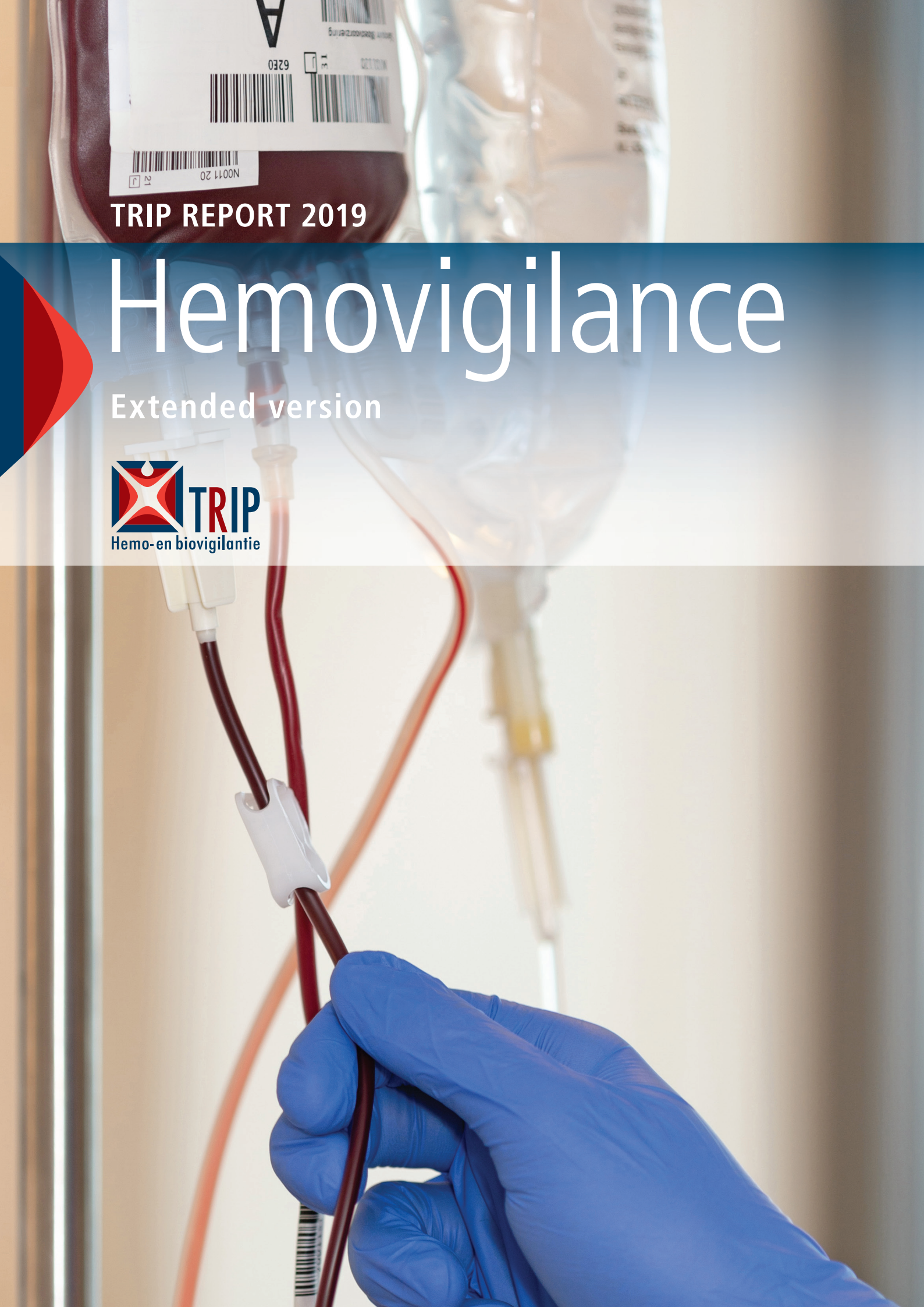

TRIP REPORT 2019

Hemovigilance

Extended version

TRIP
Hemo-en biovigilantie

TRIP REPORT 2019

Hemovigilance

Extended version

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Table of contents

Foreword

I am honoured to succeed Martin Schipperus as TRIP President. Thanks to your work, Martin, and that of many others, TRIP is running on a clear course.

Year by year, TRIP's reporting provides transparency on the general state of safety in the transfusion chain. In addition to providing transparency, the aim of hemovigilance is to improve the safety of transfusions. Over the past 15 years, our data have shown significant trends concerning lung complications. First, we saw an increase in reports of transfusion-related acute lung injury (TRALI), followed by a decrease after the 2007 implementation, by Sanquin (the Dutch National Blood Establishment), of male plasma for transfusion purposes. In addition, it became apparent that transfusion associated circulatory overload (TACO) is also a major cause of transfusion-associated pulmonary morbidity. With the awareness of this an increase in reports of TACO was observed. As a result, in 2018, experts, together with TRIP, developed a tool aimed at identifying patients who are at an increased risk of TACO and taking action on this pre-emptively (for example by adjusting transfusion speed). Further investigation is needed to determine whether the use of this tool has contributed to the decrease in the number of reports of TACO in 2019.

Yet it should be noted that examples such as the one described above are exactly what we strive to do at TRIP. In addition to continuing to detect (trends in) incidents and reactions - vigilance - we also endeavour to expressly support the professionals of the transfusion chain in reducing avoidable adverse events and reactions. Defining best practice for utilising transfusion products in the safest, but also most efficient way possible, is a clear goal to us. Tangibly, this means we aim to develop campaigns in support of such improvements in transfusion care. For instance, we are awaiting the results of the blood group discrepancies research project (data collection throughout 2019 and 2020), and the planned 'Dyspnea Year (2021) should contribute not only to advancing knowledge and understanding of respiratory deterioration in association with blood transfusion but also to reducing the problem and providing better care.

Throughout the 18 years since TRIP's establishment, the Dutch hemovigilance system has matured into a robust and internationally acclaimed system. Of course, this has been achievable only because of the joint efforts of everyone in the transfusion chain. Enormous gratitude is due for all the reports of reactions and certainly also of incidents, and in the future, possibly also of sub-optimal use of blood components. We will continue to learn from these together.

Jaap Jan Zwaginga
President, TRIP Foundation

CHAPTER 1

Main 2019 findings

1.1 Hemovigilance trends in 2019

In total, TRIP received 2064 reports of transfusion reactions and incidents in the transfusion chain in 2019, compared to 2195 in 2018. Relative to the number of red blood cell concentrates distributed, which remained approximately the same, and the number of platelet concentrates distributed, which declined by 4%, the number of reported reactions has decreased (Figure 1 and 2, Table 3, Figure 5a and 5b).

With transfusions of platelets, notably the number of (non-serious) allergic reactions decreased by approximately 40% from 2018 to 2019; from 1.8 to 1.1 reactions per 1000 units (Figure 5a). In the course of 2018, Sanquin moved to the use of PAS-E as a storage solution for platelets. The formal post-marketing surveillance by Sanquin will help determine whether the decrease of allergic reactions may be explained by this change, and if so, to what extent. The number of allergic reactions with transfusions of red blood cell concentrates also shows a decrease, albeit a more modest one (from 0.16 to 0.11 per 1000 units), so other factors must also be considered.

Transfusion-associated circulatory overload (TACO) is reported most often with transfusions of red blood cell concentrates (RBC); reported cases show a decrease of approximately 30% (from 0.30 to 0.22 reports per 1000 RBC units distributed). Increased emphasis on this adverse reaction and the application of preventive measures in clinical transfusion practice may have contributed to the fluctuations observed in the number of reports of TACO year by year (Figure 5b, Figure 8). Another factor that may have been of influence in 2019 is the implementation of the revised definition for TACO and the resulting application of more detailed assessment criteria.

At TRIP's request, 36 hospitals, which collectively account for 53% of the nationwide total number of blood components distributed, supplied data on transfusions given to patients aged 70 and older. This data showed that over 45% of the blood components transfused in these establishments was used in this group of patients, with a larger proportion being used for male than for female patients. The total number of reports per 1000 blood components transfused is the same as that for younger patients. However transfusion-associated circulatory overload and other reactions were reported more often in the older group of patients, whereas allergic and non-hemolytic febrile reactions were reported less often.

In addition to the analysis of transfusion-associated adverse reactions, analysing and reporting incidents in the transfusion chain is important. This can provide new insights and this can lead to targeted safety measures. The number of reports of incorrect blood components transfused (42) remained stable in comparison to 2018. Among these were five reports in which an underlying ICT issue was involved (three different issues in three different hospitals). The increased number of near misses (from 35 to 70) predominantly concerns cases of blood group discrepancies. These are often the result of identification errors. As part of TRIP's blood group discrepancy project, which continues in 2020, further investigation is being carried out in hospitals in order to uncover underlying factors which may contribute to this type of error. TRIP will aggregate the results into a nationwide analysis.

Comparing the number of reports received by TRIP to that received by Sanquin has shown that three potential TRALI (transfusion-related acute lung injury) reactions in 2019 were reported to Sanquin, because of the recommended investigation of causative antibodies in donors, but were not reported to TRIP. Because suspicion of TRALI - regardless of the ultimate diagnosis - indicates a serious reaction and reporting to TRIP is considered the standard in the field, this discrepancy in reporting indicates under-reporting, which may be detrimental to the value of the nation-wide registration by TRIP.

In 2019, one serious reaction occurred from transmission of a bacterial infection (Staphylococcus aureus) through transfusion of a pooled platelet concentrate. TRIP did not receive any reports of viral transmissions. This shows, yet again, that the incidence of transmissions of infections through blood transfusions is in the Netherlands is very low, occurring once for over 500,000 units transfused in 2019.

Based on the annual analysis of the number of transfusions and the number of reports in 2019, TRIP has concluded, as in previous years, that generally the level of safety of blood transfusions in the Netherlands is high. However, alertness to transfusion reactions with respiratory symptoms and the detection of identification errors are requested through the recommendations below. TRIP expresses thanks to all contact persons in the various hospitals for their indispensable contributions to this report.

1.2 Recommendations

Recommendation	Who?
Attention to correctly checking (orally or through the use of a wrist band) the details on the label with the patient who is to have a sampel taken or who will receive the blood component. Confirming whether the correct blood component is being administered to the recipient if a reaction occurs, in accordance with protocols, and always reporting a reaction to the laboratory for further investigation and registration.	Hemovigilance professionals in collaboration with the blood transfusion committees and clinicians
Continued alertness to the risk of TACO: additional monitoring of at-risk patients and implementation of preventive measures when necessary.	Hemovigilance professionals in collaboration with the blood transfusion committees and clinicians
Always immediately reporting reactions to TRIP and Sanquin when they may be related to donor-specific causes or component quality, for instance with a suspicion of TRALI. The TRIP reporting system allows for (a PDF of) the report to be made available to Sanquin and, if relevant, to the Healthcare Inspectorate. Through this path for reporting, all parties involved can view an up-to-date status of the assessment.	Hemovigilance professionals in collaboration with clinicians

CHAPTER 2

Overview of 2019 hemovigilance data

2.1 Overview of 2019 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 definitions and in the relevant sections of this report. In 2019, TRIP received 2064 reports. In total, 1870 reactions and 235 incidents (events) were reported; 41 reports concerned a combination of both an incident/event and a reaction. These 41 combined reports are included in both Table 1 (incidents) and Table 2 (reactions).

The reported data are presented in the following tables and figures:

** Supplementary tables available as online annexe*

Table 1. Reported incidents, 2010-2019*

Incident	2010	2011	2012	2013	2014	2015	2016	2017	2018*	2019*	No. of hospitals with reports in 2019
Incorrect blood component transfused	58	43	51	43	71	53	43	44	41	42	24
Near miss	71	45	50	39	33	40	52	31	35	70	23
Other incident	118	138	139	107	120	93	112	72	94	87	29
Calculated risk situation#	-	-	-	-	-	-	7	6	11	17	9
Total	**247**	**228**	**240**	**189**	**224**	**186**	**214**	**153**	**181**	**216$**	**49**

* *All reported incidents have been included, including those that were registered as an additional category*
\# *The reporting category calculated risk was introduced in 2016, see also the discussion in chapter 3.1*
$ *Additionally, TRIP received 6 reports of look-back and 13 reports with the reporting category or additional reporting category of bacterial contamination of product.*

Table 2. Reported transfusion reactions, 2010-2019

Reaction	2010	2011	2012	2013	2014	2015	2016	2017	2018*	2019*	>2 dpp#	No. of hospitals with reports in 2019
Post-transfusion bacteremia/sepsis	41	61	50	47	56	79	64	73	72	83$	8	36
Post-transfusion viral infection	1	5	2	5	0	2	3	1	0	0	0	0
TRALI	17	12	9	9	6	9	6	6	4	6	5	4
Transfusion-associated circulatory overload	47	39	56	69	76	76	87	106	134	90	30	44
Transfusion-associated dyspnea (TAD)+	-	-	-	-	-	-	8	7	5	4	1	4
Anaphylactic reaction	73	67	59	70	53	43	62	69	58	25	11	20
Other allergic reaction	184	191	180	193	153	151	126	127	134	95	2	32
Acute hemolytic transfusion reaction	21	17	7	11	17	18	18	16	16	16	8	11
Delayed hemolytic transfusion reaction (DHTR)	7	9	8	4	5	6	8	5	4	3	0	2
DHTR as additional category	14	19	10	6	8	7	5	3	1	4	0	2
New allo-antibody formation	814	831	851	849	763	697	649	672	654	712	0	62
Non-hemolytic TR	506	504	456	442	419	448	407	358	360	305	17	66
Mild non-hemolytic febrile reaction	363	366	383	340	311	336	365	319	326	277	1	49
Other reaction	164	218	225	221	191	205	215	259	289	251	18	61
Other small categories of TR¶	4	5	1	5	17	3	4	3	0	3	1	3
Total TR	**2242**	**2325**	**2287**	**2265**	**2067**	**2073**	**2022**	**2021**	**2056**	**1870**	**102**	**78**
Total grade 2 or higher#	93	101	100	108	96	112	108	121	121	102		
Total reports	**2594**	**2630**	**2580**	**2504**	**2318**	**2289**	**2248**	**2131**	**2197**	**2064**		

* *All transfusion reactions reported have been included, including those that were registered as an additional category*

\# *Imputability definite, probable or possible; for types of reactions not categorized as severe, grade 2 applies when a reaction led to (prolongation of) hospital admission*

$ *Only one of the reports was categorized as TTBI based on the culture result of the unit, see chapter 3.3*

\+ *Reporting category introduced in 2016, see discussion in Chapter 3.2*

¶ *Concerns reports of post-transfusion purpura, other post-transfusion infection (3 in 2019) or hemosiderosis.*

Abbreviations: TRALI=Transfusion-related acute lung injury; TR=transfusion reaction

