TRIP REPORT 2021

HEMOVIGILANCE

EXTENDED VERSION

TRIP
Hemo- en biovigilantie

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The TRIP report 2021 hemovigilance, extended version, is published under the responsibility of the TRIP (Transfusion and Transplantation Reactions in Patients) Foundation.

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FOREWORD

This is TRIP's Hemovigilance Report 2021. First of all, I would like to extend my sincere thanks to you all for making this overview of the transfusion chain possible, not only through your reports but also through other broad participation, for example on our advisory boards or on the clinical day.

Although, in a strict sense, hemovigilance should also describe the chain from donor to product delivery to the hospitals, the current focus 'from hospital laboratory to patient' will be clear. It is true that, of the approximately 500,000 transfusions that are annually performed in the Netherlands, some 1,000 to 2,000 cause transfusion reactions, and of these, fortunately, only 10-15% are more serious (severity grade 2 or higher). However, adverse reactions are always unexpected and impressive, and they hit extra hard, because the affected patients are already seriously ill; after all, only the sicker patients receive transfusions.

Learning from such adverse effects can only be done by analysing them as aggregate data collected throughout the country. Only in this way can we detect trends and prevent avoidable adverse effects. Of the 119 more serious adverse events with possible or higher imputability reported in 2021, 32% involve cases of transfusion-associated – and thus essentially avoidable – circulatory overload. Five patients even had a grade 4 adverse reaction. This percentage is comparable to 2020, and performing a restrictive, slower transfusion especially in cardio-renally compromised and already overfilled patients is paramount.

Following on from the 'COVID-dominated year 2020', 2021 might be more a year of 'business as usual', but there is also time to think again about the future of hemovigilance. In this respect, the decrease in transfusion reactions in 2021 compared to 2020 and 2019 could be real, but in such a case, underreporting should also be factored in. The Dutch voluntary reporting system has proven to be as good as mandatory reporting systems.

However, continued and even increasing enthusiasm for reporting certainly also depends on what reporting and TRIP give back to all of you. For me personally, the lessons from the case histories and incidents described in detail – essentially the canary in the coal mine, warning of the risk of avoidable transfusion reactions – are perhaps the most valuable. Precisely with regard to those avoidable adverse reactions, in addition to analysing 'what went wrong', we should perhaps focus more on where exactly 'things are going best' and 'how this is achieved'. We do not pay attention to it yet (!), but such benchmarking and 'best practice' analyses could also reduce the number of returned and/or destroyed blood components, the percentage of transfused O - RBCs, and the percentage of 'non-restrictively administered blood components'. So there are plenty of opportunities to improve the transfusion chain through aggregation of quality indicators that are available to all, feasible and highly relevant to all. TRIP looks forward to opportunities to discuss this with you in the coming year.

Prof Jaap Jan Zwaginga,
Chairman of TRIP Foundation

1 MAIN 2021 FINDINGS

1.1 Hemovigilance in 2021

In 2021, a total of 1279 reports were submitted to TRIP before the closing date of this report. These included 1152 reports of reactions and 145 reports of adverse events (incidents), with 18 reports describing a combination of an incident and reaction. The numbers of transfusion reactions show a decrease in allergic reactions compared to previous years, with the switch to PAS-E preservative in platelet concentrates possibly playing a role. A lower number of reports were registered as 'other reactions', reactions that cannot be classified in any of the regular categories. Incident reports were also lower than in 2019 and 2020, which can be partly explained by the conclusion of the blood group discrepancy project, which called for additional attention to reporting incidents. As in previous years, reports were received regarding the administration of units to the wrong recipients, this year resulting in two non-fatal acute hemolytic transfusion reactions.

The absolute number of reports is lower than in 2020 due not only to the aforementioned decreases but also to the policy that, as from 2021, TRIP will only register reports of new allo-antibodies in cases where there is an error or incident, a situation in which the national recommendations for optimal matching to prevent antibody formation could not be met, or when a transfusion reaction has occurred. This policy change by TRIP was made because, for several years all hospitals have been registering new antibodies in the TRIX registry.

The numbers of reports should be seen in relation to numbers of units distributed and transfused (Figures 1 and 2). A similar number of red blood cell and platelet concentrates were distributed in 2021 as in 2020. TRIP did not receive distribution figures for Omniplasma® in 2021 from Prothya Biosolutions, which was formed in 2021 by integration of Sanquin Plasma Products and Plasma Industries Belgium. This report therefore uses the numbers of units administered reported by the hospitals. The number of reported transfusion reactions (excluding reports of new antibody formation) is 2.27 per 1000 blood components compared to an average of 2.52 in 2016-2020, and the number of severe reactions is 0.23 per 1000 blood components (2016-2020: 0.24).

In 2021, one serious report of posttransfusion bacteremia, which showed *Bacillus cereus* in both the patient's blood culture and the culture of the residual blood component, was probably a case of transfusion-transmitted bacterial infection (TTBI). This infection probably contributed to the patient's death. There were no reports of viral transmissions. The reports indicate a very low incidence of infections transmitted by blood transfusion: 1 in about 489,000 units transfused.

As in other years, the participation of hospitals in hemovigilance is high, 80 out of 82 transfusing hospitals (98%) provided information. Besides hospitals, there are eight designated institutions in the Netherlands that can independently request and administer blood components; information was received from all eight institutions.

Intensified monitoring is required when introducing new (labile) blood components and when changing production methods, such as the transition to the PAS-E storage solution for platelet concentrates or the validation of non-DEHP blood bags. TRIP has a facilitating role here, sharing anonymized information about reports received with Sanquin under specific agreements. No reports have so far been registered for Fitrix® (two-component fibrin glue) or serum eye drops which have been prepared from donor blood and distributed by Sanquin since 2017 and 2019, respectively.

In conclusion, this annual report shows that, under the difficult circumstances of the corona pandemic, the level of transfusion safety is similar to previous years.

1.2 Recommendations

Recommendations	Who?
Strengthen post-authorization monitoring of new blood components by facilitating routes for reporting and supporting hemovigilance professionals in the additional tasks, including conducting clinical research. This also applies to products not applied through transfusion such as serum eye drops.	Sanquin; TRIP
Pay continual attention to the risk of respiratory transfusion reactions when prescribing, administering and monitoring transfusion-dependent patients and, in the event of a reaction, ensure adequate reporting and analysis to promote transfusion safety.	Nurses, physicians and hemovigilance professionals

1.3 Follow-up to previous recommendations

1 Reactions that may be related to donor -specific causes or component quality, for instance with a suspicion of TRALI, should immediately be reported to both TRIP and Sanquin.(Recommendation in TRIP Report Hemovigilance 2019 and 2020.)
Development: In 2021, one report with suspicion of TRALI was reported to Sanquin and subsequently not to TRIP. However, this turned out to be a report in which the initial suspicion was clinically adjusted (possible TACO, imputability unlikely), and therefore there was no missing TRALI case in the TRIP registration.

2 Ensuring that staff remain competent and capable of requesting and administering blood components, both in clinical settings and outside the hospital. (Recommendation in TRIP Report Hemovigilance 2020.)
Development: The recommendation stemmed from concerns about low numbers of transfusions in private clinics licensed to receive and administer blood transfusions to their patients (licensed institutions). In 2021/2022, TRIP, in collaboration with the hospitals, surveyed practices related to another category of transfusions outside hospitals, viz. scheduled transfusions outside the hospital. The findings were presented at the NVB-TRIP symposium and show that in the majority of cases nurses are present throughout the transfusion process. However, there is still insufficient clarity on maintaining competences of nurses working for organizations that administer small numbers of transfusions.

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2 OVERVIEW OF 2021 HEMOVIGILANCE DATA

2.1 Overview of 2021 hemovigilance data in comparison with previous years

Of the 1279 reports received by TRIP before the closing date of this report, 1152 concerned reactions. A total of 145 incidents were reported, with 18 reports describing a combination of an incident and a reaction.

TRIP records reports of transfusion reactions and incidents in all types of labile blood components, as well as SD plasma (Omniplasma®, see Section 2.3). Definitions of incident types, transfusion reactions, severity and imputability can be found at http://www.tripnet.nl under 'hemovigilance' and definitions as well as in the relevant chapters of this report. As TRIX has been implemented in all hospitals, as of 2021, TRIP will only register the formation of new antibodies if there are particular abnormalities or circumstances. This refers to incidents, such as incorrect blood component transfused, and reactions, such as acute hemolytic reactions. As might be expected, this report contains fewer reports of 'new allo-antibody formation'.

Two labile blood components (prepared from small pools of donor units) have been supplied by Sanquin for several years now and are not among the 'classic' blood components for transfusion. Fitrix® is a fibrin glue made of two components (cryoprecipitate and thrombin, frozen) from donor blood for local administration on wounds. Serum eye drops are prepared as a 50% preparation from small pools of male AB donor blood. Reports on these products are in principle registered by TRIP and are important because of the need for intensive monitoring of these newly authorized products. No reports on these products have been received to date.