Table 3. Reports per type of blood component in 2019

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	408275	392526	1729	79	4,23	0,19
Platelet concentrate	53832	52311	165	11	3,07	0,20
Fresh frozen plasma	1607	1255	2	1	1,24	0,62
SD-plasma[1]	59782	54953	16	3	0,27	0,05
Fitrix® fibrin glue	36	15	0	0		
Serum eye drops	284	209	0	0		
Blood management techniques[2]			0	0		
Combinations[3]			64	8		
Not stated			89	-		
Total	**523816**	**501269**	**2064**	**102**	**3,94**	**0,19**

* *Data received from 82/84 hospitals (98%)*

\# *Imputability definite, probable or possible*

[1] *SD = solvent-detergent treated plasma; Omniplasma® in the Netherlands; source: Bloedkatern (Sanquin publication with distribution figures for hospital users)*

[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 2019

Tabel 3b Types of reactions and incidents for each type of blood component in 2019

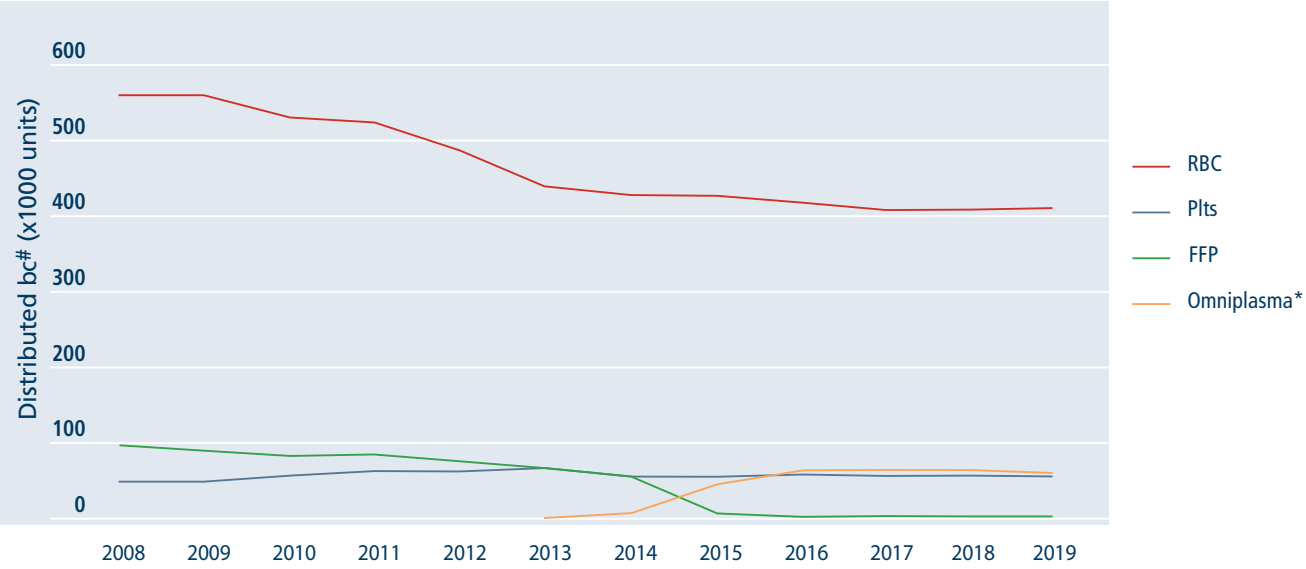

Figure 1. Distributed units of blood components, 2008-2019

* *For SD-plasma (Omniplasma®) the distributed units have been used in 2013-2015 because of the transition*

\# *Data from Sanquin*

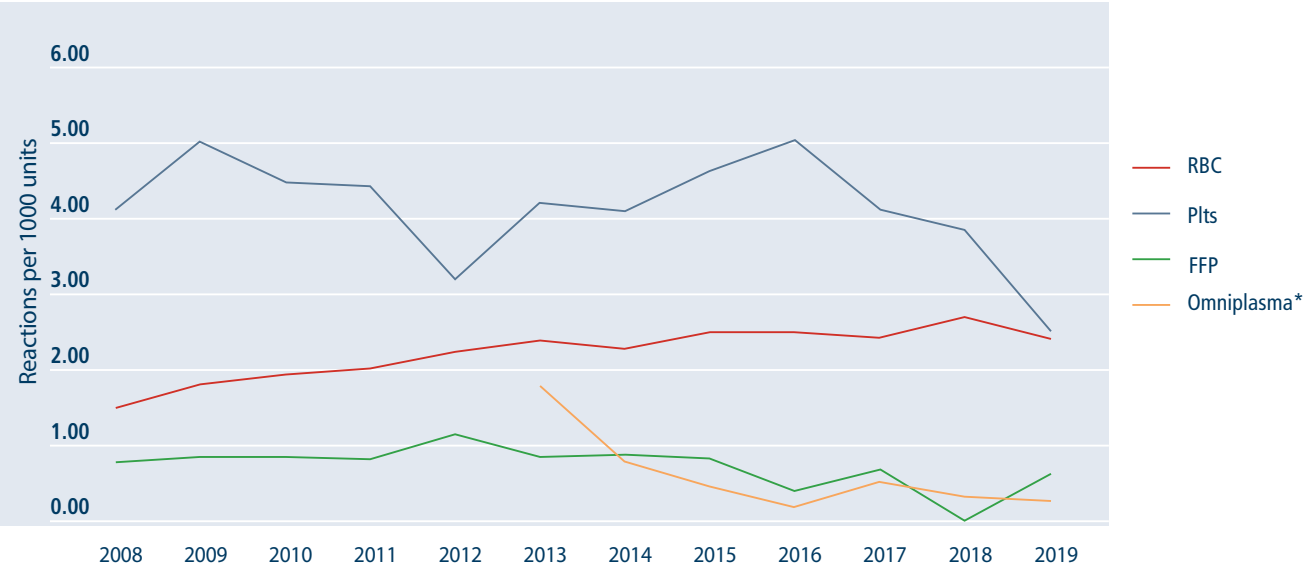

Figure 2. Transfusion reactions excluding new allo-antibodies per type of blood component, 2008-2019

This figure displays the transfusion reactions reported with the use of only one type of blood component

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

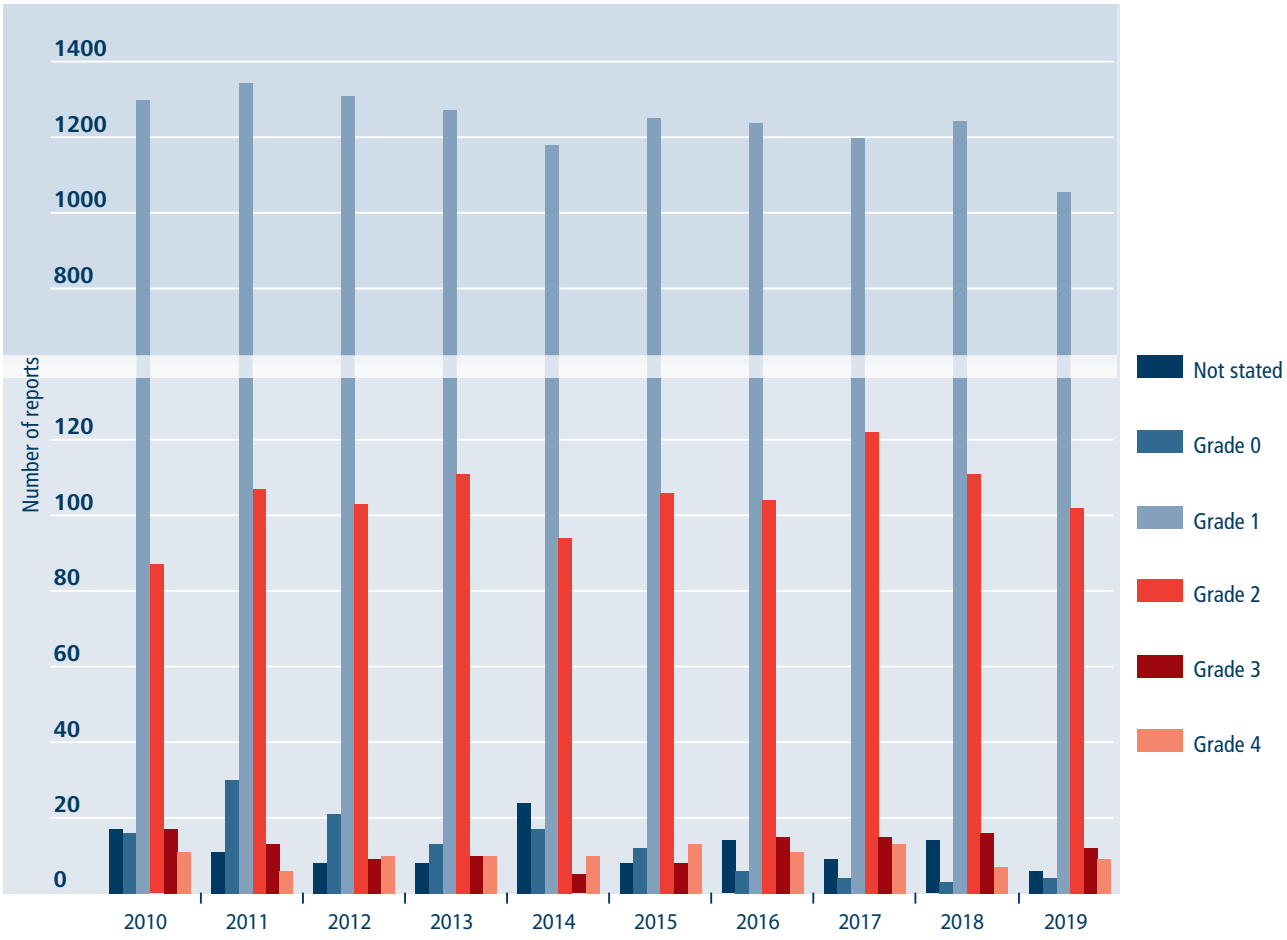

Figure 3. Severity of the transfusion reactions*, 2010-2019

* *All transfusion reactions except new allo-antibody formation are included in this figure*

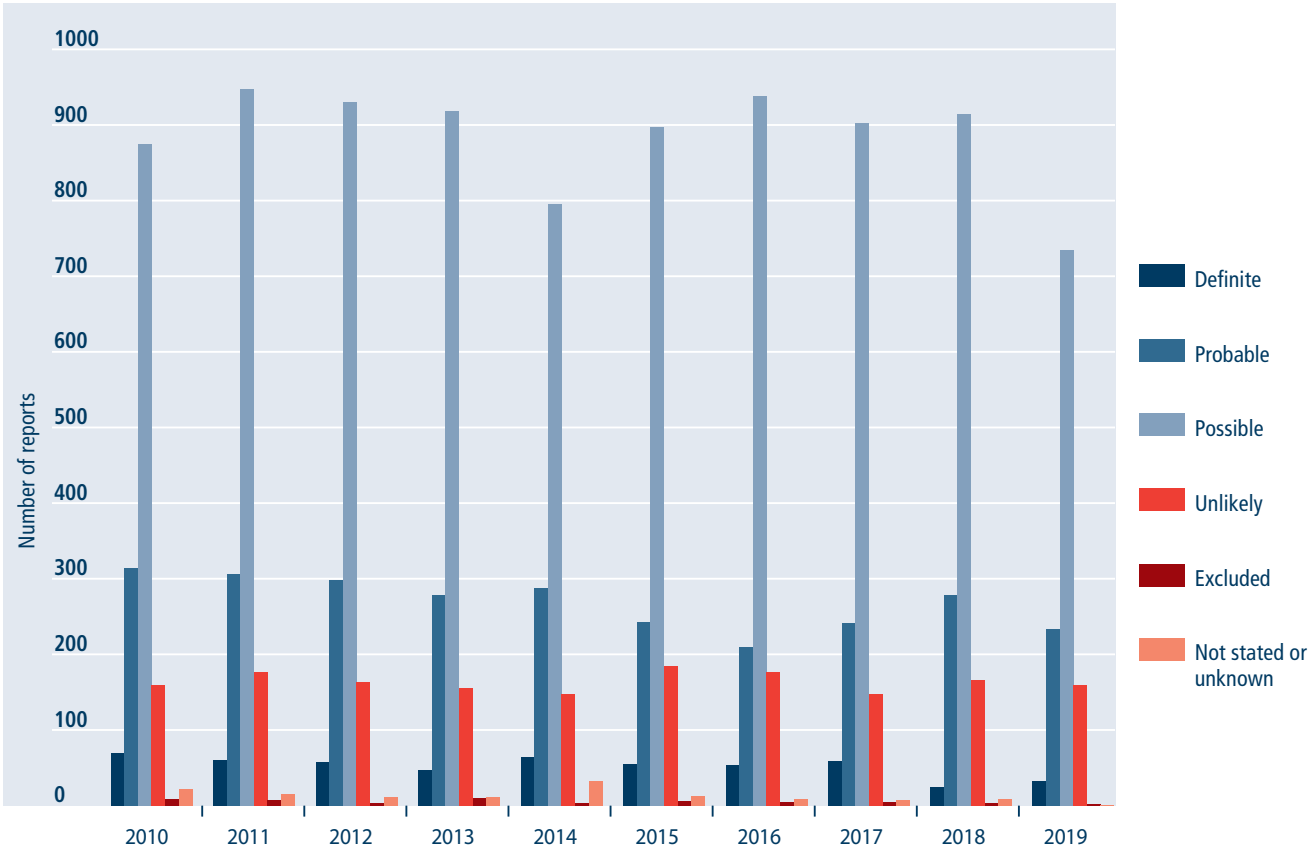

Figure 4. Imputability of the transfusion reactions*, 2010-2019

* *All transfusion reactions except new allo-antibody formation are included in this figure*