Reported data are presented in the following tables and figures:

* *Additional online tables can be accessed through hyperlink*

Table 1 Reported incidents, 2017-2021

Incident	2017	2018*	2019*	2020*	2021*	No. of hospitals with reports in 2021
Incorrect blood component transfused	44	41	42	44	26	18
Near miss	31	35	70	41	29	15
Other incident	72	94	87	100	74	22
Calculated risk situation	6	11	17	8	8	6
Total[$]	**167**	**196**	**236**	**203**	**145**	**37**

* *All reported incidents have been included, including those that were registered as an additional category with a reaction.*
[$] *This includes look-back reports and the reporting category or additional reporting category of 'bacterial contamination of product' (8 in 2021), see Chapter 3.3*

Table 2 Reported transfusion reactions, 2017-2021

Reaction	2017	2018*	2019*	2020*	2021*	Severity grade ≥2[$]	No. of hospitals with reports in 2021
Post-transfusion bacteremia/sepsis	73	72	84	74	56	12	30
Post-transfusion viral infection	1	0	0	0	0	0	0
TRALI	6	4	6	2	1	1	1
Transfusion-associated circulatory overload	106	134	91	112	101	38	40
Transfusion-associated dyspnea	7	5	4	8	5	1	5
Anaphylactic reaction	69	58	25	46	20	7	13
Other allergic reaction	127	134	104	86	91	4	32
Acute hemolytic TR	16	16	16	15	9	6	7
Delayed hemolytic transfusion reaction	5	4	3	6	5	2	4
DHTR as additional category	*3*	*1*	*4*	*7*	*2*		*2*
New allo-antibody formation	672	654	724	598	5	0	5
Non-hemolytic TR	358	360	317	304	299	15	67
Mild non-hemolytic febrile reaction	319	327	284	298	323	1	61
Other reaction	259	288	257	330	237	32	59
Other categories of TR[#]	3	0	3	0	0	0	0
Total TR	**2021**	**2056**	**1917**	**1819**	**1152**	**119**	**75**
Total severity grade ≥2[$]	**121**	**121**	**104**	**140**	**119**		
Total reports	**2183**	**2198**	**2112**	**2081**	**1279**		

* *All reported incidents have been included, including those that were registered as an additional category.*
[$] *Imputability definite, probable or possible.*
[#] *Concerns reports of post-transfusion purpura, other post-transfusion infection or hemosiderosis.*

Table 3 Reports per type of blood component in 2021

Type of blood component (BC)	Units distributed in 2021	Units administered in 2021*	No. of reports		Reports per 1000 BCs	
			All	Serious[$]	All	Serious[$]
Red blood cell concentrate	402003	388386	1033	77	2.66	0.19
Platelet concentrate	52827	51669	150	22	2.90	0.42
Fresh frozen plasma	2487	736	1	0	1.36	0.00
SD plasma[#]		47861	9	3	0.19	0.06
Fitrix® fibrin glue	30	29	0		0.00	
Serum eye drops	1085	262	0		0.00	
Anti-COVID-19 plasma[**]	322	525	18	3		
Blood management techniques			0			
Other blood components			0			
Combination[‡]			39	14		
Not specified			29			
Total	**458754**	**489468**	**1279**	**119**	**2.53[&]**	**0.24[&]**

* *Data received from 80/82 hospitals (98%). One of the 82 contact addresses of hospitals was not included in 2020 due to unclear status.*
[$] *Imputability definite, probable, possible.*
[#] *SD=solvent-detergent treated plasma; Omniplasma® in the Netherlands, only units transfused are reported because the manufacturer declined making distribution data available.*
[**] *Units transfused can include COVID-19 study units of fresh frozen plasma unit in which presence of COVID-19 antibodies was unknown to treatment team; this was also the case for a small number of the reported reactions (see 2.4).*
[‡] *See Section 3.4; one report related to combinations concerned an adverse reaction after transfusion of cell saver blood followed by Omniplasma® ; combinations of labile blood components with SD plasma are also included here.*
[&] *Reports in relation to total units of red blood cell concentrates, platelet concentrates, fresh frozen plasma, and SD plasma units transfused..*

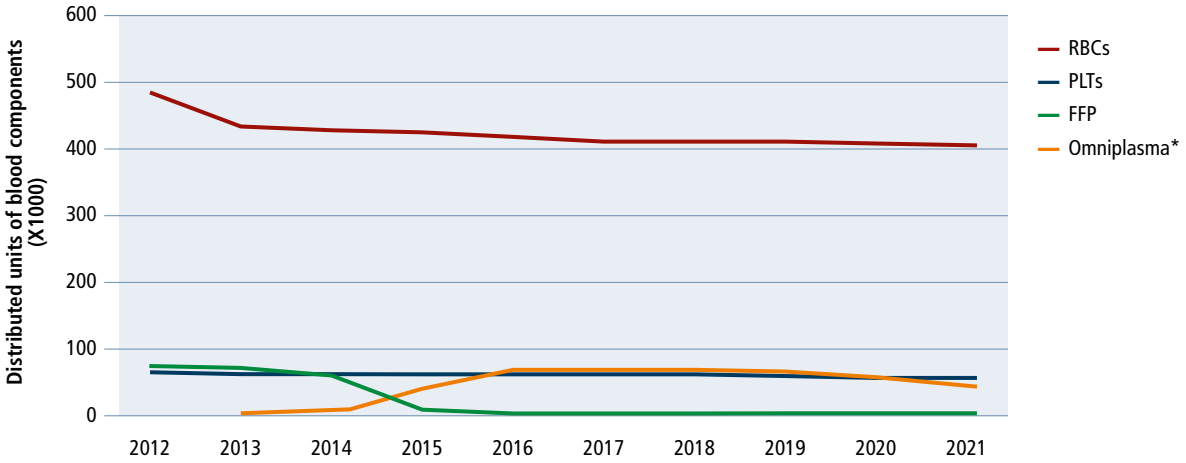

Figure 1 Distributed units of blood components, 2012-2021

* *For SD plasma (Omniplasma®), the distributed units are reported in 2013-2015 because of the roll-out phase; the distributed units in 2021 are reported because the manufacturer declinedmaking distribution data available.*

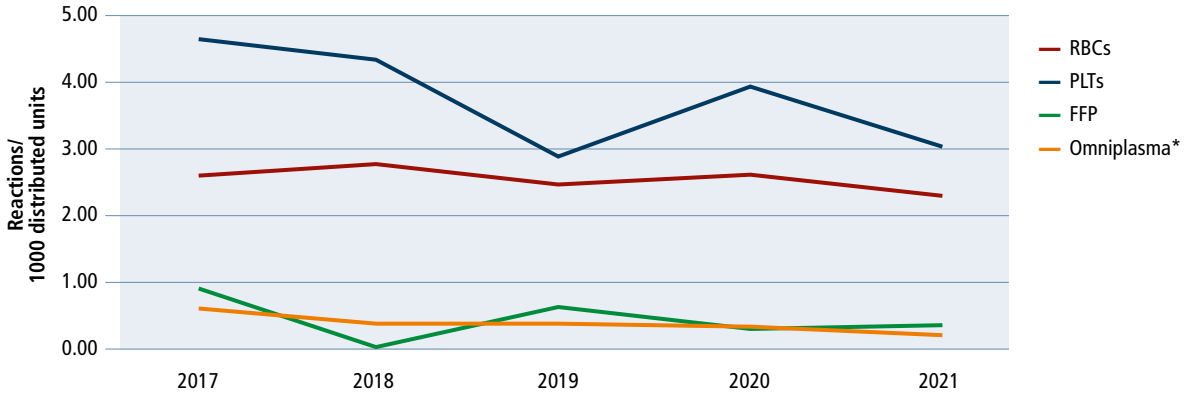

Figure 2 Transfusion reactions per type of blood component, 2017-2021

Included are all transfusion reactions with the exception of new allo-antibody formation.
** For SD plasma (Omniplasma®), only units actually transfused are reported in 2021 because the manufacturer refrains from making distribution data available.*
The graph shows transfusion reactions (all imputabilities) excluding new antibodies, with reactions in a combination of blood component types attributed proportionally to the respective types (i.e. a reaction in a patient who received both platelets and red blood cells is counted as 0.5 reaction with platelets and 0.5 reaction with red blood cells, etc.).