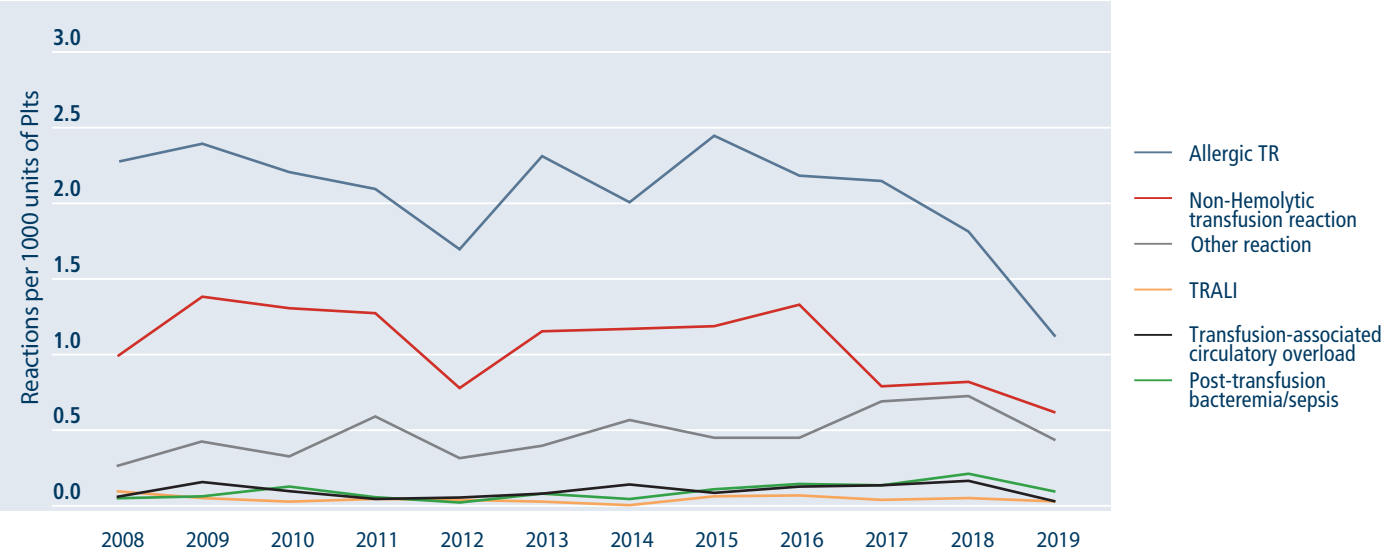

Figure 5a. Reactions reported with platelet concentrates, 2008-2019

This figure shows reports from the main reaction categories with definite, probable, or possible imputability; significant decrease of allergic reactions (anaphylactic or other allergic reactions), other reactions and transfusion-associated circulatory overload in 2019

Abbreviations: TR=transfusion reaction; TRALI=Transfusion-related acute lung injury; Plts=Platelet concentrate

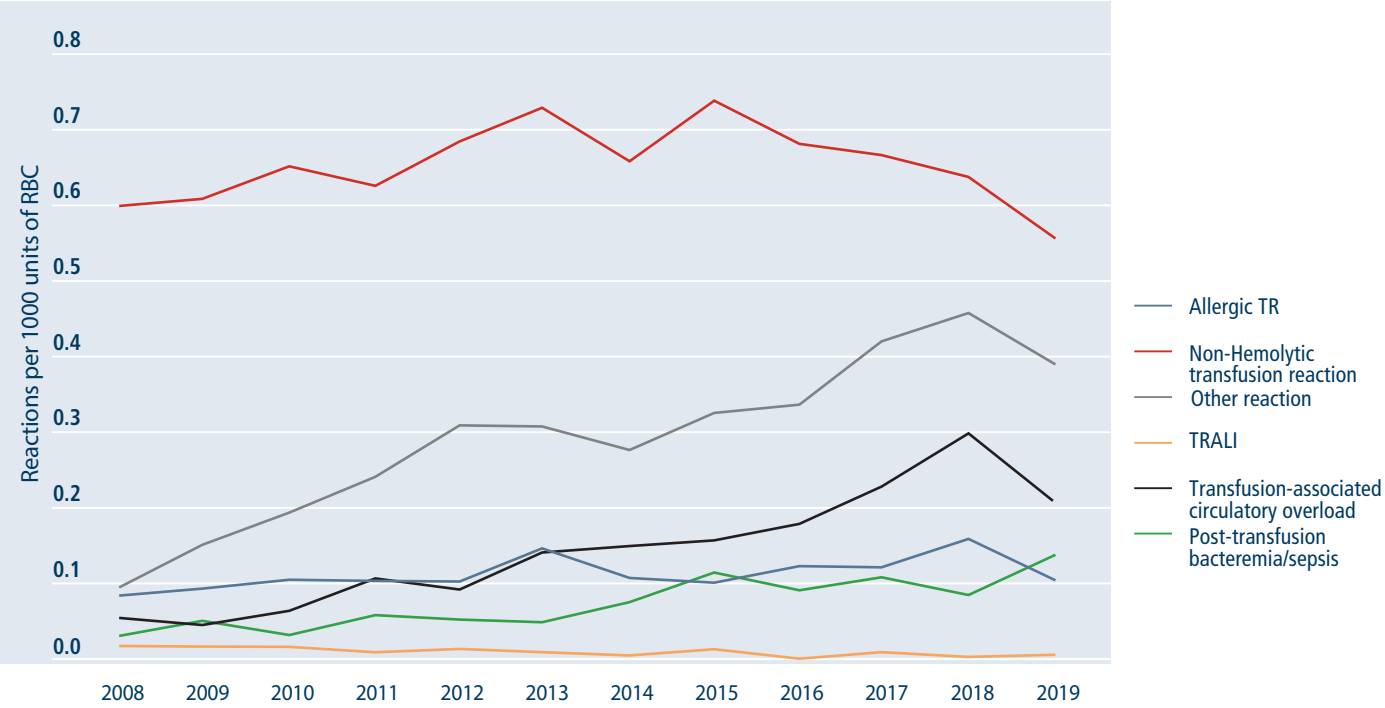

Figure 5b. Reactions reported with red blood cell concentrates, 2008-2019

This figure shows reports from the main reaction categories with definite, probable, or possible imputability; significant decrease of transfusion-associated circulatory overload and allergic reactions (anaphylactic and other allergic reactions) in 2019

Abbreviations: RBC=Red blood cell concentrate; TR=transfusion reaction; TRALI=Transfusion-related acute lung injury

2.2 Overview of mandatory reports of serious transfusion reactions

Every year TRIP compiles an overview of mandatory serious transfusion reaction reports (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 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 the different legal status (medicinal) and vigilance requirements of that product.
- 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).

Table 4. Number and imputability of reports of grade 2 and higher in 2019, in accordance with EU overview

Severity grade	2 or 3			4	Total
Imputability	Definite	Probable	Possible	Possible	
Hemolytic transfusion reaction (ABO)	1	0	0	0	1
Hemolytic transfusion reaction (immunological, not ABO)	1	1	1	0	3
Hemolytic transfusion reaction, (not immunological)	1	1	2	0	4
Allergic reaction	2	6	5	0	13
Febrile reaction	1	1	16	0	18
Other reaction	0	8	10	0	18
TAD	0	1	0	0	1
Transfusion-transmitted bacterial infection	1	0	0	0	1
TRALI	1	1	2	1	5
Transfusion-associated circulatory overload	1	15	12	2	30
Total	**9**	**34**	**48**	**3**	**94**

2.3 Transfusion reactions with fatal outcome (Grade 4)

In 2019, TRIP received nine reports of transfusion reactions after which the patient did not recover and eventually passed away; only three of these reports were of definite, probable or possible imputability. These reports are summarized in Table 5. Table 6 lists all Grade 4 reports with definite, probable or possible imputability that TRIP has received from 2010 onward.

Table 5. Grade 4 reports 2019*

Reaction	Sex, age	Blood component	Imputability	Symptomatology
Transfusion-related Acute Lung Injury (TRALI)	M, 69y	RBC	Possible	Myelofibrosis, admitted with month-long fever and diarrhoea, dehydration; increasingly dyspnoeic after 2 units RBC and saline solution; good L/R ventricular function on cardiac echo; bilateral pulmonary infiltrates on chest X-ray. Ventilated, progressive ARDS and multi-organ failure.
Transfusion-associated circulatory overload (TACO)	M, 71y	RBC and Plts	Possible	Patient with moderate aortic stenosis, admitted with to hypotension and Hb 3.9 mMol/L following gastric hemorrhage. Decreased bp and saturation after 3 RBC and 1 unit Plts; extensive pulmonary oedema on chest X-ray, considerably raised troponin and BNP, no improvement despite ventilation and vasopressors.
Transfusion-associated circulatory overload (TACO)	F, 60y	RBC	Possible	Liver cirrhosis COPD, and kidney failure; Tf because of rectal blood loss. Cardiac asthma and cardiorespiratory arrest after 2 units of RBC.
Other reaction	M, 65y	RBC	Unlikely	Chemo started for AML, admitted to ICU due to progressive hypoxia, circulatory arrest after 3rd unit of RBC; resuscitation not attempted because of poor prognosis.
Other reaction	M, 55y	RBC	Unlikely	Liver cirrhosis, pancytopenia and kidney failure; syncope and cardiorespiratory arrest during Tf.
Other reaction	M, 88y	RBC	Unlikely	Hospitalisation for high energy trauma and multiple fractures, clinically stabilised; decreased blood pressure during transfusion, shock with acute splenic arterial hemorrhage.
Other reaction	M, 91y	RBC	Unlikely	Coronary atherosclerosis in 3 vessels, Tf for chronic anemia; clinically stable during 2 RBC transfusions, expectoration of blood during 3rd unit of RBC, unresponsive, death.
Other reaction	F, 72y	RBC	Unlikely	Patient with permanent tracheostomy after malignancy, operated for aneurysm, AKI afterwards; became confused at end of 1st unit of RBC (0.5 mg haloperidol); died 50 min. later, do-not-resuscitate order.
Transfusion-related Acute Lung Injury (TRALI)	F, 16y	RBC	Unlikely	Patient with Fontan circulation (univentricular heart), transferred with intrathoracic hemorrhage. Hemodynamic instability and respiratory deterioration with pulmonary oedema and fluid from the tube shortly after 2 units of RBC, cardiorespiratory arrest.

Abbreviations: AML=acute myeloid leukemia; AKI=acute kidney injury; ARDS=acute respiratory distress syndrome; BNP=Brain-type natriuretic peptide; COPD=chronic obstructive pulmonary disease; Plts=platelet concentrate; RBC= red blood cell concentrate; Tf=transfusion

Table 6. Grade 4 reports (imputability definite, probable, possible) 2010-2019

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
AHTR		1	1			2					4
Other reaction	3	1	1	2		1	1	1	2	0	12
Post-transfusion bacteremia/sepsis*			1		2						3
Post-transfusion purpura					1						1
TRALI	2		1			2	1	1	1	1	9
Transfusion-associated circulatory overload	2	1	1		3	2	3	6	2	2	22
Totaal	**7**	**3**	**5**	**2**	**6**	**7**	**5**	**8**	**5**	**3**	**51**

** Only one of the reports (from 2014) was confirmed to be TTBI based on the culture result of the unit*

2.4 Transfusion of blood components and reports in patients aged 70 and older

After inquiries from the Dutch Blood Transfusion-Related Research Consortium concerning the use of blood components in elderly patients, and in order to align with the theme Aging at the 2020 NVB-TRIP symposium, TRIP asked hospitals to supply 2019 data on the number of units administered to patients aged 70 and older (70+), in addition to the standard reporting of reactions and incidents and annual data on the total number of blood components administered.

Out of the 84 hospitals reporting to TRIP, 36 (43%) supplied data on use of blood components for this older group of patients; among these were five University Medical Centres. Table 7 shows the number of blood components applied in these 36 establishments which collectively account for 53% (267724/501269) of all blood components transfused in the Netherlands). In these establishments, 45.5% of all blood components were administered to patients aged 70 and older, whereas only 13.4% of the general population is in this age group.

Table 7. Transfusion of blood components per age group; information received from 36/84 hospitals

	<70	%	70+	%	Total
Red blood cells	97675	48.0%	105680	52.0%	203355
Platelets	24255	74.2%	8449	25.8%	32704
Omniplasma	23332	75.3%	7657	24.7%	30989
FFP	484	99.6%	2	0.4%	486
Other	187	98.4%	3	1.6%	190
Total	**145933**	**54.5%**	**121791**	**45.5%**	**267724**

The total use of red blood cell concentrates across all age groups is estimated to be 22.5 units per 1000 people in the Dutch population, based on an extrapolation of the data supplied by 36 hospitals to 100%. In 2015, the EDQM reported that, in the Netherlands, approximately 25.1 units of red blood cell concentrates, 7.3 units of platelet concentrates, and 0.4 units of fresh frozen plasma were distributed per 1000 inhabitants (Janssen MP, Rautmann G. The collection, testing and use of blood and blood components in Europe, 2015 report, Council of Europe Publishing, Strasbourg, 2015). The overall use of blood components in the Netherlands is lower than in many other European countries.

Thirty-two hospitals were able to supply data on the number of blood components administered to 70+ patients according to sex, see Table 8.

Table 8. Transfusion of blood components to 70+ patients, subdivided according to sex: information received from 32/84 hospitals

	Male	%	Female	%	Total
Red blood cells	54028	56.1%	42311	43.9%	96339
Platelets	5066	70.0%	2169	30.0%	7235
Omniplasma®	4272	63.2%	2490	36.8%	6762
FFP	0	0.0%	2	100..0%	2
Other	2	66.7%	1	33.3%	3
Total	**63368**	**57.4%**	**46973**	**42.6%**	**110341**

TRIP received data from 31 hospitals (including three university hospitals) on the use of blood components in the 70+ age group with a further breakdown according to age (or age group) and sex. Figure 6 displays this data in relation to the total number of inhabitants in each age band in the Netherlands in 2019 (source: StatLine Statistics Netherlands.