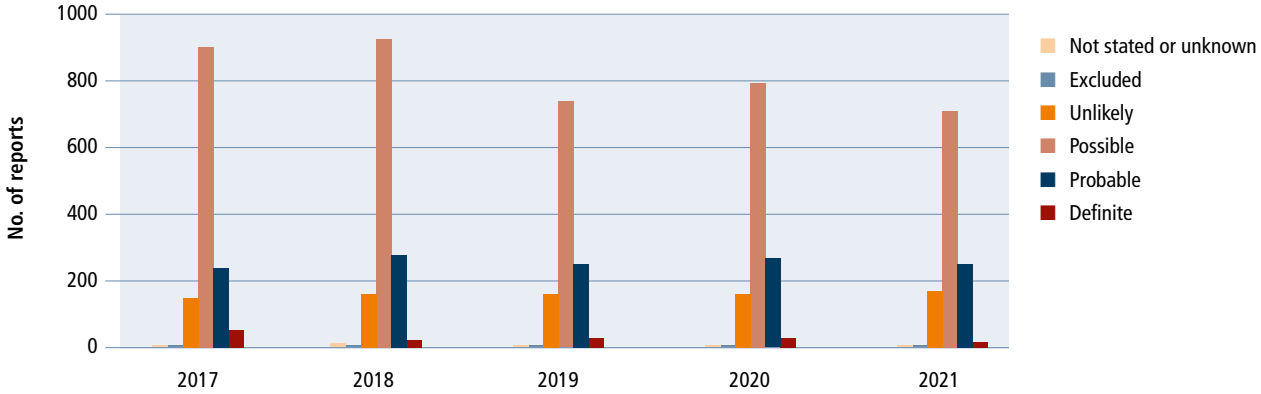

Figure 3 Imputability of the transfusion reactions, 2017-2021

Included are all transfusion reactions with the exception of new allo-antibody formation.

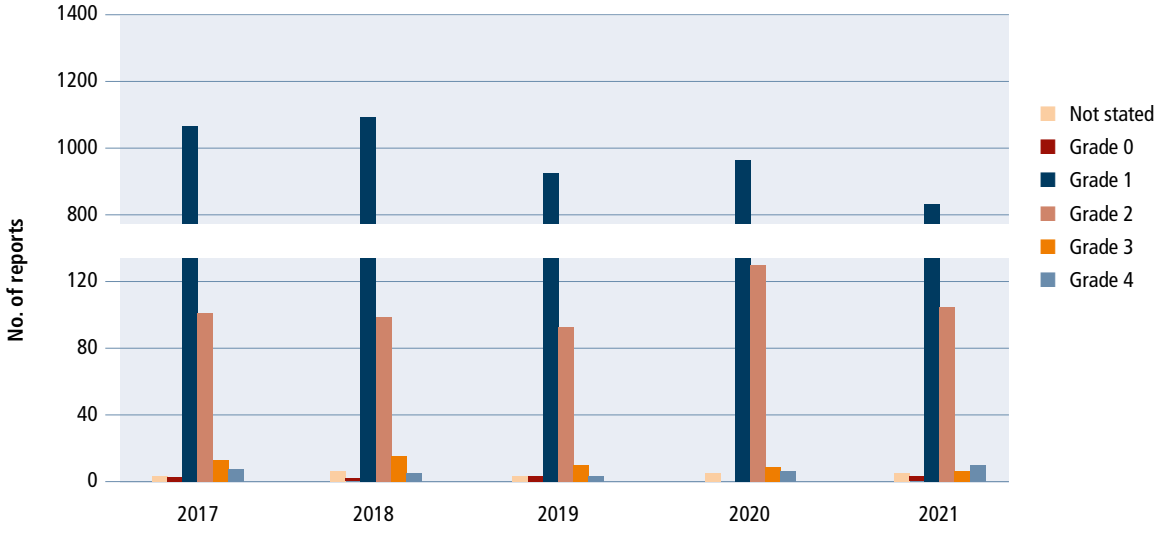

Figure 4 Severity of transfusion reactions (imputability definite, probable, possible), 2017-2021

Included are all transfusion reactions with the exception of new allo-antibody formation.

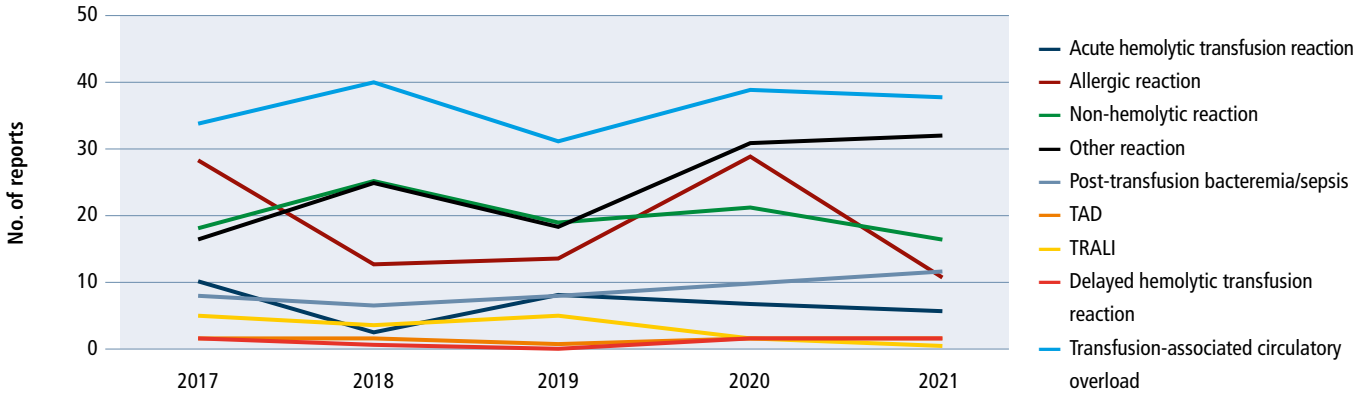

Figure 5 Serious transfusion reactions (imputability definite, probable, possible), 2017-2021

Table 4 Severity grade 4 reports in 2021

Reaction	Blood component	Sex age group	Imputability	Symptomatology
Post-transfusion bacteremia/sepsis	PLT	F, 70-79	Definite	Patient with thrombo- and leukopenia; fever and increasing malaise more than 3 hours after start of Tf; deterioration despite meropenem. B. cereus in blood culture and unit.
Delayed hemolytic transfusion reaction	RBC & PLT	M, 20-29	Probable	Tf during surgery in patient with sickle cell anemia and allo-antibodies; after 1 week hemolysis, profound anemia and hypoxia, deterioration despite corticoids, IVIg, eculizumab and most compatible Tf.
Transfusion-associated circulatory (TACO)	RBC	M, 80-89	Probable	Iron-deficiency anemia, Hb 4.9 mmol/L during rectal blood loss. Pt with atrial fibrillation overload and valve disease, oedema in lower legs and slight crepitation in lung bases. Slow transfusion, however saturation drop after 2 hrs, further deterioration despite diuretics.
Other reaction	RBC	F, 30-39	Possible	Patient with AML, thrombopenia with HLA antibodies, pulmonary abnormalities on CT and need for oxygen and platelets, scheduled bronchoscopy, deterioration 1 hr after Tf, no improvement after therapy.
Other reaction	COVID-19 convalescent plasma	F, 80-89j	Possible	Multiple myeloma, admission indication: oxygen requirement with COVID-19 pneumonia; 5.5 hrs after start Tf: confusion, respiratory insufficiency, no recovery with diuretics and increase in oxygen support. Non-ICU policy had been agreed beforehand.
Incorrect blood component transfused and acute hemolytic transfusion reaction	RBC	M, 70-79	Possible	See Section 3.1
Transfusion-associated circulatory overload	RBC	M, 80-84	Possible	Rectal blood loss, non-STEMI; dyspnea during first EC, improved with nitroglycerine and 15L oxygen via non-rebreathing mask; after 2nd EC: respiratory deterioration, no improvement with furosemide.
Transfusion-associated circulatory overload	RBC	M, 70-79	Possible	Hb 3.1 mmol/L, iron deficiency, ischemic ECG abnormalities, aortic valve stenosis; TACO symptoms and tightness in the chest after 30ml, deterioration despite therapy.
Transfusion-associated circulatory overload	RBC	M, 70-79	Possible	Septic patient after surgery for aneurysm with complicated course; Hb 4.7 mmol/L for which 2 ECs; heart failure before Tf already, deterioration with saturation drop despite medication incl. furosemide.
Transfusion-associated circulatory overload	RBC	M, 90-99	Possible	Patient with cardiovascular risk profile, drop in oxygen saturation to 60% after 100ml; BNP and vital parameter course consistent with TACO, remained oxygen dependent despite some diuresis; death within 1 week with comfort policy.
Other reaction	RBC	M, 80-89	Unlikely	Hemodynamically unstable patient, hypotension 30 min after start of Tf.
Other reaction	COVID-19 convalescent plasma	M, 70-79	Unlikely	Respiratory deterioration in patient with COVID-19.
Post-transfusion	RBC	F, 80-89	Unlikely	Patient with CML in blast crisis showed a rise in temperature, respiratory deterioration and pos. blood culture at the end of the Tf.

Table 5 Severity grade 4 reports (imputability definite, probable or possible), 2012-2021

Reaction	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Totaal
Acute hemolytic TR	1			2						1	4
Other reaction	1	2		1	1	1	2			2	10
Post-transfusion bacteremia/sepsis	1		2							1	4
Post-transfusion purpura			1								1
TRALI	1			2	1	1	1	1			7
Delayed hemolytic TR										1	1
Tf-associated circulatory overload (TACO)	1		3	2	3	6	2	2	6	5	30
Total	**5**	**2**	**6**	**7**	**5**	**8**	**5**	**3**	**6**	**10**	**57**

2.2 Late reports from 2020

After the deadline for submitting reports for reporting year 2020, 98 reports were still received from that year (Table 6). The reports came from six hospitals. These late reports have been incorporated into the figures and tables in this report for the respective reporting year. Among the late reports were four serious reactions with severity grade 2; one anaphylactic reaction (imputability possible), two non-hemolytic transfusion reactions (imputabilities unlikely and possible) and one other reaction (imputability possible).

Table 6 Late reports from 2020 in the 2021 report (N = 98)

Reporting category	Severity grade		
	Not specified or 0	1	2
Acute hemolytic transfusion reaction		2	
Anaphylactic reaction		1	1
Other allergic reaction		7	
Mild non-hemolytic febrile reaction		15	
Non-hemolytic transfusion reaction	1	16	2
New allo-antibody formation	30		
Other incident	6		
Other reaction		12	1
Post-transfusion bacteremia/sepsis		1	
Incorrect blood component transfused	2		
Transfusion-associated circulatory overload (TACO)		1	

2.3 Overview of mandatory reports to the European Commission

Every year, TRIP compiles an overview for the European Commission of mandatory reporting of serious reactions and events in the transfusion chain. The 'Common Approach' prepared by the European Commission together with member states provides the following guidance:

— Reactions with imputability definite, probable or possible should reported; late reports from the previous year should be included.
— Reactions that occurred after administration of an incorrect blood component or other incident are taken into account in the relevant category.
— Hemolytic reactions are subdivided into immunological (ABO), immunological (not ABO) and non-immunological (e.g.run-in along with hypotonic fluid).
— Reactions to SD plasma only are not counted due to the legally different route.
— On the form, reports are subdivided according to type of blood component transfused.

The febrile reactions listed in the table were assessed as serious due to (prolongation of) hospitalization (Table 7).

Table 7 Number and imputability of reports of severity grade 2 or higher in 2021 or late reports from 2020, in accordance with EU overview

Severity grade	2 of 3			4		
Imputability	Definite	Probable	Possible	Probable	Possible	Total
Hemolytic transfusion reaction (ABO)	1				1	2
Hemolytic transfusion reaction (immunological, not ABO)		3		1		4
Hemolytic transfusion reaction (not immunological)		1	1			2
Allergic reaction	1	7	2			10
Febrile reaction		6	11			17
Other reaction		8	22		2	32
TAD		1				1
Transfusion transmission of bacterial infection				1		1
TRALI						0
Transfusion-associated circulatory overload (TACO)	2	20	11	1	4	38
Total	**4**	**46**	**47**	**3**	**7**	**107**

2.4 Application of COVID-19 convalescent plasma (CCP) and reports

Plasma collected from patients who have recovered from infection with SARS coronavirus type 2, COVID-19, and whose levels of anti-COVID-19 antibodies are sufficiently high, may potentially be effective in the treatment of some patients with COVID-19. Studies on this have been carried out both in the Netherlands and internationally, some of which have already been published. In 2021, CCP was applied in the CoV-Early study and sometimes on a compassionate use basis. Table 8 presents the reactions reported to TRIP. Five reports of non-serious allergic reactions indicated that they were study products, for which, because of the study, it was not known whether COVID-19 convalescent plasma or control unit FFP without anti-COVID-19 antibodies was involved. In the reported transfusion figures, hospitals were not always able to distinguish between study units with COVID-19 antibodies and control units (fresh frozen plasma). Thus, the number of reports per 1000 units of CCP distributed cannot be reliably calculated. Furthermore, study participation leads to more observed reactions due to active monitoring.

Table 8 Reports regarding CCP in this hemovigilance report (N = 19*)

	Reactions
Reports (concern reactions only)	19*
Reporting hospitals	9, 1-7 reports per hospital
Reactions with imputability definite, probable, possible	17 (further analysed below)
Median age (IQR)	Median 57 years (52-63 years)
Sex	4 female (24%)
	13 male (76%)
Severity	2 serious (one grade 4, one grade 2)
Imputability	Definite 1 (6%)
	Probable 8 (47%)
	Possible 8 (47%)
Reaction	Number (% of total)
Anaphylactic reaction	2 (11.8%)
Other allergic reaction	10 (58.8%)
Non-hemolytic transfusion reaction	2 (11.8%)
Other reaction	3 (17.6%)

* *Including 1 late report from 2020: grade 1 other reaction, possible*

Impact of pandemic on reports in 2021

Unlike in 2020 (dip in reports in April to June), there was no clear impact on the number of reports received during the peaks of hospital occupancy by corona patients (Figure 6).

During the reporting year, patients with COVID-19 also received regular blood components. Was the pattern of reported reactions different in that patient group than in patients who did not have the disease? The reports to TRIP do not always provide information on the underlying clinical picture. A total of 22 patients were reported to have COVID-19, in addition to the 18 patients who received CCP. (In the 2020 report: 26; in the late reports, two reactions and one other incident). The types of reports are summarized in Table 9 and Figure 7. There was no difference in blood component type, reaction severity or sex.

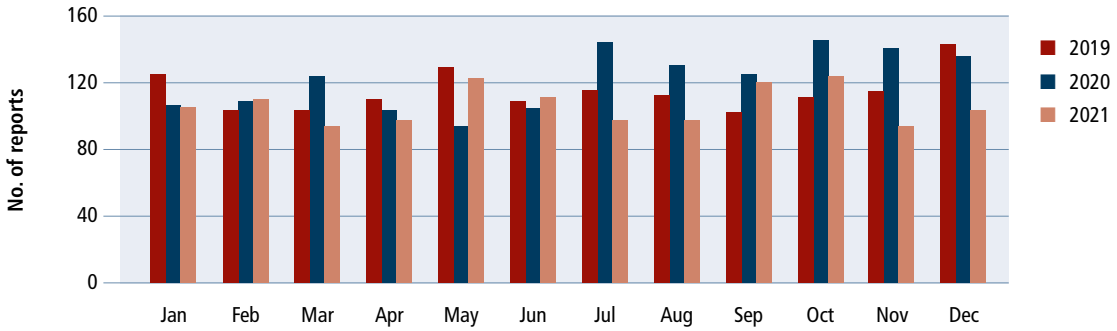

Figure 6 Reports to TRIP of transfusion reactions and incidents per month in 2019-2021

Included are all transfusion reactions with the exception of new allo-antibody formation.

Table 9 Reports concerning patients reported as having COVID-19 compared with patients where this was not the case (excluding patients treated with CCP)

Report	Patients with COVID-19 (Total 22 reports)			Patients without COVID or unknown (Total 1239 reports)		
Incidents (incl. those registered as additional category with reactions)	1 (other incident)		4,5%	144		11,6%
Total reactions, excluding new allo-antibody formation	21 reactions (see Figure 7)			1126 reactions (see Figure 7)		
Reactions with imputability definite, probable or possible analysed further below	16 reactions (see Figure 7)			933 reactions (see Figure 7)		
Sex (%)	Female	8	50%	Female	442	47%
	Male	8	50%	Male	491	53%
Severity	Grade 4	0		Grade 4	9	1,0%
	Grade 3	0		Grade 3	6	0,6%
	Grade 2	2	12,5%	Grade 2	101	11%
	Grade 1	14	87%	Grade 1	825	87%
Imputability	Definite	0	0%	Definite	16	1,7%
	Probable	3	19%	Probable	233	25%
	Possible	13	81%	Possible	684	73%
Type of blood component	RBC	14	88%	RBC	767	82%
	PLT	1	6,2%	PLT	127	13,6%
				SD plasma	6	0,6%
	Combi	1	6,2%	FFP	1	0,1%
				Combis	32	3,4%