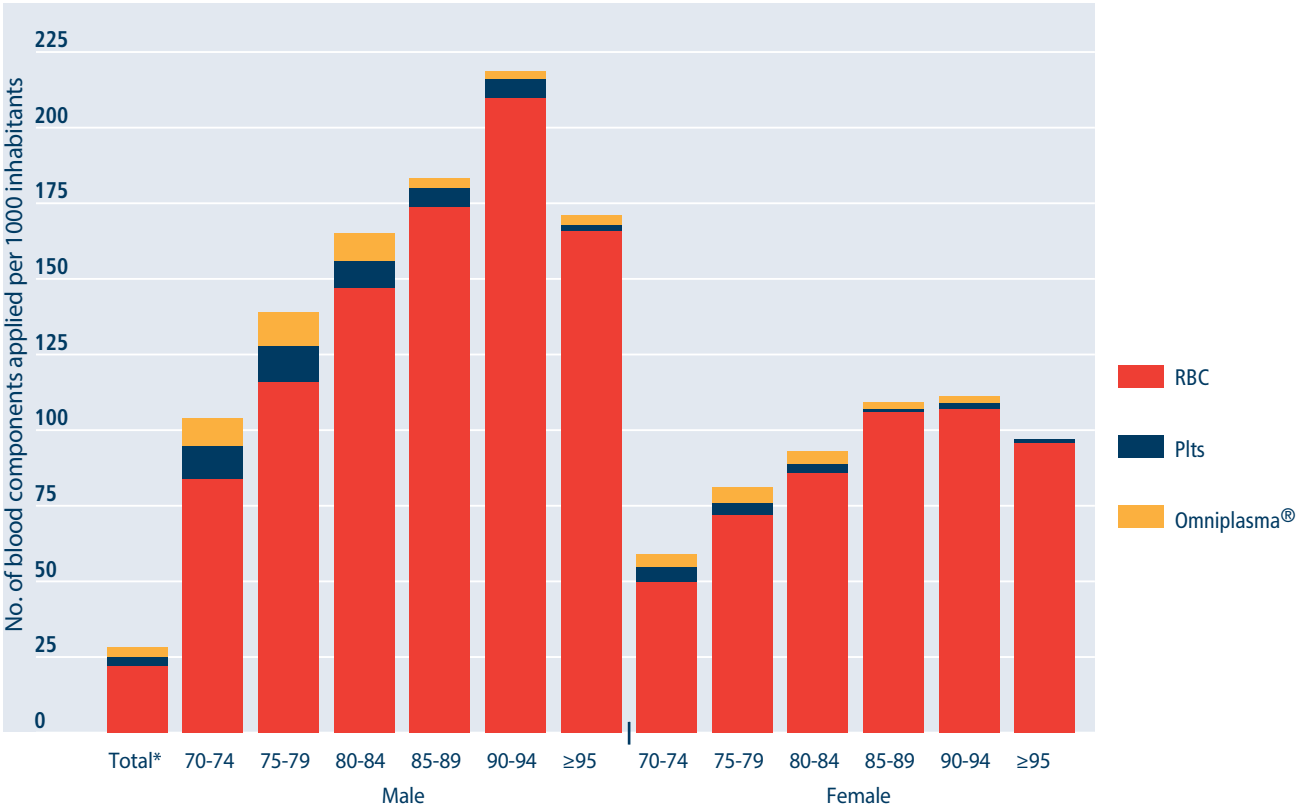

Figure 6. Number of units of red blood cells, platelets, Omniplasma®, and other blood components transfused by age group and sex, per 1000 in the general population

* *Total use of blood components in the 31/84 hospitals that provided transfusion data for 70+ patients subdivided according to age, collectively accounting for 44% of all transfused blood components in the Netherlands (data extrapolated to 100% of blood components transfused)*

As shown above (Table 8 and Figure 6), by comparison, a larger number of blood components is transfused to older men than to older women. In the Netherlands men over 70 years old are admitted to hospital more often (4690 hospitalisations/10,000 inhabitants) than women over 70 years old (3436 hospitalisations/10,000 inhabitants) and are more often admitted due to haematological malignancies (118 as opposed to 70/10,000 inhabitants; source: StatLine Statistics Netherlands). This difference in the number of hospitalisations accounts for part of the difference in the number of blood components used in men and women over 70 years old.

Reports

TRIP received a total number of 1399 reports from the 36 establishments that supplied data on 70+ patients. 1238 of these reports concerned (only) adverse reactions, 128 concerned incidents and 33 concerned incidents with adverse reactions. Four incidents were excluded from the analysis because there was no age indicated in the report. After excluding the categories for new allo-antibody formation (n=478), mild non-hemolytic febrile reaction (n=181), calculated risk (n=14), bacterial contamination of blood component (n=10), incorrect blood component transfused in the past (n=1), and look-back by the blood establishment (n=4), 726 reports were included in our analysis, of which 598 concerned adverse reactions, 114 concerned incidents and 14 concerned incidents with adverse reactions. The imputability of 521 of the adverse reactions was assessed as definite, probable or possible.

Table 9. Number of transfusion reactions and incidents in 36/84 hospitals by age and sex

Transfusion reactions	<70			70+		
	M	F	Total	M	F	Total
Acute hemolytic transfusion reaction	3	4	7	4	1	5
Anaphylactic reaction	5	7	12	3	2	5
Other allergic reaction*	30	27	57	9	6	15
Non-hemolytic transfusion reaction*	56	56	112	27	36	63
Other reaction*	32	25	57	33	35	68
Post-transfusion bacteremia/sepsis	14	12	26	11	6	17
Other post-transfusion infection	0	0	0	1	0	1
TAD	0	0	0	2	1	3
TRALI	4	0	4	0	0	0
Delayed hemolytic transfusion reaction	0	2	2	2	1	3
Transfusion-associated circulatory overload*	7	12	19	21	24	45
Reactions total	**151**	**145**	**296**	**113**	**112**	**225**
Serious reactions	13	16	29	15	15	30
Number of reactions reported per 1000 bc			2.03			1.85
Incidents						
Near miss	4	21	25	9	8	17
Other incident	11	16	27	17	15	32
Incorrect blood component transfused	8	9	17	7	3	10
Incidents total	**23**	**46**	**69**	**33**	**26**	**59**
Number of incidents reported per 1000 bc			0.47			0.48

* *Statistically significant difference between 70+ and <70 years age groups*
Abbreviations TAD=transfusion-associated dyspnea; TRALI=transfusion-related acute lung injury; bc=blood components

Conclusion

This analysis based on data on approximately half of the national use of blood components concludes that over 45% of all blood components are transfused to patients aged 70 and older, and more blood components are transfused to male patients than to female patients. In some age groups, male patients receive as much as 150 units of red blood cell concentrates per 1000 inhabitants of that age group, compared to the average 22.5 units of red blood cell concentrates per 1000 inhabitants for the general population. The total number of transfusion reactions and incidents reported per 1000 blood components applied does not differ between 70+ patients and younger patients. Transfusion-associated circulatory overload and other reactions are reported more often in patients aged 70 and older, whereas other allergic reactions and non-hemolytic febrile reactions are reported less often.

2.5 Late reports from 2018

After the deadline for submitting reports to be included in the 2018 report, three more reports concerning this year were received (Table 10). This number is lower than in previous years, which is to be attributed to flexibility concerning the inclusion of reports that were finalised after the official closing date in the 2018 report.

Table 10. Late 2018 reports included in the 2019 report

Reporting category	Severity grade					No Reaction, severity not applicable	Incidents: Risk assessment
	Not stated or 0	1	2	3	4		
Non-hemolytic transfusion reaction		1					
Incorrect blood component transfused						1	Other preventive policy*
Near miss						1	ABO risk, mix-up of bc#

* *Erroneously not complying to preventive component selection for policy other than prevention of irregular antibody formation or irradiatiated bc: a 3 year-old child received Omniplasma rather than FFP*

\# *This was a report about the second patient in a case of incorrect blood component transfused that was included in the 2018 report; the digital check revealed this error.*

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.

42 reports from 24 hospitals (29%), 1-4 reports per hospital

- 7x a reaction was observed first and it was discovered afterwards that IBCT preceded it (1x AHTR, 1x anaphylactic reaction, 1x other reaction, and 4x new allo-antibody formation with additional category IBCT), see Table 11. One report of new allo-antibody formation was connected to an IBCT that occurred years earlier (2013; additional category IBCT in the past), that incident was not counted along with the 2019 reports of IBCT.
- In 4 cases, an error occurred in the investigation or procedures following a reaction or an incident, which allowed for (another) IBCT to occur (1x new allo-antibody formation, 1x bacterial contamination of blood component, 1x other incident with additional category IBCT, and 1x IBCT with a separate report describing IBCT in a 2nd patient).
- 6x the analysis of an IBCT showed that the same error had occurred before and resulted in the same patient receiving one or more incorrect blood components, of which no report had been made yet. These incidents were not counted as additional cases IBCT in 2019.

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 received the blood which was intended for patient Y the worst risk would be for the unit to be ABO incompatible – regardless of what the two patients' blood groups turned out to be. The descriptions of the risk groups which TRIP includes in this analysis can be found on www.tripnet.nl (under hemovigilance, tools). 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. The most marked change in the number of reports across the different risk categories was observed with TA-GvHD. In 2019 TRIP did not receive any IBCT reports in this subgroup in 2019. The subgroups for reports concerning ABO-risks and reports concerning prevention Irrab are the largest, but the number of reports in these categories has not changed much over the past five years (Figure 7). For more details, see Table 11.

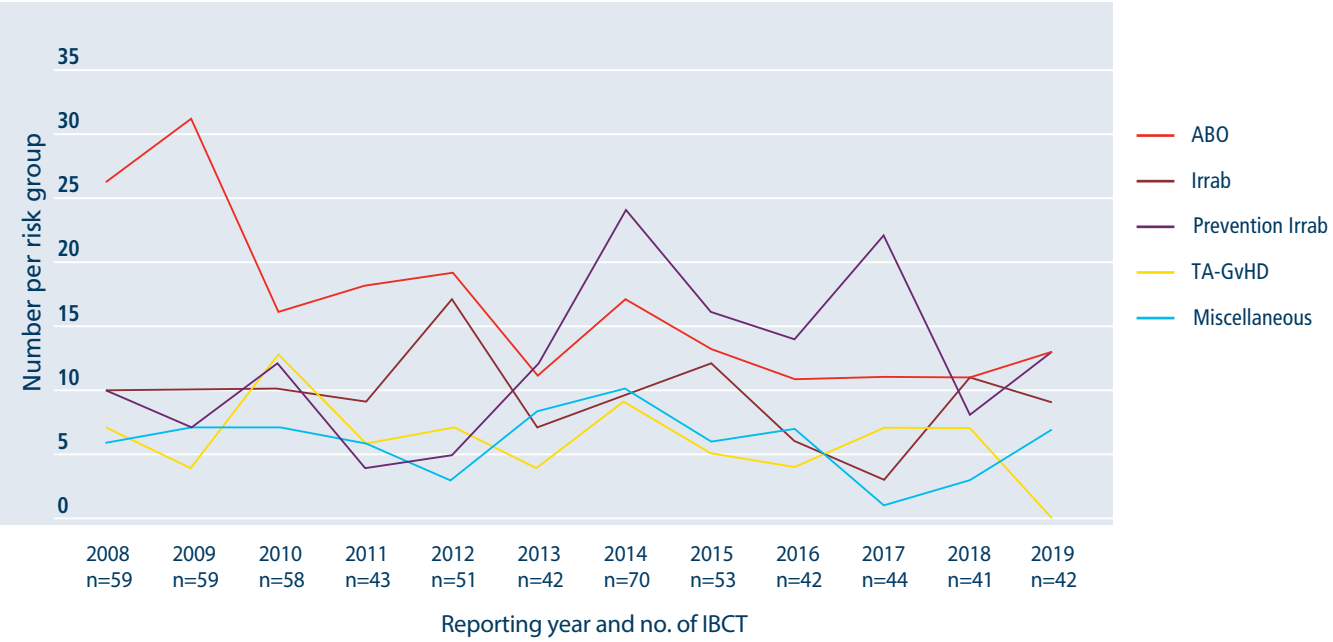

Figure 7. Incorrect blood component transfused broken down according to risk group, 2008-2019

Abbreviations:
ABO=risk of an ABO incompatible blood transfusion
Irrab=risk of an irregular antibody incompatible transfusion
Prevention irrab= guidelines not followed with regard to prevention of irregular antibody formation
TA-GVHD=risk of transfusion-associated graft versus host disease (after transfusion of a non-irradiated blood component)
Miscellaneous= risks related to, among other things, administration of bc with positive bacterial screening; administration of a leaking blood bag or a bag that has been spiked before or has been stored incorrectly (damage/quality); or erroneously not complying with a preventive policy other than the ones named above (B-19 safe, washing, after transplant of solid organ, etc.)

Of the 13 reports classified as ABO risk, 12 cases concern mix-ups of blood bags, patients, or patient details and one report concerned a patient who had previously received an O positive stem cell transplant in a different hospital and who erroneously received A positive RBC based on the (incompatible) historically determined blood group, from before the stem cell transplant. This blood group discrepancy was detected during the blood group determination for T&S. Information was requested and received from the other hospital's laboratory, but this information was not acted on correctly.

- 1x in a case in which a reaction was observed, the administration of approximately 200 mL of a blood component (A positive RBC) intended for a different patient was not detected until two hours after the reaction started. After approximately 2.30 hours of infusion, the patient developed symptoms (slight rise in temperature, chills, tachypnea, dyspnea, stridor, saturation decreased to 94%, blood pressure increased to 132/106, tachycardia), at which point the transfusion was stopped and the patient was given paracetamol and 20g of furosemide intravenously. Later, in view of increased blood pressure and continued dyspnea, the patient was also administered 1L of O2 for several hours. After this, the patient swiftly recovered.
- 1x a case concerned erroneous administration of O positive red blood cells to a patient (O positive) who still had to be assessed by a physician and for whom, logically, there was no transfusion prescription (yet).
- 1x a unit of RBC was erroneously partly administered to the intended recipient (patient 2) after a small part of this same unit had mistakenly been transfused into a different (incorrect) patient (patient 1), due to a mix-up.

In 2019, TRIP received five reports of IBCT from three different hospitals concerning three different situations in which there were ICT issues. In all cases, a situation emerged in which there was a risk of repetition for the same patient or for other patients. Additionally, the same ICT issue could occur in different hospitals. The first case concerns the request form for blood components, in which automatic population of certain

data fields (that are subject to change) with patient data, such as a recent organ transplant, turns out to be cause for the transmission of incorrect information to the lab.

The case in a second hospital concerns a transfer to a new digital information system, for which adjustments were made to patient numbers. With this transfer, "old" transfusion advice and/or data from the patient's transfusion history were not linked to the new patient number and as a result a new blood group determination and serological screening had to be carried out for all known patients. This played a role in the T&S issuing of blood components to patients who had recently screened negatively, but whose history of irregular antibodies was known in the former laboratory information system.

In the lab at a third hospital, entering typed platelet concentrates under the name of a specific patient had previously led to problems: these blood components could not be released to general storage if they no longer needed to be stored for the originally intended recipient. In consequence the hospital had decided to enter typed platelet concentrates that were ordered for a specific patient as "regular" platelet concentrates, a method that was never adjusted after the original problem had been resolved. This contributed to an incident in which the typed platelet concentrates for patient 1 had not been delivered to the lab yet and platelet concentrates that had been matched for patient 2 (and had already been delivered in advance for the next day) were issued and administered to patient 1.

- In 4 of the incidents with irregular antibody risk, TRIX information on antibodies (demonstrated elsewhere) was available which could have prevented the error, or could have led to detection of an earlier error, but was overlooked during the processing of the request.
- For 3 of the 7 IBCTs with irregular antibody risk, a longer interval (several months) occurred between the administration of incompatible RBC and the detection of the error, so it is plausible that in some of these cases any (mild) hemolytic reaction that may have occurred has gone unnoticed.
- In contrast to previous years, TRIP did not receive any reports of a patient erroneously receiving non-irradiated blood components. Underreporting of this type of incident had been suspected already.