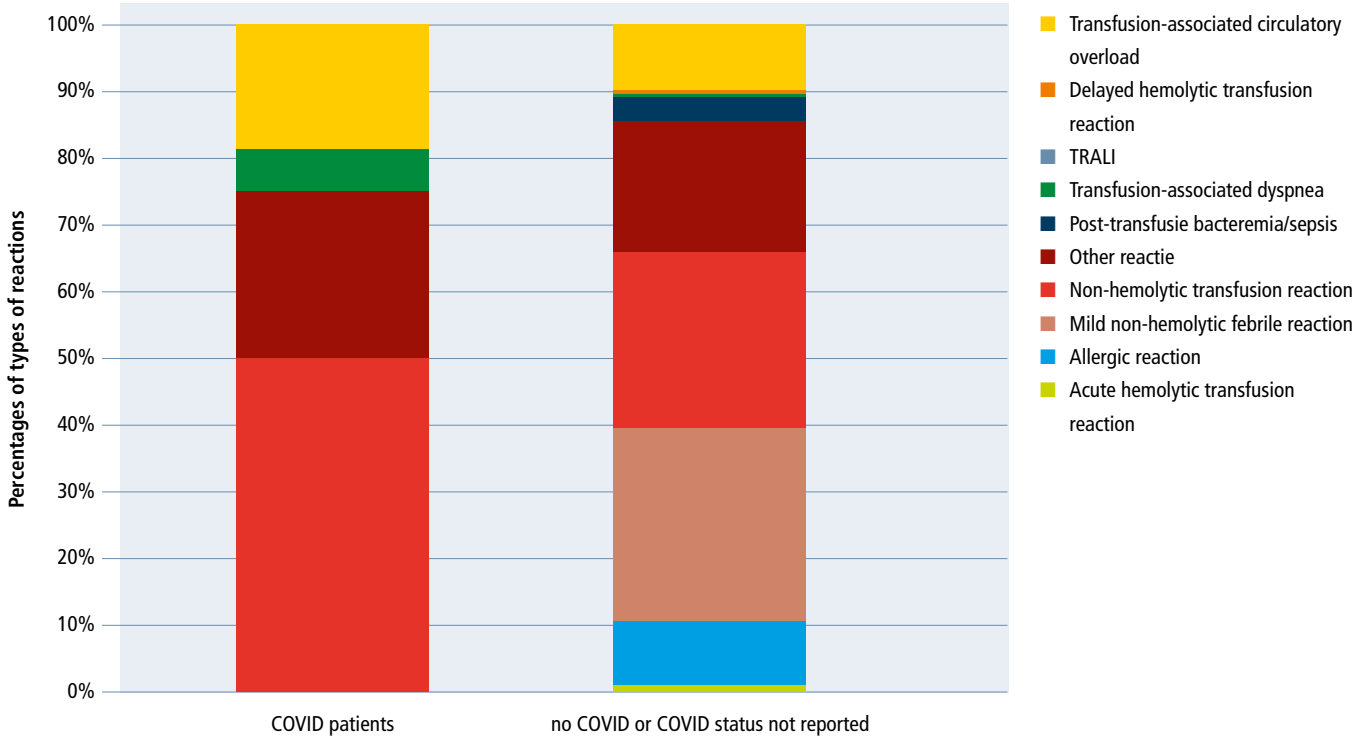

Figure 7 Reported reactions (imputability definite, probable or possible) in patients with COVID-19 (N = 16 reactions) and in patients without COVID-19 or with COVID-19 status not reported (N = 933) in 2021
Reports associated with COVID-19 convalescent plasma transfusion are not included.

3 DISCUSSION OF REPORTS PER CATEGORY

3.1 Incidents in the transfusion chain

Incorrect blood component transfused (IBCT)
All cases in which the patient was transfused with a blood component that did not meet all the requirements of a suitable component for that recipient or that was intended for another patient.

26 reports, decrease compared to last year (41%)
Number of reporting hospitals: 18 (22%), range 1-7 reports per hospital.

- Three x a reaction was detected first and then discovered to have been preceded by an IBCT and once an incident was detected and followed by the reaction (in all 2x AHTR, 1x other reaction and 1x TACO).
- Nine times preventive policy (irregular antibodies, Parvo B19 negative and after transplantation) was not followed, which led to the formation of a new antibody (anti-Kpa, Anti-E and anti-K) in two cases.
- Out of the five ABO risk cases, four cases involved a mix-up of blood bags, patients or patient data. Twice it resulted in an acute hemolytic transfusion reaction (see below).
- In three of the seven irregular antibodies prevention policy (irrab prevention) risk cases, TRIX information or information from third parties on antibodies (detected elsewhere) was present, which could have prevented the error or detected a previously made error, but the information was missed when processing the request.

TRIP risk classification
As in previous years, TRIP assessed all the reports of incorrect blood component transfused to establish which was the worst potential risk to which a patient was exposed through transfusion of an incorrect blood component. The risk classification used by TRIP is described on the website (www.tripnet.nl: hemovigilance/forms under explanation).

In 2021, damage/quality constitutes the largest risk group (10). In this group, units were disconnected by the patients and then reconnected to the same cannula (2) or the units ran subcutaneously and were transferred to a new cannula (6). Once the unit was found not to be connected to the IV cannula at the start of transfusion and after discovery it was reconnected (for five minutes) and once a new spike was inserted into an already punctured unit.

Disconnecting and transferring a transfusion line on to a new IV is not described as such in the blood transfusion policy guidelines. However, there is a recommendation under the module 'Medication and blood transfusion through the same IV' that says 'The transfusion should not be interrupted for more than 2 hours and the transfusion line should never be temporarily disconnected due to the risk of bacterial contamination'. It is up to the hospital how this recommendation is followed when continuing transfusion using a new infusion cannula.

Twice a reaction was reported in addition to the incident, namely TACO and other reaction with saturation drop, however there was no suspicion that the reaction was related to the incident.

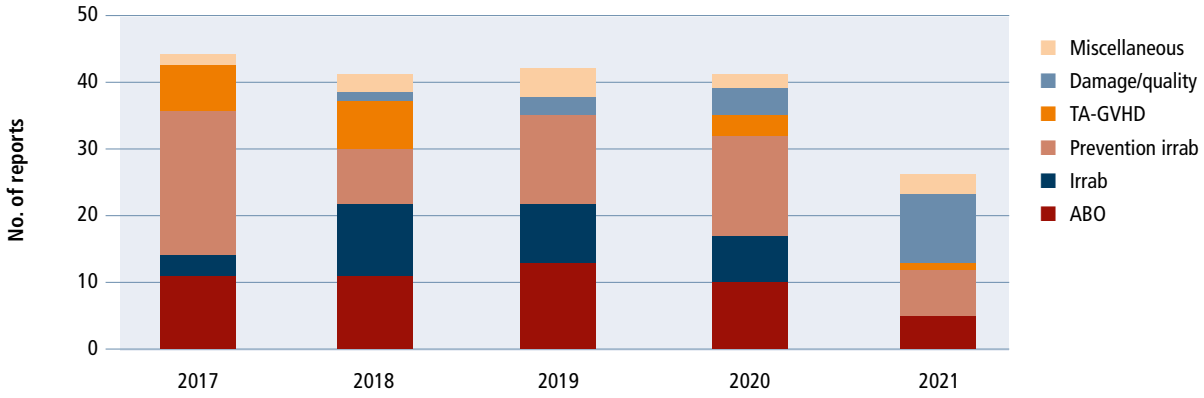

Figure 8 Incorrect blood component transfused 2017-2021 subdivided according to risk group

ABO = Risk of an ABO incompatible blood transfusion
Irrab = Risk of an irregular antibody incompatible transfusion
Prevention irrab = Risk of alloimmunization due to non-compliance with preventive selection criteria
TA-GVHD = Risk of transfusion-associated graft versus host disease (after transfusion of a non-irradiated blood component)
Damage = Administration of a blood bag that has been spiked before.
Miscellaneous = Administering a 0-negative uncrossed unit that was not selected for the patient concerned (other; 1 in 2021) or erroneously not complying with a preventive policy other than the above (B19-safe, after bone marrow transplantation; 2 in 2021)

Incorrect blood component transfused (ABO risk) with acute hemolytic reaction

- Nurse 1 gives nurse 2 a patient sticker and asks them to collect an RBC unit for patient X (O pos). Unit is collected and checked by nurse 2 and laboratory technician when issued. Nurse 1 connects the RBC unit to patient X. After 20 minutes, patient develops symptoms of an acute hemolytic reaction: temperature rise ≥2°C, chills, drop in oxygen saturation (96% to 91%), hypertension (111/75 to 177/106), tachycardia and low back pain; patient is transferred to ICU. It turned out that the unit was blood group B pos and was not intended for patient X, as the wrong patient sticker was given to nurse 2. Within a day the patient recovered fully from the transfusion reaction.
- Two reserved RBC units are ready for two patients (X: O pos and Y: A pos) in the blood refrigerator at the recovery unit. Patient X is hemodynamically unstable and will go to ICU. At the recovery unit, it is decided to administer an RBC unit. As digital identification fails, a decision is taken not to use the digital system and to administer the unit anyway. When the RBC unit for patient Y is sent back to the laboratory, the mix-up is discovered. More than an hour after completion of the transfusion, hemolysis parameters are taken and compared with pre-transfusion values: Hb decreased from 5.6 to 5.1 mmol/ml; LDH was not measurable due to hemolysis; increase in bilirubin (21 to 50 µmol/l) and a decrease in haptoglobin (2.78 to 1.67 g/l). Patient X dies the same day from their underlying condition.

- One TA-GVHD risk case involved a patien, who had an indication for irradiated RBC units in connection with the treatment their underlying disease. This was not known to hospital B, as this information from hospital A had not yet been communicated. During transfusion, the parent asked if it was an irradiated unit, and the transfusion was discontinued. The incident did not lead to a reaction in the patient.
- One miscellaneous risk case involved an RBC unit (O neg, without patient sticker), which was issued for a neonate. The neonate was found not to be in need of transfusion and the unit was to be collected. However, this was found to have been administered to the mother in the meantime (emergency situation). The case was considered an IBCT, as the unit was initially not selected for the mother and the lab had not yet been informed that it concerned an emergency situation.

More descriptions of 2021 Incorrect blood component transfused cases (in Dutch) can be found at www.tripnet.nl in the Report of the Month section:
Report of the Month 2022 - 3: Pneumatic tube transportt
Report of the Month 2022 - 4: IV fails during transfusion

Near miss (NM)

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.

29 reports, number of reporting hospitals 15 (18%), 1-9 reports per hospital

- 17 near misses were detected in time because of blood group discrepancy.
- In 12 cases, the incidents were prevented by conscious and unconscious alertness of laboratory staff, nurses or patient (5; 6; 1).
- In 19 incidents, it concerned a (probable) mix-up of patients or patient data, labels, blood samples, blood components, test materials, etc.
- One case concerned the finding on internal checks that there were 14 instances of blood group discrepancies, the cause of which was not clear. These were all reported back to the relevant departments (see Table 10: Other).
- In 24 reports, there was a potential ABO risk.

Table 10 Near miss reporting

Occurrence*	N	Manner of discovery	N	Description	N
Request	3	Blood group discrepancy	1	— Mix-up of labels on request form	1
		Alertness of lab technician	2	— Whilst matching parent-child data, technician discovers the unit is linked to the wrong child	1
				— Indication for irradiated units, which was not known to the requester	1
Investigation prior to transfusion (request)	16	Blood group discrepancy	13	— Mix-up of tubes/labels/patient data at the laboratory	3
				— Mix-up of tubes/labels/patients at the department	9
				— Lab system shows results automatically before the outcomes are known	1
		(unconscious) alertness of departmental staff	2	— Mix-up of tubes/labels in clinical department	2
		(unconscious) alertness of laboratory staff	1	— Mix-up of tubes/labels in clinical department	1
Investigation for indication	3	(unconscious) alertness of departmental staff	2	— Mix-up of tubes/labels in clinical department	2
		Blood group discrepancy	1	— Patient is linked to the wrong patient data in the EHR in clinical department	1
Processing of request	3	(unconscious) alertness of laboratory staff	2	— TRIX data is initially clicked away, but seen later after all	1
				— The results of the penultimate cross-matching are mistaken for recent cross-matching. This is discovered when recent results are released	1
		(unconscious) alertness of patient	1	— Patient speaks of recent stem cell transplant. This had not yet been reported in TRIX by the transplant centre	1
Other$	4	(unconscious) alertness of departmental staff	2	— Patient is linked to the wrong patient data in the EHR on the ward due to identification error	1
				— Red blood cell unit was collected with wrong patient sticker/data	1
		Blood group discrepancy	2	— In the past, patient had another person registered at the hospital under his/her name	1
				— Internal audit finds that 14 reports of blood group discrepancy were made during the year	1

** Place in the transfusion chain where the incident occurred. See website TRIP*
$ Other = Hospital outside transfusion chain (1); administration (1); situation outside hospital and transfusion chain (1); unknown (1)

More descriptions of 2021 Near Miss cases (in Dutch) can be found at www.tripnet.nl in the Report of the Month section:
Report of the month 2022-1: Two tasks

Other incident

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.

74 reports, number of reporting hosp[itals: 22 (27%), range 1-25 reports per hospital.

- Four cases where a reaction was also observed (1x other reaction; 1x NHTR, 1x TACO, 1x post-transfusion bacteremia/sepsis).
- 43 units were (partially) lost, of which 24 were not 'errors' (see below).

Classification by type of error

In order to better identify the types of errors and what the consequences are for the blood components, TRIP, unlike previous years, distinguished the cases in the other incident category by type of error and also whether or not a blood component was lost. As reported above, more than half of the incidents involved led to loss or partial loss of the blood component. They fall into the 'lost' group when the blood bag could not be returned to stock or could not be fully transfused because of an incident. The classification by type of error gives a biased view because some of the lost blood units were classified as transfusion errors and 'other cases' . Among 'other cases', most do not involve a real error, but 'things that happen'. Examples include accidentally puncturing a bag, a unit running subcutaneously despite correct checks, or patients consciously or unconsciously disconnecting the unit. Sometimes similar incidents are reported by hospitals as transfusion errors. This included 11 reports in 2021 that, on closer inspection, were not transfusion errors (no indication of any errors during transfusion). Better classification in future years should lead to a better picture of to what extent incidents/errors lead to the loss of blood components.

Table 11 Reports of other incidents in 2021, subdivided according to type of error

Type of error	N	Lost (or partially lost)	N	Description	N
Administrative error	1	No	1	— Blood group of twin brother was listed under patient's name	1
Assessment error	11	Yes	7	— Assessment by doctor/indication revised during transfusion or initially incorrect	4
				— Units collected/spiked/requested too soon	2
				— Transfusion discontinued without consulting laboratory	1
		No	4	— Non-crossmatched blood transfused without indication	1
				— Reaction was reported too late, which prevented ancillary investigation	2
				— Delay of transfusion	1
Storage error	2	Yes	2	— Unit was stored for too long/wrongly at the department	2
Blood sampling error	6	Yes	1	— Initial indication based on diluted blood sample	1
		No	5	— Transfusion based on Hb determination from diluted blood sample*	4
				— Transfusion based on erroneous Hb determination (cause unclear)	1
Communication error	2	No	2	— Delay of transfusion because patient's admission for transfusion was not reported	1
				— Full unit given while otherwise prescribed	1
Donor or Product error	1	No	1	— Clot in infusion system after transfusion	1
Identification error	1	No	1	— Transfusion and associated test requested for the wrong patient, detected before sampling	1
Procedural error in lab	3	Yes	1	— Units not issued in coolbag due to urgency	1
		No	2	— Erroneous result not checked but forwarded automatically	1
				— Units not prepared	1
Technical error	4	Yes	1	— Infusion system does not work as required	1
		No	3	— Lab system shows a result automatically before the actual results are known	3
Transfusion error	25	Yes	15	— Infusion/infusion pump was not checked (infusion does not run; runs subcutaneously; not disconnected)	3
				— Unit was not spiked properly or ran subcutaneously despite checks	8
				— Unclear whether checks were performed and unit ran subcutaneously	4
		No	10	— Infusion/infusion pump possibly not checked (incorrect infusion rate; infusion does not run or runs subcutaneously)	4
				— Unit runs subcutaneously despite checks	3
				— Unclear whether checks were performed and unit ran subcutaneously	2
				— Unit interrupted for too long (> 2 hours)	1
Other	18	Yes	16	— Checks were done, but unit ran subcutaneously or patient became suddenly unwell (2) or unknown reason for not starting (1)	7
				— Unit consciously or unconsciously disconnected by patient	2
				— Unit accidentally punctured when spiking (leak)	7
		No	2	— Transitional period for introduction of new transfusion protocol	1
				— Unit was sent to wrong hospital, transfusion delayed	1

** One transfusion reaction reported caused unit to be discontinued; not because of incident*

Several 2021 Other incident cases have been described in the Report of the Month series on the TRIP website (in Dutch): Examples:
Report of the Month 2022 - 4: IV fails during transfusion
Report of the Month 2022 - 5: Unnecessary transfusion because of blood sampling errors

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.

Eight reports, number of reporting hospitals: 6 (7%), range 1-3 reports per hospital

- All eight reports concerned emergency situations.
- None of the situations resulted in a reaction.

Table 12 Calculated risk cases in 2021

Case description	Number
— Circumstances made it impossible to take a patient's known irregular antibodies into account	3
— Patient with massive blood loss received non-crossmatched units	2
— Emergency situation during which 0 neg red blood cell units are given and mistakenly 0 plasma. According to protocol, this should have been AB plasma. Because of emergency, administered anyway under the doctor's ultimate responsibility; unit turned out to be ABO compatible later on.	1
— In an emergency situation, a spike shoots out from a red blood cell unit into the nurse's hand. The spike is disconnected and a new spike is placed in the same unit; this was done because of the high transfusion requirement at the time.	1
— Emergency surgery in neonate, during which cross-matching tests with the mother were all positive. Neonate was infused with a unit of red blood cells that were weakly positive on cross-matching. Cross-matching test afterwards (unit/neonate) was negative.	1

Conclusion Incidents in the transfusion chain

For incorrect blood component transfused, a decrease from 41 to 26 reports is seen. A decreasing trend is seen in all risk groups, but is most noticeable in irrab risk while the decreasing trend of recent years is continued for ABO risk. The largest risk group is damage/quality (10/26). In this group, units were transferred to a new infusion cannula after the infusion needle was broken or the unit was detached from the infusion cannula and reconnected. In the blood transfusion guidelines, there is no conclusive advice on this and it is up to hospital policy whether reconnecting a unit is permitted. If this is not the case, it is a case of IBCT.

Near misses also saw a decrease from 41 to 29 reports. This is partly explained by the closing of the blood group discrepancy project, which called for extra attention to reporting these events in 2019 and 2020. This year, the table is organized according to the place in the chain where the incident almost occurred and then based on how the incident was discovered. Most near misses arise on the ward (19/29) and they are most often discovered because of a blood group discrepancy (17/29). In previous years too, a near miss was most often detected due to blood group discrepancy.