IBCT case descriptions (in Dutch) of 2019 reports can be found in the Report of the Month (Melding van de maand) series on www.tripnet.nl, e.g.:
Report of the Month April 2019: Where has the patient gone?
https://www.tripnet.nl/melding-van-de-maand-april-2019-waar-is-de-patient-gebleven/
Report of the Month January 2020: Work smarter, not harder..... (1)
https://www.tripnet.nl/melding-van-de-maand-januari-2020-het-gemak-dient-de-mens/
Report of the month February 2020: Work smarter, not harder..... (2)
https://www.tripnet.nl/melding-van-de-maand-februari-2020-het-gemak-dient-de-mens-2/
Report of the Month May 2020: Patient observed well, but..... (1)
https://www.tripnet.nl/melding-van-de-maand-mei-2020-patient-goed-geobserveerd-maar/

Table 11. Incorrect blood component transfused in 2019: breakdown according to type of risk, blood component and observed reaction

Type of risk*	Blood component	N	Blood component coincidentally compatible or negative for	Blood component (possibly) incompatible for	N	Reaction or New allo-antibody	N	Imputability%	Severity grade%
ABO	RBC	11	Rhesus D	ABO	3	AHTR	1	Definite	2
						None$	1		
						None#	1		
			ABO rhesus D		8	None¶			
	Plts	2	ABO rhesus D		1	None			
			Rhesus D	ABO	1	None			
Irrab	RBC	8		anti-Jkb	1	None			
				anti-K	1	Not followed up on&			
				anti-Lea	1	None+1			
				anti-c and -Jka	1	None			
				anti-K, -E and -Cw	1	None			
				anti-E	1	None			
			Antibody/antibodies previously demonstrated in patient		2	None			
	Plts	1		HLA-antigens previously demonstrated in patient		Anaphylactic reaction	1	Definite	2
Prevention irrab	RBC	13		Rhesus / K	10	None+2	2		
						Anti-E€1	2		
						Anti-K€1	1		
						None€2	4		
						None@	1		
				Rhesus	3	None	1		
						None@	2		
Miscellaneous	RBC	6	Not applicable			Other reaction£	1	Possible	1
						None	5		
	Plts	1	Not applicable			None¥			

* *ABO = risk of an ABO incompatible blood transfusion*
Irrab = risk of an irregular antibody incompatible transfusion
Prevention irrab = guidelines not followed with regard to prevention of irregular antibody formation
TA-GVHD = risk of transfusion-associated graft versus host disease (after transfusion of a non-irradiated blood component)
Miscellaneous = risks related to, among other things, administration of bc with positive bacterial screening; administration using a leaking bag or a bag that has already been punctured before or has been stored incorrectly (damage/quality); or erroneously not complying with a preventive policy other than the ones named above (B-19 safe, washing, after transplant of solid organ, etc.)

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

$ *Concerns transfusion based on historically known (former) blood group to patient who had undergone an incompatible stem cell transplant*

\# *Incompatible RBC (AB neg) infused for approximately 20 minutes, no clinical symptoms observed in O pos recipient, possibility of some degree of hemolysis not excluded in lab reports*

¶ *In 1 of these cases, the blood component was not returned to the lab immediately after it was disconnected, but subsequently, in contravention of the protocol, administered to the intended recipient (separate report registered in Other risk subgroup)*

& *Patient wished not to receive any further examinations or treatments, palliative care provided*

+1 *Patient with known irregular antibody, SOP not adhered to correctly: forgotten to look in TRIX before selecting units. In this case compatible units should have been found and IAT crossmatching performed*

+2 *Patient with known irregular antibody, in 1 case antibody screening afterwards demonstrated anti-C in a patient in whom previously only anti-M had been detected; the administered uncrossmatched blood components were erroneously C positive.*

€1 *Chronic blood transfusion protocol/MDS patient, preventive Rh/K policy erroneously only started recently and/or Rh phenotyping established based on unreliable result (after previous Tf)*

€2 *Chronic blood transfusion protocol/MDS patient, according to most recent information at the time of writing of this report no new antibodies were demonstrated*

@ *F < 45 years, according to most recent information at the time of writing of this report no new antibodies were demonstrated*

£ *After a blood component had partially infused subcutaneously the unit was disconnected, but transfusion was subsequently continued using a new IV line, against advice from the lab. Several hours later, at the conclusion of the administration, the patient showed chills, a slightly increased temperature (to 38.4 °C), a decrease in blood pressure (118/70 to 96/54) and tachycardia. Further examination (a culture and blood group serology) did not uncover any irregularities. Patient recovered from the reaction spontaneously.*

¥ *After a notification from Sanquin of a positive bacterial screening, the incorrect Plts were returned by mistake and the Plts that had screened positively were nearly administered in full to the patient; no clinical symptoms observed in patient, no cultures performed.*

Abbreviations: AHTR = acute hemolytic transfusion reaction; Bp = blood component; RBC = red blood cell concentrate; Tf = transfusion

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.

70 reports from 23 hospitals (27%), 1-11 reports per hospital

- In 58 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
- In 63 cases there was a potential ABO risk
- In 55 of these cases this error was detected after finding a blood group discrepancy.
- The other near misses were detected during various other planned (including 3x during checks when issuing a bc and 2x because of a positive crossmatch) and unplanned checks, by coincidence and/or personal attentiveness.

Analysing regularly occurring types of near miss incidents can be of value for determining what circumstances lead to these situations. Following a recommendation by the Hemovigilance Advisory Board, hospitals were asked to register all cases of blood group discrepancies throughout the 2019 reporting year, analyse these to the extent possible, and report them to TRIP. See also the TRIP Blood Group Discrepancies Project (https://www.tripnet.nl/wp-content/uploads/2019/01/Bloedgroepdiscrepanties-bijlage.pdf). (In Dutch)

It is a misconception to think that the analysis of unusual incidents and the registration of exceptional contributing factors are the main ways of contributing to improving the safety of the transfusion chain. Systematically collecting and thoroughly analysing relatively common near misses and other incidents that were detected (in part) as a result of a blood group discrepancy contributes to the uncovering of the underlying causes of identification errors in particular. This may also help substantiate the importance of introducing certain measures, e.g. digital identification when collecting blood samples.

Regardless of what the cause of a blood group discrepancy turns out to be, further examination must be carried out to definitively determine the patient's blood group (again). The detection of blood group discrepancies is important on the one hand, as a safety net for identification errors and other errors, but on the other hand it can lead to delays in the process and additional costs. It may be expected that situations in which blood group discrepancies were discovered in time are to a large extent comparable to errors which result in an incorrect blood component being transfused. Reducing the frequency of this type of error is desirable. In consultation with the Hemovigilance Advisory Board, TRIP will continue the TRIP Blood Group Discrepancy Project into 2020.

Analysis of the first results from the Blood Group Discrepancy Project

TRIP received 65 reports, from 21 hospitals, in various reporting categories, that are suitable for the TRIP project. Of these 65 reports, 54 contain sufficient information for further analysis

Table 12. Reports of detected blood group discrepancies in 2019

	Reporting category				
	Near miss	Calculated risk	Other incident	IBCT	Total
Unknown whether ABO or Rh D discrepancy was found	13				13
ABO discrepancy*	36	1	3	1	41
Rh D discrepancy#	7		4		11
Total	**56**	**1**	**7**	**1**	**65**

* *Includes 3 cases of ABO discrepancies after SCT and 1 case of A2 variant blood group.*
 # Includes 7 cases of Rh D variants and 1 case of Rh discrepancy after IUT
Abbreviations: IBCT=incorrect blood component transfused; IUT=intra-uterine transfusion; SCT=stem cell transplant

There are 37 cases with a (probable) mix-up and a (potential) ABO blood group discrepancy:

- In eight cases, it was not established what error was made: in five of these cases the initially determined blood group turns out to be incorrect, four cases concerning a patient's first blood group determination and one case a patient's definitively established blood group (from years before).
- In 25 cases an error occurred as a result of which a label is placed onto a blood tube with patient data that do not belong to the patient whose blood was collected into the tube. In 14 of these cases, the mislabelling was named as the error, in most of these cases the correct patient was sticked (n=11). In 11 further cases the entry of the request and printing of a label were done for a different patient than intended, but the correct patient was sticked. Only in a small minority of these cases was the underlying cause of these errors uncovered.
- For three of the cases, the report describes a situation in which a different patient was sticked from the person for whom this was requested and in one case a blood sample from a patient other than the intended person was used for a blood group determination in the lab.

In 15 cases in which (presumably) no mix-ups occurred, a different probable or definite cause was uncovered for the discrepancy. Two of these cases concern a discrepancy with a blood group that was determined many years earlier, during infancy (< 3 months), and of which it is no longer possible to determine what error may have caused it.

Preliminary conclusions

Situations in which labels for patients may be mixed up (such as the use of a single printer by multiple requesters) or in which a computer system may unnoticeably skip from one patient's data to another's, carry a high risk. Correctly verifying patient data on labels to be put on tubes for blood is an important check to carry out in order to detect these errors.

Descriptions of 2019 Near miss cases (in Dutch) can be found in the Report of the Month series on www.tripnet.nl:
Report of the month October 2019: What is your date of birth?
https://www.tripnet.nl/melding-van-de-maand-oktober-wat-is-uw-geboortedatum/
Report of the month September 2020: The label in the lead.
https://www.tripnet.nl/het-etiket-in-de-hoofdrol-3-bijna-ongeluk-meldingen/

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.

87 reports from 29 hospitals (35%), 1-19 reports per hospital (one report of calculated risk in which other incident was reported as an additional category is included in the analyses in this section)

- 20 reports of incidents with which a reaction was also observed (12x Other reaction; 4x Mild NHFR; 1x other allergic reaction; 3x TACO)
- 35 incidents with wastage of (part of) 1 or more blood components

Table 13. Reports of other incidents in 2019, subdivided according to risk group

Type of risk*	N	Subgroup	N	Description	N
ABO	7	Delay in determining Hb/blood group	3	Mix-up of tube/label detected due to blood group discrepancy resulted in delay of emergency operation.	2
				When Plts are requested, a patient's SCT turns out not to have been communicated to the lab, but is coincidentally discovered as a result of a blood group discrepancy.	1
		Bc administered to intended (correct) recipient	3	Unclear whether complete identity check was carried out; accompanying form for blood not countersigned by 2nd nurse.	2
				Check before starting Tf not carried out at patient's bed, label with a different patient's data scanned and warning signal ignored.	1
		Wastage of blood component	1	2 units of FFP (O pos) thawed, subsequently it was not possible to assign the units to the patient (A pos).	
Prevention Irrab	4	Delayed distribution	1	A1 special delivery took > 1 hour following emergency request for O pos, c neg RBC and Plts for F <45 yrs.	
		Result of blood group/Irrab or full typing not processed correctly	3	Treatment with Daratumumab already started, but sampling for full blood typing had been forgotten (performed by Sanquin at a later time point).	1
				2+ reaction with Rhesus D determination erroneously not investigated further, later it was established out that patient should be considered as D neg.	2
Damage/quality	22	Wastage of blood component	16	Accidental puncture of unit during spiking.	2
				Bc collected but Tf cannot take place (yet), due to symptoms in patient (3x) or failure of the IV during an intermediate CT scan (1x), bc punctured prematurely in these cases. In 1 case the symptoms that developed as a result of a previous transfusion were classified as TACO.	4
				Bc collected but Tf cannot take place (yet) or is no longer needed and Bc returned to the lab late or not at all.	5
				Bc collected but Tf cannot take place (yet) or is no longer needed and Bc are erroneously stored outside refrigerator or in an incorrect refrigerator.	3
				Temperature of refrigerator for blood storage too high for a prolonged period due to undetected open door.	1
				Unit no longer usable because of felt-tip pen writing on bag.	1
		Bc administered to intended (correct) recipient	6	Infusion together with medication or unsuitable IV solution. 1x patient developed symptoms of itching several hours after Tf: Other allergic reaction.	5
				Infusion pump set to incorrect setting (too slow) and subsequently exceeding of maximum infusion time.	1
Undertransfusion and/or overtransfusion	35	(nearly) Delayed Tf	5	Extra time needed for delivery of washed RBC not taken into account.	2
				Anti-M in mother erroneously not taken into account when requesting pedipack.	1
				Request for Tf not processed correctly in the lab, RBC not ready.	1
				Request for Tf for a different (incorrect) patient because of mix-up with tube/label for Hb determination, detected at a later time due a blood group discrepancy with a determination from the same tube.	1
		Delay of Tf and wastage of blood component	1	Administration of Plts recorded in Electronic Health Record, but not carried out. By the next day, Plts had expired; new Plts were ordered and administered prior to operation .	

Undertransfusion and/or overtransfusion		Wastage of blood component	16	IV impaired and subcutaneous infusion, sometimes with considerable symptoms in the arm/hematoma (3x other reaction). In 1 case the bc was disconnected, but not returned to the lab, against advice from the lab. Subsequently administration of the RBC was resumed through a new cannula and a new line (additional category IBCT).	13
				IV line failed and blood bag drained beside the cannula.	1
				Tf stopped immediately after observing reaction (mild NHFR), in hindsight unnecessary. (Report of the Month June 2020)	1
				Infusion time of infusion pump set to 6 hours, final 30 ml of RBC not administered because maximum infsuion time of 6 hours after distribution was reached.	1
		(nearly) Administering unnecessary Tf and wastage of bc	1	Request for RBC, Plts and plasma based on diluted blood sample (drawn from IV arm).	
		(nearly) administering unnecessary Tf	9	Administration of RBC selected for the patient in case of need, but not required.	1
				Tf based on Hb determination from diluted blood sample (drawn from IV arm).	5
				Excess of RBC administered to neonate as a result of an incorrect calculation.	1
				After administration of 4 units of RBC to bleeding patient without interim check of Hb level, Hb found to have increased from 5.2 to 12 mMol/L	1
				Request for RBC based on WBC result (5.9) instead of Hb result (7.0).	1
		(nearly) Administering unnecessary Tf + delayed Tf	3	Other component type requested/issued from intended. (Report of the Month November 2019)	3
		Delay in determination of Hb/blood group	1	Label of different (incorrect) patient put over label of correct patient on tube for Hb and blood group determination, detected as a result of blood group discrepancy.	
Traceability	1	Failure in checks/ surveillance of Tf		Registration of administration not according to protocol when electronic device failed.	
Other	18	Reaction reported to the lab late or not at all	12	Symptoms during or following the Tf, were reported to physician. 8x Other reaction, 3x Mild NHFR, 1x TACO.	
		Failure in checks/ surveillance of Tf	2	Deterioration of patient during Tf, not related to administration of bc, RBC administered in full, no further investigation in the lab (hemolysis/blood group serology) nor was the bc cultured. Reporting category TACO.	1
				Infusion pump set too fast for patient with cardiac decompensation, detected after shift change of nurses and adjusted. Symptoms of increased dyspnea at the end of the Tf, improved without further treatment. Additional category Other reaction. (Report of the Month April 2020)	1
		Miscellaneous	4	No Plts card provided on issue of minor incompatible Plts.	1
				Blood group of neonate registered as D neg, later it transpired that this was incorrect and 5 IUTs had been administered.	1
				Blood group determined as Rhesus D neg in the past turns out to be variant of Rhesus D that is considered as D pos.	1
				Against protocol, patient is not supervised by a nurse during an endoscopy while receiving a Tf, administration had been halted temporarily.	1

** ABO = risk of an ABO incompatible blood transfusion*
Prevention irrab = guidelines not followed with regard to prevention of irregular antibody formation

Abbreviations: bc=blood component; FFP=fresh frozen plasma; IUT=intrauterine transfusion; NHFR=Non-Hemolytic Febrile Reaction; Plts=platelets; RBC=red blood cells; SCT=Stem cell transplant; TACO=Transfusion-Associated Circulatory Overload; Tf=transfusion; WBC=White Blood Cells

A number of 2019 Other incident cases have been described (in Dutch) in the Report of the Month series on www.tripnet.nl:
Report of the month October 2019: Was the patient administered an incorrect blood component?
https://www.tripnet.nl/melding-van-de-maand-november-2019-kreeg-de-patient-een-verkeerd-bloedproduct/
Report of the month June 2020: Patient observed well, but..... (2)
https://www.tripnet.nl/melding-van-de-maand-juni-2020-patient-goed-geobserveerd-maar/
Report of the Month April 2020: Were preventive measures successful in preventing TACO?
https://www.tripnet.nl/melding-van-de-maand-april-2020-heeft-preventief-beleid-taco-effectief-voorkomen/
Report of the month July 2020: To measure is to know
https://www.tripnet.nl/melding-van-de-maand-juli-2020-meten-is-weten/
Report of the month August 2020: Three TACO patients
https://www.tripnet.nl/melding-van-de-maand-augustus-2020-drie-patienten-met-taco/

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.

17 reports from 9 hospitals (11%), 1-6 reports per hospital
- 1 report with additional category other incident due to delay of delivery in emergency situation
- 2 reports of a reaction with additional category of calculated risk situation: Other reaction (1x) and new allo-antibody formation (1x)

Nearly all reports of calculated risk situations in 2019 concern emergency situations (in five cases transfusion by trauma medical services in helicopter air ambulance) in circumstances which did not allow for consideration of antibodies previously demonstrated in a patient (n=5), or irregular antibodies that had not previously been demonstrated in the patient, but were subsequently demonstrated in the pre-transfusion sample when the screening was performed (n=1), or preventive transfusion advice for a defined at-risk group (n=8).

Only three of the cases did not concern an emergency situation. One of these cases involved a patient for whom blood components with very specific typing were required, such that no fully compatible blood components were available in the Netherlands. In a second case, anti-Lua was coincidentally demonstrated in a patient while this patient was being transfused with a T&S unit of RBC after an earlier screening with a test panel without Lua positive cells. A mix-up of the blood tube/patient label occurred with this patient's blood samples (detected due to blood group discrepancy and reported as a Near miss) and anti-Lua was found with a different test panel incorporating Lua positive cells. Crossmatching with the transfused RBC gave a negative result however and the unit of RBC turned out to be Lua negative as well. Additionally, detecting a blood group discrepancy between the first blood group registered for the patient in 1991, as a neonate, and the second blood group determination, as part of a pregnancy screening 28 years later, gave cause to report the case as a Calculated risk situation to draw attention to the potential risks of such a registration.

3.2 Non-infectious transfusion reactions

Transfusion-associated circulatory overload (TACO)

Respiratory problems during or within 12 hours after transfusion, manifested by at least one pulmonary feature (criterion A or B). In all, at least 3 of the criteria below must be met.
See also notes 1 to 6 on www.tripnet.nl
A. New or worsening respiratory problems (see note 1)
B. Features of new or worsening pulmonary oedema, based on:

- *Physical examination (see note 2) and/or*
- *Chest X-ray or other imaging of the chest (see note 3)*

C. Relevant changes in the cardiovascular system (see note 4)
D. Findings suggestive of relevant changes in fluid balance (see note 5)
E. Biomarker result(s) consistent with TACO (see note 6)
https://www.tripnet.nl/wp-content/uploads/2019/06/TRIP-TACO-definition_2019

90 reports from 42 hospitals (50%), 1-11 reports per hospital

- In 3 reports, other incident was added as an additional category (1x unnecessary wastage of blood component; 2x reaction not reported to laboratory)
- Transfusion-associated circulatory overload was reported as an additional category 9 times: with Other reaction (2x), Post-transfusion bacteremia/sepsis (2x), AHTR, Other allergic reaction, Mild NHFR, NHTR and TRALI

The steady rise in recent years wasabsent in 2019. Both the total number of reports of TACO and the number of TACO reports with severity grade 2 or higher (n=30) decreased (total number of TACO reports in 2015: 76; 2016 89; 2017 106; 2018 134). TACO was reported most often with transfusions of red blood cell concentrates, and there was a decrease from 0.30 to 0.22 reports per 1000 units in comparison to 2018. The decrease in the number of reports may be explained by several different factors, such as: stricter assessment as a result of the implementation of the new TRIP definition; increased awareness of preventing TACO; the workload in hospitals. The TRIP office has examined some of these factors more closely, to determine to what extent they possibly were influential.

Was a larger number of reports concerning respiratory symptoms been registered in a different reporting category as a result of stricter assessment criteria? The 2019 TACO reports were reviewed to determine whether at least three criteria from the revised definition were met, as this definition requires. For 83 of the 90 cases, the registered data provide adequate groundsto determine unambiguously that sufficient criteria from the definition were met. For five cases, some doubts arise, for instance if the report mentioned low oxygen saturation, but did not explicitly state that dyspnea or a decrease in saturation occurred. In two cases, the report was accepted on the physician's or the reporting hospital's assessment, and no results from a physical examination or other patient levels or values were detailed in the report - which was considered sufficient for registration as TACO up to and including. The TACO reports from 2018 were re-assessed according to the 2019 definition, and the results from both years were compared to each other (Table 14). It seems probable that the implementation of the revised definition for TACO and the resulting use of more elaborate assessment criteria has been of some influence.

Table 14. TACO reports: Does the reported reaction meet the criteria set for TACO as of 2019?

	2019		2018	
	Number	Percentage	Number	Percentage
Yes	83	92.2	87	64.9
Insufficient information	2	2.2	37*	27.6
Uncertain	5	5.6	10	7.5
Total	**90**	**100.0**	**134**	**100.0**

* *Most likely, further data from a number of these cases is available, and if this data were requested and assessed, these reports would meet the 2019 criteria.*

Have there been any noticeably large fl uctuations in certain hospitals, for instance as a result of increased attention, for example with clinical teaching on the subject? The pattern in the number of reports of TACO and other reaction per hospital from 2016 to 2019 was mapped out. In the majority of the hospitals which reported at least one case of TACO during this period (n=66), the number of reports of TACO from year to year varies from 0 to 4 per year. Remarkably, 18 hospitals (21% of the total number of contact addresses in 2019) did not reported any cases of TACO in this period. Presumably, underreporting of TACO still occurs. In a limited number of hospitals (n=12 from a total of 66) a clear peak in the number of TACO reports above the level of other years can be discerned (2017 n=5; 2018 n=8; 2019 n=2), with at least 5 reports of TACO in that year. Table 16 and Figure 8 in the annex display these results: in 2018, more hospitals than in the other years submitted a relatively high number of TACO reports. Additional analyses of the fl uctuations in numbers of TACO and Other reaction with respiratory features are described in the annex (with Table 15 and 16, Figure 8 and 9).

The imputability of the reported TACO cases remains high, nearly 50% of the 2019 reports have been assessed as probable or defi nite. Additionally, 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.

Most reports of TACO are related to the administration of one or more red blood cell concentrates (n=87), or the administration of both red blood cell and platelet concentrates (n=3). In 2019, TRIP did not receive any reports of TACO related to transfusion with massive hemorrhaging or with the administration of plasma or solely platelet concentrates.

Table 17. Severity and imputability of TACO cases in 2019

Imputability	Total number of reports*	Severity grade			
		1	2	3	4
Definite	2	1	1		
Probable	39	24	14	1	
Possible	48	34	12		2
Totaal	**90***	**60***	**27**	**1**	**2**

* *The imputability of one grade 1 report was not assessed*

In three reports TACO occurred in combination with an incident classified as other incident, see also Table 13 (section on other incidents). One of these cases concerns a patient with, among other things, acute kidney failure, who, at an Hb of 2.2 mMol/L, had already received three units and in whom a reaction was observed (slight increase in temperature to 38.0 °C, decrease in saturation to 95%, tachypnea and fluctuating blood pressure), just moments before attaching the fourth unit of RBC. As a result, the transfusion was postponed, but unfortunately, the blood component had already been spiked and thus was unnecessarily wasted. In the other two cases, the reaction was wrongly not reported to the lab.

Conclusions TACO

Retrospectively, the number of reports of TACO in 2018, assessed using the 2019 definition , is at least as high as the number in 2019. There appears to be a decrease in the number of reports of TACO in 2019 that cannot be ascribed to lower use of blood components or the implementation of the new TACO definition. Fairly sizeable fluctuation in the individual reporting patterns of a (small) number of hospitals seems to have played a part in the decrease of the number of reports of TACO.

A number of 2019 TACO cases have been described (in Dutch) in the Report of the Month series on www.tripnet.nl: Report of the Month April 2020: Was preventive policy successful in avoiding TACO?
https://www.tripnet.nl/melding-van-de-maand-april-2020-heeft-preventief-beleid-taco-effectief-voorkomen/
Report of the month August 2020: Three TACO patients
https://www.tripnet.nl/melding-van-de-maand-augustus-2020-drie-patienten-met-taco/

TRALI

Dyspnea and hypoxia within six hours of the transfusion; chest X-ray shows bilateral pulmonary infiltrates.

- Six reports of TRALI in 2019, five of which had an imputability assessed as definite, probable, or possible.
- The severity grade of these five reports was 1x grade 4; 3x grade 3; and 1x grade 2
- One report of TRALI (imputability possible) was reported with the administration of SD-plasma to a patient with no recognised ARDS risk factor.
- Additionally, three 2019 reactions were reported as suspected TRALI to Sanquin, but not to TRIP. TRIP urgently requests for all TRALI reactions to be reported to TRIP as well (at an early stage, because there is a risk this might be forgotten at a later point and the case will be missing from the national data. This is no less important when a different diagnosis, such as TACOI, is ultimately assigned.

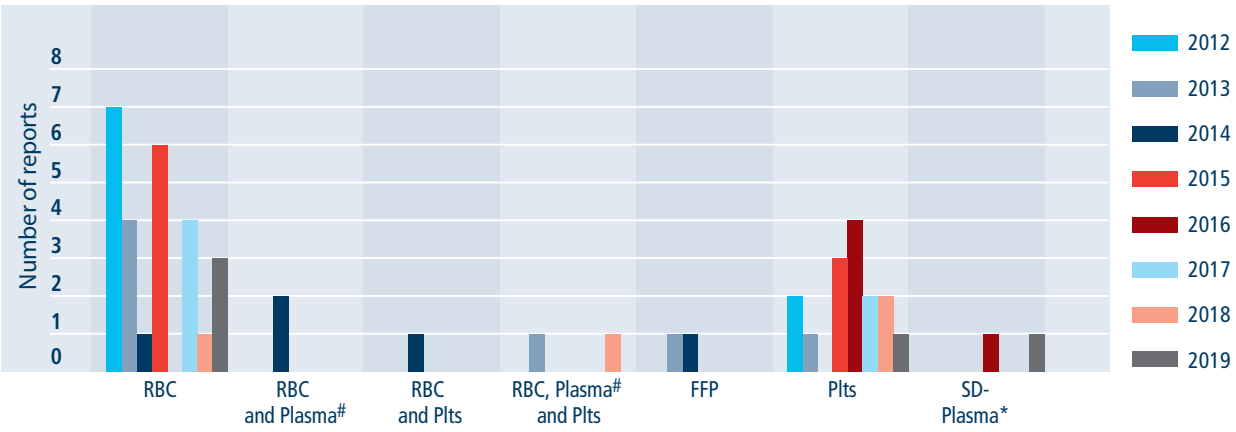

Figure 10. Type of blood component in TRALI reports of certain, probable or possible imputability, 2012-2019

 # The plasma was FFP up to 2014 and SD-plasma from 2016 to 2019

** See discussion in 2016 TRIP report: TRALI report from that year concerns patient at risk of ARDS and TACO could not be ruled out.*

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 anaphylactic 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.

- Four reports of TAD in 2019
- A total number of 24 reports since this reporting category was introduced in 2016 (Table 18).

Table 18. Transfusion-associated dyspnea (TAD), 2016-2019

TAD N=24	No. of reporting hospitals: 15
Age	Median 63 years, range 14-84 years
Sex	11 F, 13 M
Interval	Median 2hrs 13 min, range 15 min to 4 hrs 15 min from start of transfusion
Previous Tf and/or pregnancy	Known in 9/11 of female patients Previous Tf known in 8/13 of male patients
Severity grade	5x grade 2, 19x grade 1
Imputability	5 probable, 17 possible, 2 unlikely
Symptoms	24x dyspnea and/or decrease in oxygen saturation: median decrease to 85% (recorded in 19 reports) 13x Increase in temperature and/or chills 4x systolic ≥ 30 mm Hg (<50 mm Hg) increase in blood pressure (no relevant increase in diastolic) 4x systolic ≥ 20 mm Hg (<40 mm Hg) decrease in blood pressure, decrease in diastolic max. 13 mm Hg 3x distress, nausea 2x chest pain Other symptoms: 1x headache

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.

- 17 reports (16 with RBC, one with platelets; see Table 19)
- One report of severity grade 2 as a result of transfusion of an ABO-incompatible blood component, transfusion stopped 15 minutes after onset of transfusion when first symptoms occurred, (IBCT registered as additional category).

Table 19. Acute hemolytic transfusion reaction (AHTR) in 2019

AHTR N=17	No. of reporting hospitals: 10
Age	Median 69 years, range 22-91 years
Sex	7 F, 8 M (two female patients with two reactions)
Interval	Interval median 2hrs 13 min, range 15 min to 5 hrs 51 min
Previous Tf and/ or pregnancy	Known for 7/8 male patients and 6/7 female patients with AHTR Pregnancy 2x none, 5x unknown, 2x not stated
Severity grade	9x grade 2, 8x grade 1
Cause	1x (as a result of IBCT) ABO incompatibility (grade 2) 3x with Hemoglobinopathy (1x heterozygote Hb Savannah; 1x sickle-cell disease; 1x thalassemia) 1x patient with paroxysmal nocturnal hemoglobinuria 4x in three patients with autoimmune hemolytic anemia 3x in two patients with irregular antibodies that had not been demonstrated before Tf (a-Wra and a-Fya+anti-P1 respectively) 1x with A+ Plts in PAS with recipient (O+) with high titre anti-A For the remaining reactions (3) no direct cause was determined; these occurred with patients with chronic hemolysis and auto- or nonspecific antibodies.
Imputability	6x definite; 3x probable; 8x possible

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.

- Three reports of DHTR and four of DHTR recorded as an additional category with demonstration of new allo-antibody formation; all reported with transfusions of RBC
- Gradual decrease from year to year, number in 2019 comparable to that in 2017-2018 (Figures 11 and 12)
- Preventive measures include preventive matching of RBC transfusions, following the transfusion guidelines and TRIX, the National Transfusion Register of Irregular antibodies and X(crossmatch) problems.