This year, other incidents have been grouped by type of error. Most take place during transfusion or assessment by the doctor or nursing staff. In 43 of the 74 events, a unit was partially or completely lost, with 24 cases not involving an error. These cases involved the unit running subcutaneously despite scheduled controls, accidentally puncturing a bag, or the patient disconnecting a unit.

All reports of calculated risk situations concern emergency situations.

3.2 Non-infectious transfusion complications

Respiratory transfusion reactions

Transfusion-associated circulatory overload (TACO)

Respiratory problems during or within 12 hours after blood 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 www.tripnet.nl.

A New or worsening respiratory problems
B Features of new or worsening pulmonary oedema based on:
  – Physical examination, and/or
  – Chest X-ray or other imaging of the chest
C Relevant changes in the cardiovascular system
D Findings suggestive of relevant changes in fluid balance
E Biomarker result(s) consistent with TACO

101 reports of TACO reported by 40 hospitals (49%), with a range of 1 to 10 reports per hospital.
- 95 (94%) reports of TACO with imputability definite, probable or possible.

TACO definite, probable, possible:
- 9.8% of all transfusion reactions, 32% of all serious reactions.
- Five reactions with severity grade 4, in which the patient died after transfusion.
- Because of additional findings that did not fit with TACO, TACO was recorded four times with another type of reaction in the additional category. Four times TACO was reported as an additional category with another type of transfusion reaction and twice in combination with an unrelated incident.

Table 13 Overview of TACO reports with imputability definite, probable or possible

	TACO N = 95
Sex (%)	
Female	53 (56%)
Male	42 (44%)
Age (years)	76 (66-83)
Time interval between start of transfusion and occurrence of transfusion reaction (hrs:min)	3:45 (1:48-6:47)
Severity grade of transfusion reaction (%)	
Severity grade 1	54 (57%)
Severity grade 2	30 (32%)
Severity grade 3	3 (3%)
Severity grade 4	5 (5%)
Unknown/not assessable	3 (3%)
Imputability (%)	
Definite	2 (2%)
Probable	53 (56%)
Possible	40 (42%)

Values are expressed as numbers (%) or medians (IQR)

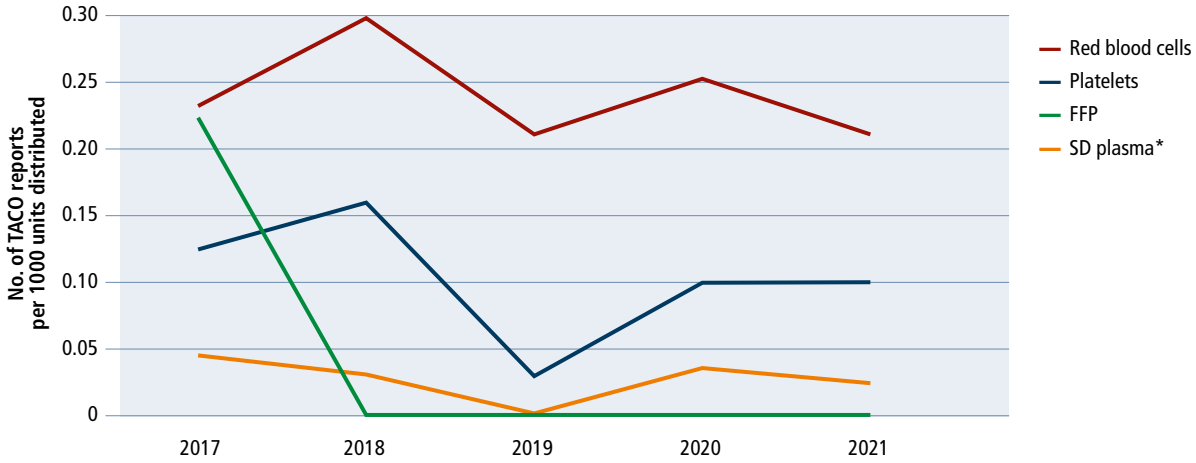

Figure 9 Number of TACO reports with imputability definite, probable, possible per 1000 blood components distributed

Reactions when given combinations of blood components are proportionally attributed to the respective blood component types
**In the absence of distribution figures for SD plasma in 2021, reactions are shown per 1000 units transfused.*

Transfusion-related acute lung injury (TRALI)

Symptoms of acute lung injury such as dyspnea and hypoxia, occurring during or within 6 hours of transfusion, chest X-ray shows bilateral pulmonary infiltrates.

- In 2021, one TRALI report was received, with imputability likely and severity grade 3. The main features were dyspnea and tachycardia. TRALI occurred after administration of units of SD plasma.
- TRALI was recorded once as an additional category together with the transfusion reaction TACO. In addition to symptoms appropriate to TACO, it was concluded on the basis of imaging that elements of TRALI were also present. The new international TRALI definition allows for a combination of these two reactions. One reaction was reported to Sanquin as a suspected TRALI, but is not known as such to TRIP. After the initial suspicion, Sanquin judged that there was no TRALI and no further investigation was performed.

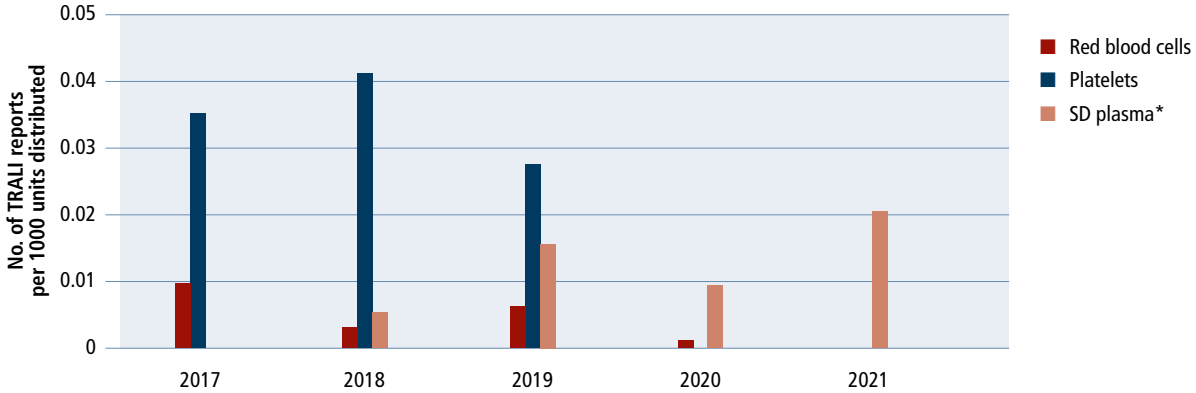

Figure 10 Number of TRALI reports with imputability definite, probable or possible per 1000 blood components distributed.

Reactions associated with combinations of blood components are proportionally attributed to the respective blood component types.
** In the absence of distribution figures for SD plasma in 2021, reactions are shown per 1000 units transfused.*

Transfusion-associated dyspnoea (TAD)

Shortness of breath or hypoxia during or within 24 hours of transfusion, and the criteria for TRALI, TACO 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.

- Five reports of TAD, all with definite, probabe or possible imputability.
- Because of additional findings that did not fit TAD, TAD was registered once with a different type of reaction in the additional category.
- In all cases symptoms of dyspnea occurred within 6 hours of termination of the transfusion.

Table 14 Overview of TAD reports with imputability definite, probable or possible

	TAD N = 5
Sex (%)	
Female	2 (40%)
Male	3 (60%)
Age (years)	78 (56-91)
Time interval between start of transfusion and occurrence of transfusion reaction (hrs:min)	01:07 (0:20-04:39)
Severity grade of transfusion reaction (%)	
Severity grade 1	4 (80%)
Severity grade 2	1 (20%)
Imputability (%)	
Probable	1 (20%)
Possible	4 (80%)

Values are expressed in numbers (%) or medians (ranges)

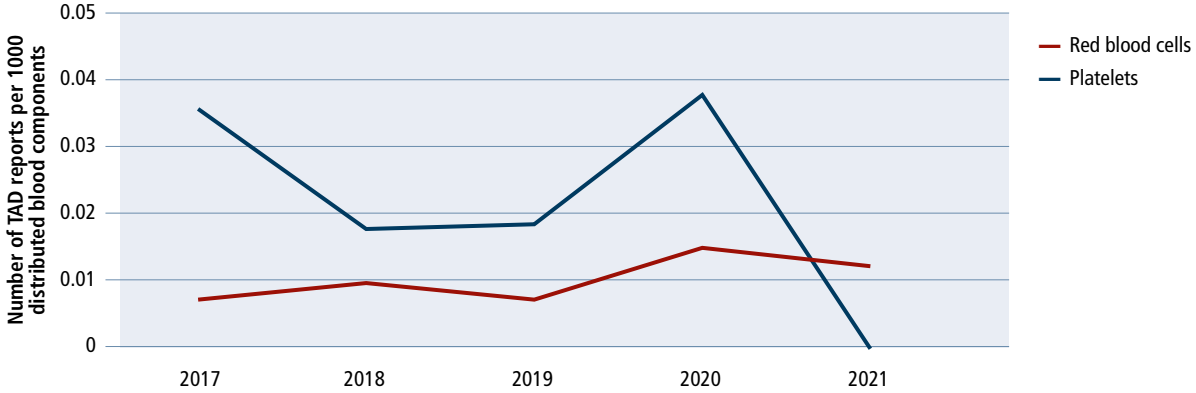

Figure 11 Number of TAD reports with imputability definite, probable or possible per 1000 blood components distributed.