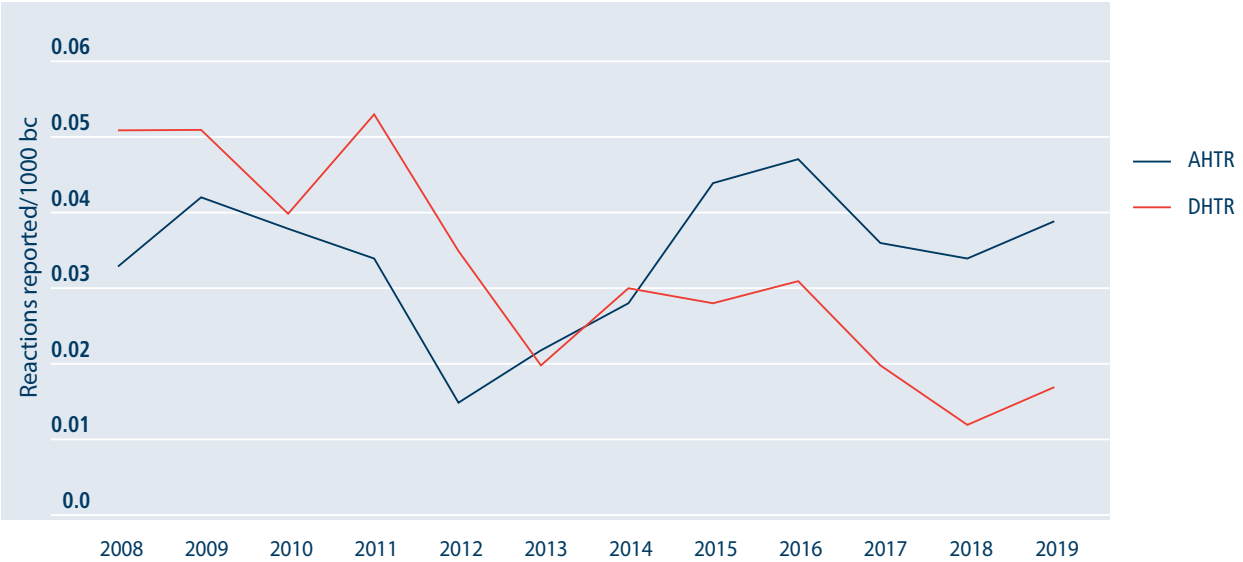

Figure 11. Reports of acute and delayed hemolytic transfusion reactions relative to the number of red blood cell concentrates distributed, 2008-2019

Encompasses all reports with definite, probable and possible imputability, including hemolytic reactions with incorrect blood component transfused or demonstration of new allo-antibody formation

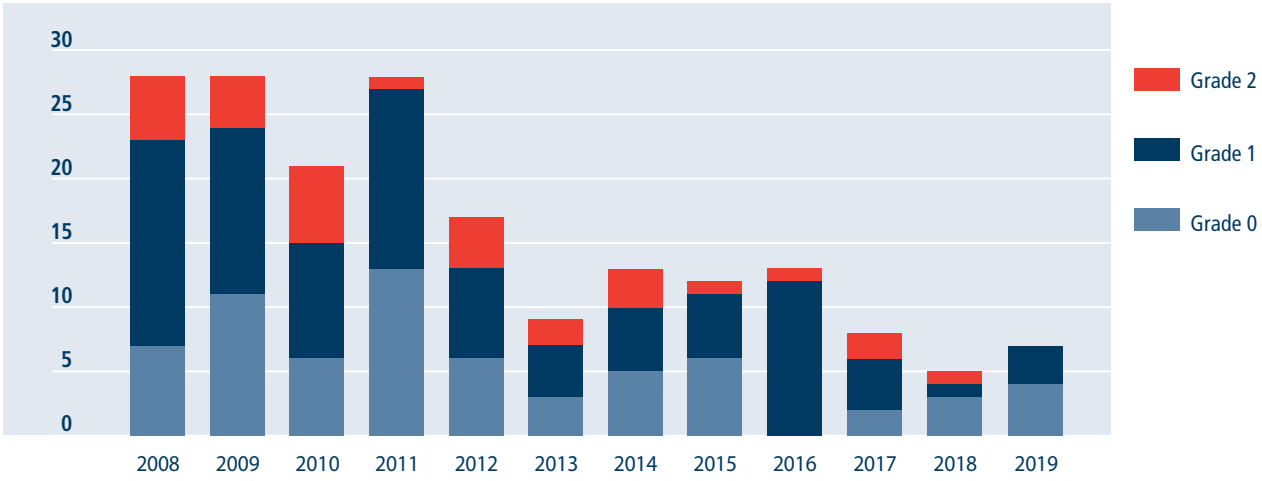

Figure 12. Severity of reports of delayed hemolytic transfusion reactions (main/additional category; imputability definite, probable, possible), 2008-2019

Anaphylactic reaction and other allergic reaction 2019

Anaphylactic reaction

Rapidly developing allergic reaction occurring within a few seconds after the start of transfusion or up till a short time after transfusion with features such as stridor, fall in systolic and/or diastolic blood pressure ≥ 20mm Hg, nausea/vomiting, diarrhoea, back pain, skin rash.

Other allergic reaction

Allergic phenomena such as itching, redness or urticaria without objective respiratory, cardiovascular or gastrointestinal features, arising from a few minutes of starting transfusion until a few hours after its completion.

- A total number of 120 reports (25 and 95 respectively), the number of non-serious reports has decreased by approximately 30% in comparison to 2016 to 2018.
- Most reactions (both the absolute number and the number in relation to the number of blood components) occurred with platelet concentrates, but these also saw the largest decrease in number of reports (Figure 13).

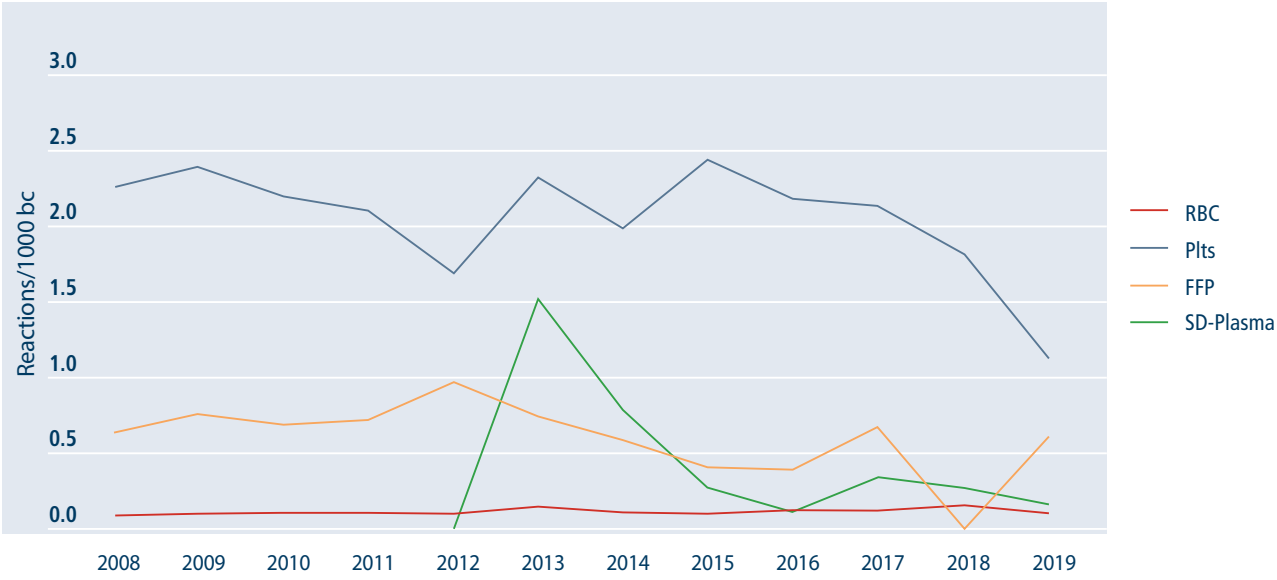

Figure 13. Reports of allergic transfusion reactions (anaphylactic reactions and other allergic reactions combined) relative to the number of blood components distributed, 2008-2019

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).

- 712 reports (723 including reports with new allo-antibody formation as an additional category), 843 new allo-antibodies
- 59 reporting hospitals (70%), range of 1-64 reports per hospital.
- 287 M and 436 F
- 27 new allo-antibodies in women < 45 years old at the time of transfusion
- Specificities displayed in Table 20
- Formation of anti-E or anti-K in 8 women <45 years old (Table 21), no reports of incorrect selection of blood components with this subgroup.
- In 2019, 6379 new allo-antibodies were entered into the TRIX database, 1645 of which in male patients (TRIX annual report 2019).

Table 20. New allo-antibodies in 2019: Most frequent specificities in women and men

New antibody	F <45y*	F total	M	Ratio F/M	Percentage (TRIP 2019)	TRIX#
anti-E	7	143	106	1,3	31.5%	16.7%
anti-K	2	120	71	1,7	21.1%	12.9%
anti-Jka	5	34	9	3,8	2.7%	3.2%
anti-c	-	32	9	3,6	2.7%	5.3%
anti-Fya	5	39	26	1,5	7.7%	4.9%
anti-C	1	16	17	0,9	5.1%	6.2%
anti-Wra	1	17	15	1,1	4.5%	6.0%
anti-Cw	-	17	13	1,3	3.9%	3.1%
anti-S	4	16	4	4,0	1.2%	2.0%
anti-Lua	2	9	18	0,5	5.4%	-
anti-Kpa	-	12	5	2,4	1.5%	-
anti-D	-	9	3	3,0	0.9%	11.4%
anti-e	1	8	13	0,6	3.9%	0.9%
anti-Jkb	1	9	5	1,8	1.5%	0.8%
anti-Fyb	-	4	2	2,0	0.6%	0.5%
anti-M	1	9	8	1,1	2.4%	9.6%

 # From: van Gammeren et al. A national Transfusion Register of Irregular Antibodies and Cross (X)-match Problems: TRIX, a 10-year analysis. TRANSFUSION 2019;59;2559–2566.

Table 21. Reports of formation of anti-D, anti-c, anti-E and anti-K in women <45 years old in 2019

Antibody	2019		2018
Anti-D	None		1
Anti-c	None		4
Anti-E	7	2x Tf just before parturition, no antigen positive RBC 1x No known E-pos Tf 4x Tf 2011 or before	8
Anti-K	2	Tf 2002 or before	3

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 reports of transfusion reactions: 251, including four other reactions registered with other incidents.
- 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 (18 in 2019).
- Many reports with features that do not fit any of the standard categories, and that may (partly) be explained by the patient's illness. Although the patient's underlying condition may be important in the differential diagnosis for these reactions, the imputability of a quarter of these reactions was still judged to be definite or probable, based on the temporal association with the transfusion.
- Numbers and subcategorization similar to those in previous years (Table 23).
- For five reactions reported in one of the specific reporting categories, other reaction was included as an additional category: to signal the observation of a somewhat increased blood pressure (3x) with febrile reactions, and a rise in temperature that lasted for over 24 hrs (1x) and a repeat positive blood culture result (1x) found in association with TACO.

Table 22. Types of reactions that are registered as other reaction (broken down as in previous TRIP reports)

Type of reaction	2018	2019	2019 Def., Prob.	2019 Poss.	2019 ≥ severity grade 2*
Reactions with hypotension	53	58	9	38	1
Subgroup hypotensive reaction (ISBT)#	9	8	2	8	1
Reactions with dyspnea	27	21	5	10	3
Increased blood pressure	31	30	4	22	1
(Possible) cardiac symptoms	12	21	4	10	2
Did not completely fit TRIP definition for standard category	55	44	9	24	2
Unproven sepsis	1	0	0	0	0
Other symptoms	110	77	20	34	9
Total	**289**	**251**	**51**	**138**	**18**

* *Imputability definite, probable or possible*
\# *For this, systolic blood pressure must be ≤80 mm Hg*
Abbreviations: Def., Prob.=Imputability definite or probable; Poss.=Imputablity possible

Other reaction case descriptions (in Dutch) of 2019 reports can be found in the Report of the Month (Melding van de maand) series on www.tripnet.nl, e.g.:
Report of the Month May 2019: Fever again and again
https://www.tripnet.nl/melding-van-de-maand-mei-2019-steeds-weer-koorts/
Report of the Month April 2020: Was preventive policy successful in avoiding TACO?
https://www.tripnet.nl/melding-van-de-maand-april-2020-heeft-preventief-beleid-taco-effectief-voorkomen/

3.3 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 patient blood culture result; a causal link to a transfused component may or may not be confirmed (through a finding of the same bacterial species in the component or other material from the donor).

Bacterial contamination of blood component

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.

Table 23. Overview of reports from hospitals relating to bacterial problems 2010-2019

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Post-transfusion bacteremia/sepsis	41	61	50	47	55	79	64	72	72	83
(cases of TTBI, as assessed by experts)	(3)	(2)	(1)	(2)	(2)	(2)	(3)	(2)	(1)	(1)
Post-transfusion bacteremia/sepsis as an additional category (not TTBI)	17	13	14	6	10	4	2	5	1	0
Bacterial contamination of blood component* (including positive bacterial screening)	44	43	42	25	12	15	10	4	-	1 #
Bacterial contamination of blood component (including reports of positive bacterial screening) as an additional category	17	19	16	10	14	7	16	19	11	12

* *The cases in which bacterial screening by the blood establishment results in a positive culture are supplied to TRIP in the form of a single total figure by Sanquin, and since 2017 have only been registered for TRIP reporting as a separate report by a hospital if a patient showed symptoms or experienced negative consequences, such as postponement of surgery or the administration of prophylactic medication.*

\# *Led to hospital admission and prophylactic antibiotics.*

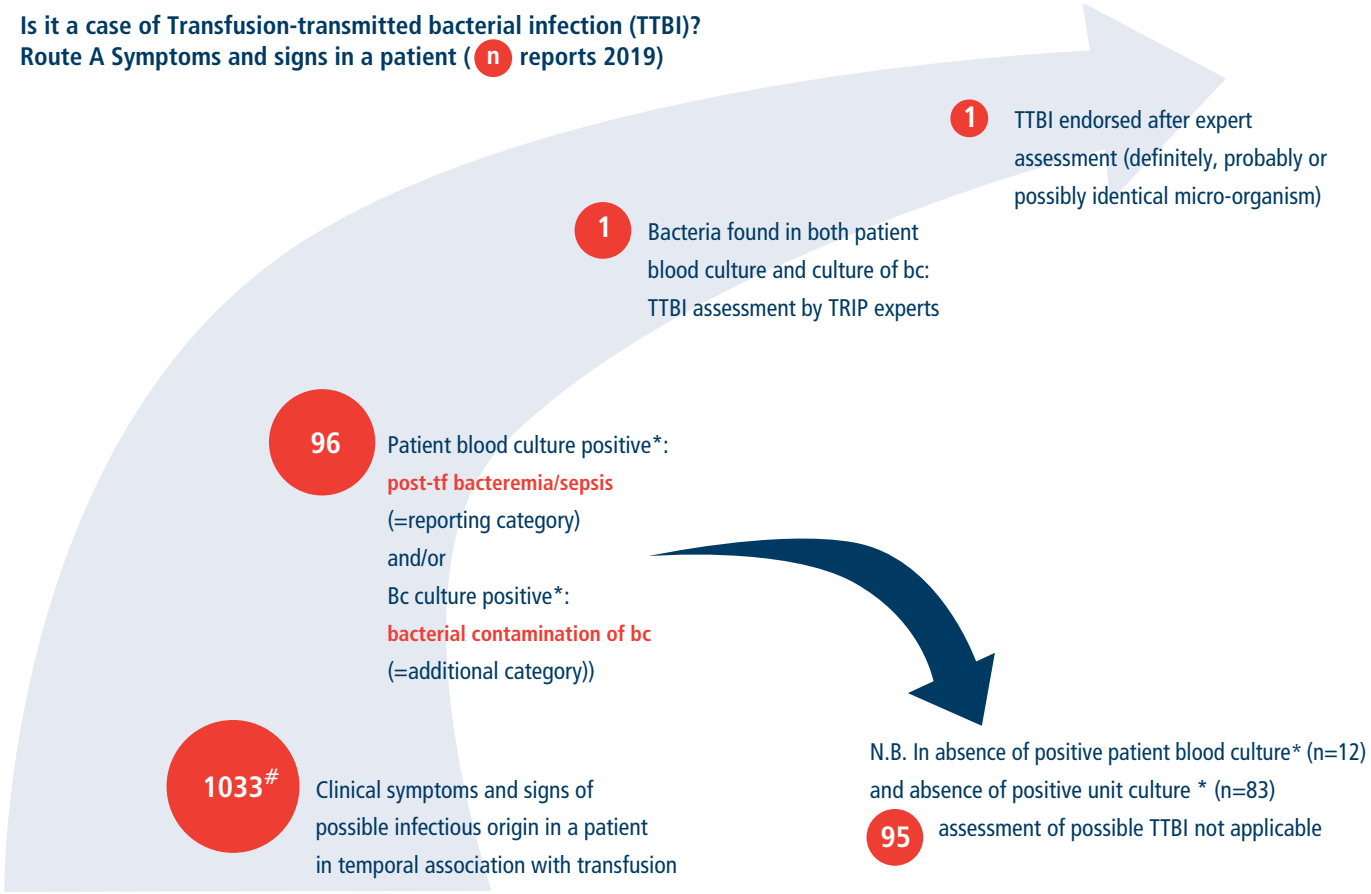

Figure 14. Assessment of TTBI 2019

 # Cases reported in 2019 with increase or decrease of patient's temperature and/or chills
** Culture result must be judged to be relevant*
Abbreviations: pt=patient; bc=blood component

Table 24. Assessment of TTBI 2019 (n=1, discussed with Hemovigilance Advisory Board)

Patient blood culture	Unit (culture result in hospital)	Blood component	BacTalert / culture by Sanquin	Reporting category	Severity grade	Imputability of reaction	TTBI assessment
S. aureus	*S. aureus*	Plts (pooled)	Negative; Sanquin cultured 3 units of RBC from the same donations after recalling (negative)	Post-transfusion bacteremia/ sepsis	2	Definite	Probable

Table 25. Overview of bacteriological screening of platelet concentrates by Sanquin

Cumulative numbers (Sanquin)	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Platelet concentrates with initial positive result	332	321	238	165	214	190	218	188	185	185
Units already transfused (Platelet concentrates and corresponding RBC units)	106	125	90	83	80	82	79	96	100	81*

** In five cases Sanquin was informed that a mild reaction had beenobserved in the patient, but the reaction was not linked to the positive result of the bacteriological screening; in six cases Sanquin did not receive a responsefrom the hospital*
Abbreviations: Plts=platelet concentrate; RBC=red blood cell concentrate

A case description of post-transfusion bacteremia/sepsis (in Dutch) in 2019 can be found in the Report of the Month (Melding van de maand) series on www.tripnet.nl, e.g.:
Report of the Month May 2019: Fever again and again
https://www.tripnet.nl/melding-van-de-maand-mei-2019-steeds-weer-koorts/

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 hospitals

In 2019, TRIP did not receive any reports concerning post-transfusion viral infection.

Look-back by the supplier/recall* (2020 definition)

Retrospective notification of a non-compliant or possibly infectious donation (other than bacterial contamination of a blood component), leading to investigation of the recipient for that infection or possible consequences.
** If there was a notification from Sanquin but the patient had no reaction or other (medical) consequences (such as prophylactic medication), hospitals should not report these cases to TRIP. Sanquin provides overall total figures to TRIP annually.*

Information from hospitals

In 2019, TRIP received six reports in the category os look-back/recall: in five cases because test results at a donor's next donation indicated a past infection. The sixth report concerned post-donation information from the donor, who had had flu-like symptoms and a fever four days after donating. In three of the six cases, extra tests of the recipient of the blood component or additional monitoring was performed; there was no indication of any transmitted infection.

As of 2020, hospitals are requested to only report look-backs and recalls to TRIP if there are consequences for the patient, such as a reaction, prolonged hospitalization, additional treatment, et cetera.

Information from Sanquin

In 2019, look-back investigations were performed according to protocol after 11 seroconversions (2x HBV; 6x Syphilis; 3x HIV) and one HEV-positive donation. Hospitals were requested to trace the recipients in order to inform them (look-back); no transmissions was found (one investigation was still in progress at the time of writing this report).

Conclusion infectious transfusion complications

TRIP received no report of a viral infection transmitted in 2019. One report of post-transfusion bacteremia/sepsis, in which Staphylococcus aureus was found both in the patient's blood culture and in the cultured remnant of the blood component, was judged to be a likely Transfusion-Transmitted Bacterial Infection (TTBI). In all, the registered reports for 2019 demonstrate that the incidence of transmissions of infections with blood transfusions in the Netherlands is low: only 1 in over 500,000 administered units.

3.4 Blood management techniques (BMT)

In 2019, TRIP received no reports from hospitals concerning transfusion reactions or incidents related to the use of blood management techniques, such as reinfusion drains or cell savers.

3.5 Reports with SD-plasma (Omniplasma®) in 2019

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 continues to supply FFP for pediatric use and other special indications.

Because SD-plasma is prepared under legislation on pharmaceutical products, hospitals draw up contracts between the hospital pharmacy and the blood transfusion laboratory. In accordance with arrangements made between TRIP and Lareb, the Dutch pharmacovigilance agency, reports of transfusion reactions and/or transfusion incidents may be submitted using the TRIP system. As of 2018, TRIP has forwarded such reactions to Lareb, with the exception of new allo-antibody formation in patients who also received cellular components were also administered and of incidents not related to component quality. (The reporting to Lareb includes 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 on page 9 shows the course of the use of SD-plasma. The 31 reports with SD-plasma from 2019 are summarized in Table 26 (2018: 34 reports, including a late report of incorrect blood component transfused concerning the use of SD-plasma rather than FFP for a child). 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. The general picture is comparable to when FFP was the standard plasma product.

Table 26. Reports associated with SD-plasma in 2019 (n=31)

	Non-serious reactions		Serious reactions	
Type of reaction	**SD only**	**SD and other blood product**	**SD only**	**SD and other blood product**
Anaphylactic reaction		2	1	
Other allergic reaction	8	1		
Mild non-hemolytic TR		1		
Non-hemolytic TR	1	1		
New allo-antibody formation		6		
Other reaction	2	3	1	1
TRALI			1	
Incidents				
Other incident*	1	1		

* *2x wastage of blood component: product thawed but unexpectedly could not be administered*

Conclusion

The side effects of the use of SD-plasma (Omniplasma®) are similar to the reactions previously reported to TRIP with 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 (Transfusion (and Transplantation) 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 (biovigilance). The biovigilance findings are reported in a separate annual biovigilance report which is also available on www.tripnet.nl under publications/reports. TRIP is advised by the Hemovigilance and Biovigilance Advisory Boards, which consist of representatives of the professional societies.

Reporting to TRIP is anonymous. Though voluntary in principle, it is regarded as the professional standard by the Healthcare Inspectorate (IGJ) and the national "CBO" transfusion guidelines (2011; the revised Guidelines for Blood transfusion policies are expected to be finalised by 2020). Reporting to TRIP is separate from the hospitals' responsibility to provide care.

All reports are submitted digitally (as of 2016). 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. This enables the TRIP physicians to assess their coherence and verify the reporting category of (potentially) serious reports. An Expert Committee (EC), consisting of experts from the Hemovigilance Advisory Board, advises on the classification of serious and complex reports.

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.
In the Netherlands, these requirements have been implemented in the Quality, Complaints and Disputes in Healthcare Act (Wet kwaliteit, klachten en geschillen zorg, Wkkgz), in the Wkkgz implementing order under the heading of "hospital blood banks" (Ziekenhuisbloedbanken), section 5.1, paragraph 3.
The hospitals can send serious reports to the Healthcare Inspectorate and Sanquin using the TRIP online reporting system. TRIP performs 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. TRIP compiles the annual mandatory overview of serious adverse events and reactions to be forwarded to the European Commission, via the Ministry of Health, Welfare and Sport.

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. With regard to reactions in 2019, three reports of serious transfusion reactions (TRALI), which had been reported to Sanquin, could not be found in the TRIP database as of March 2020. TRIP urgently requests hospitals to always report a reaction to TRIP as soon as possible after reporting it to Sanquin. If all reports to Sanquin are sent through the TRIP reporting system 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 2019, TRIP received reports from 76 hospitals. Six hospitals indicated that there had been no reports of incidents or reactions in the TRIP reporting categories in 2019. Two hospitals had not provided any information about reports or numbers of transfusions to TRIP at the time of compiling this report. The level of participation among hospitals is 82/84=98% for submitting reports and also 82/84=98% for submitting data on the number of blood components transfused.

Besides the hospitals, TRIP is in contact with four private clinics which have been licensed by the Ministry of Health, Welfare and Sport to receive and transfuse blood components to their patients; these clinics have contracts with Sanquin or other hospitals for the provision of component selection and cross-matching services. In 2020, TRIP also contacted four additional establishments, of which it became known via the Ministry of Health, Welfare and Sport that they had also been licensed. Two of the eight licensed clinics informed TRIP that no units were transfused in 2019 and two other clinics informed TRIP that reports of any reactions would be made by the transfusion labs in the hospitals with which they have contracts for the provision of blood components.

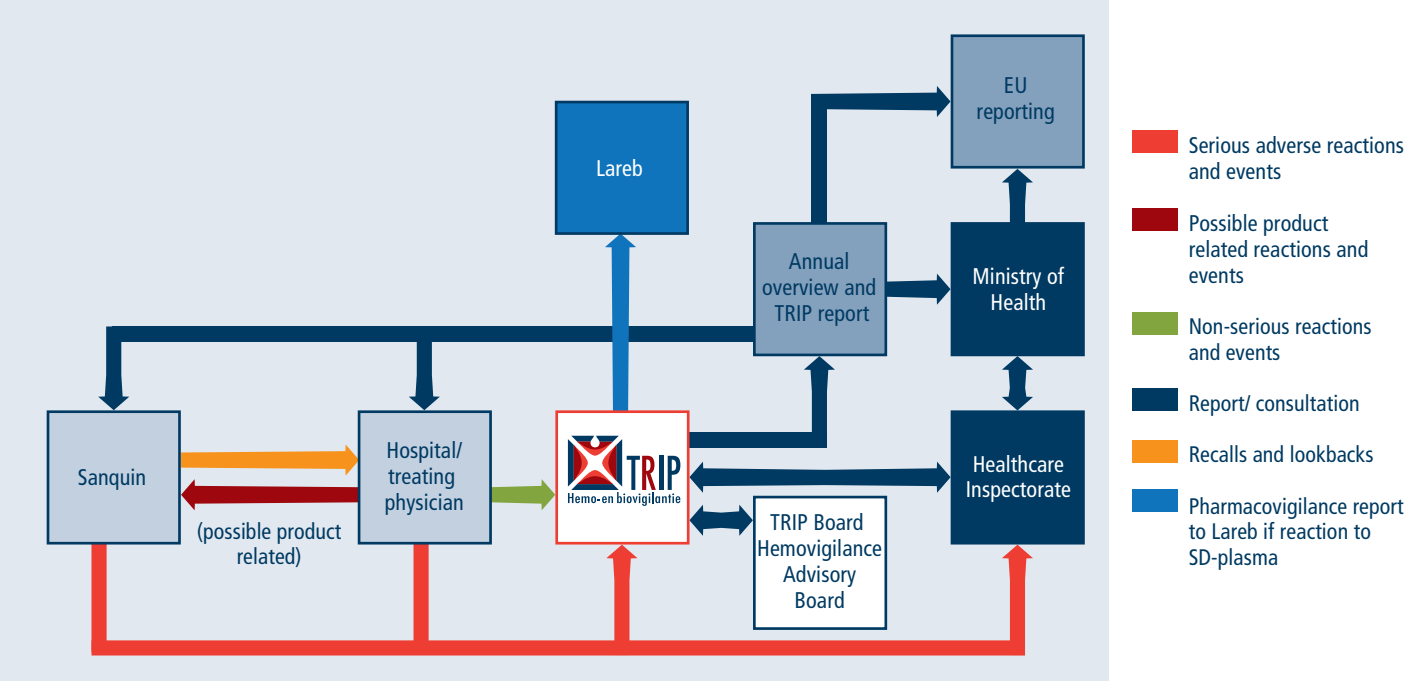

Figure 15. Flow of hemovigilance information and outputs in the Netherlands

List of terms and abbreviations

AHTR	Acute hemolytic transfusion reaction
Bc	Blood component
BMT	blood management techniques
CBO	CBO quality organisation in healthcare
DHTR	Delayed hemolytic transfusion reaction
EU	European Union
FFP	fresh frozen plasma
IBCT	Incorrect blood component transfused
ICU	intensive care unit
Irrab	Irregular antibodies
Mild NHFR	Mild non-hemolytic febrile reaction
NHTR	non-hemolytic transfusion reaction
OI	Other incident
Other all. reaction	Other allergic reaction
Plts	Platelet concentrate
Post-Tf bact/sepsis	Post-transfusion bacteremia/sepsis
Pt	Patient
PTP	Post-transfusion purpura
RBC	Red blood cell concentrate
Sanquin	Sanquin (Dutch national blood establishment)
SD	solvent detergent (a pathogen reduction method)
Sp.	Species
Sympt.	Symptoms
TACO	transfusion-associated circulatory overload
TAD	transfusion-associated dyspnea
TA-GvHD	Transfusion-associated graft versus host disease
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

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