Reactions associated with combinations of blood components have been proportionally attributed to the respective blood component types.

Case description
A 91-year-old woman with a history of renal insufficiency is dialysis-dependent. She is prescribed one RBC unit at a Hb of 4.8 mmol/L. One hour after administration of the full RBC unit, she becomes dyspneic and her respiratory rate increases from 20/minute to 36/minute. Her O2 saturation drops to 89%. There is also hypertension. On physical examination, no crepitations are heard and there is no oedema. The chest X-ray shows a normal cardiovascular picture. NT-proBNP is not determined. The patient is administered 1L O2 /min and recovers rapidly. No furosemide was given.
There is insufficient evidence for a diagnosis of circulatory overload and chest X-ray with a normal cardiovascular picture also ruled out TRALI. As there is no other explanation for the dyspnea, such as underlying pathology, this case is classified as TAD.

Distinction between respiratory transfusion reactions

TACO, TRALI and TAD are transfusion reactions consisting of respiratory complications. These respiratory transfusion reactions are often difficult to distinguish from each other and from underlying pathology, especially in ventilated patients1. Adequate diagnosis is important because optimal treatment varies between reactions. Definitions have been formulated and revised for TACO2 and TRALI3 , with the revised international TRALI definition by Vlaar and colleagues awaiting validation for use in hemovigilance.

Pulmonary oedema is present in both TACO and TRALI. Although the pathophysiology of respiratory transfusion reactions is complex, it is assumed that the oedema in TACO is related to increased hydrostatic pressure in the pulmonary vascular bed and that in TRALI there is increased capillary permeability with a non-cardiogenic, inflammatory etiology4 . Based on this difference in underlying mechanism, a number of factors contribute to the distinction between TACO and TRALI.

Increased hydrostatic pressure in TACO is associated with left atrial overload. Left atrial overload can be examined non-invasively by echocardiography. In TRALI, there is no left atrial hypertension, or left atrial overload is not the main cause of hypoxemia. To support the diagnosis of TACO, B-type natriuretic peptide (BNP) or NT-pro B-type natriuretic peptide (NT-proBNP) may be determined. These natriuretic peptides are released during stretch of the myocardium due to increased pressure. In the general patient population, normal levels exclude TACO and a 1.5-fold increase relative to pre-transfusion values is indicative of TACO5 . Natriuretic peptides are less useful as biomarkers in critically ill patients. Severely ill patients may already have elevated natriuretic peptides due to hypoxic vasoconstriction prior to transfusion, and an increase may be explained by other conditions within this population.

A chest X-ray shows bilateral pulmonary oedema in both TRALI and TACO cases. A dilated vascular pedicle and increased cardiothoracic ratio are indications of TACO6 . However, these findings are aspecific and do not rule out TRALI. In addition, several clinical variables are used to verify the role of TACO in the development of respiratory problems, such as cardiovascular function and fluid balance.

The revised international TRALI definition describes the possibility of the combination classification TRALI/ TACO, where both transfusion reactions occur simultaneously. Even when the available data do not enable a distinction to be made between the two reactions, this category can be used.

TAD is a pulmonary complication during or after transfusion that cannot be classified as TACO or TRALI, and is not related to the patient's underlying pathology. The pathophysiology of TAD is unknown and there are no specific clinical features for this diagnosis. It is possible that some of the TAD cases involve a milder or atypical form of TACO or TRALI, with the underlying mechanisms of these conditions playing a role in the development of the respiratory problem.is internationale standaardisatie van definities en datacollectie noodzakelijk. Een internationaal samenwerkingsverband waarin TRIP is vertegenwoordigd, werkt aan een uniform meldingsformulier voor respiratoire transfusiereacties, ter harmonisatie van de beoordeling van dit type reacties.

To better understand the pathophysiology and diagnostics of respiratory transfusion reactions, international standardisation of definitions and data collection is necessary. An international partnership in which TRIP is represented is working on a uniform reporting form for respiratory transfusion reactions to harmonize the assessment of this type of reaction.

Conclusion on respiratory transfusion reactions

Respiratory transfusion reactions are the group of transfusion reactions with the highest mortality and morbidity. Again this year, TACO is the transfusion reaction with the highest number of serious reports. The categorization of pulmonary complications after transfusion is complex. Monitoring, identification and analysis of respiratory transfusion reactions are necessary to better understand the pathophysiology and risk factors, and promote transfusion safety.

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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 ³20 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.

Nine reports (all relating to red blood cell transfusion, see Table 15)

- One reaction with severity grade 3 due to ABO incompatible transfusion, discontinued on occurrence of symptoms 20 minutes after start of transfusion (IBCT is the registered reporting category and the case is described in the relevant section).
- One reaction with severity grade 4 associated with an ABO incompatible transfusion, however it is unlikely that the patient died as a result of the incompatible unit (IBCT is the registered reporting category and the case is described in the relevant section).
- Three reports concern patients with previously undetected irregular antibodies, in two cases the blood components were antigen positive for the antibody elicited in the patient. In the third report, irregular antibodies had not (yet) been investigated. Two reports have new allo-antibody formation recorded as an additional category.
- Two reports involved patients with increased signs of hemolysis without serological incompatibility.

Table 15 Acute hemolytic transfusion reactions (AHTRs) in 2021

	AHTR N = 9
Sex (%)	
Female	5 (56%)
Male	4 (44%)
Age (years)	58 (51-77)
Time interval between start of transfusion and occurrence of transfusion reaction (hrs:min)*	1:58 uur (0:50-2:10)
Severity grade of transfusion reaction (%)	
Severity grade 1	3 (33%)
Severity grade 2	4 (45%)
Severity grade 3	1 (11%)
Severity grade 4	1 (11%)
Imputability (%)	
Definite	1 (11%)
Probable	3 (33%)
Possible	5 (56%)
Cause	
Patient with previously undetected irregular antibodies (anti-Wra and anti-Jkb)	3
Patient with pre-transfusion hemolysis with possible exacerbation during transfusion	1
Patient with (chronic) autoimmune hemolytic anemia	1
Transfusion of – ABO incompatible unit (reporting category: IBCT)	2
No clear cause has been demonstrated in patient	2

* *Two cases with unclear interval due to multiple transfusions*

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.

- Seven reports (all relating to RBCs; in one case platelets were also given).
- Five cases have the reporting category DHTR, two of which have new antibody formation (once anti-Jk(a) and once anti-E, anti-c and anti-K) in additional category.
- Two cases of 'new allo-antibody formation' with DHTR recorded as an aditional category (once anti-E and once anti-E and anti-S).

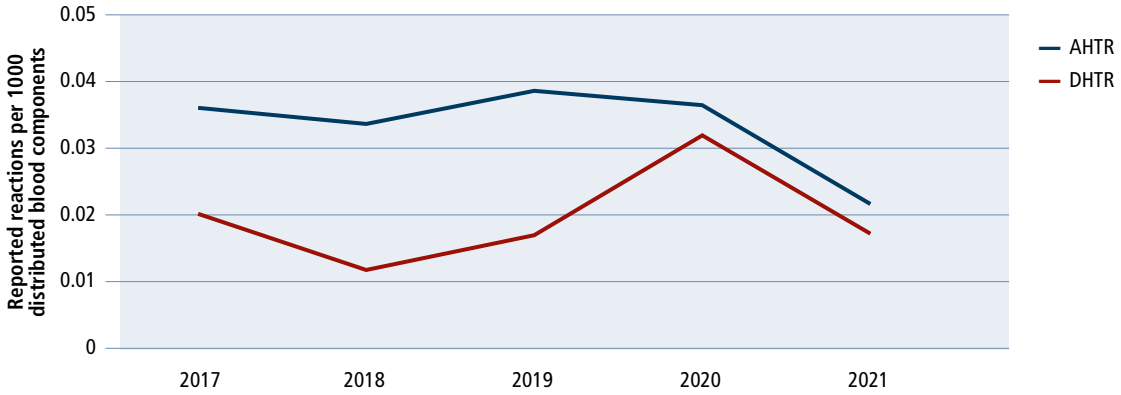

Figure 12 Reports of acute and delayed hemolytic transfusion reactions relative to the number of red blood cell concentrates distributed, 2017-2021

Figure shows reports with definite, probable or possible imputability, including hemolytic reactions associated with incorrect blood component transfused or demonstration of new allo-antibody formation.

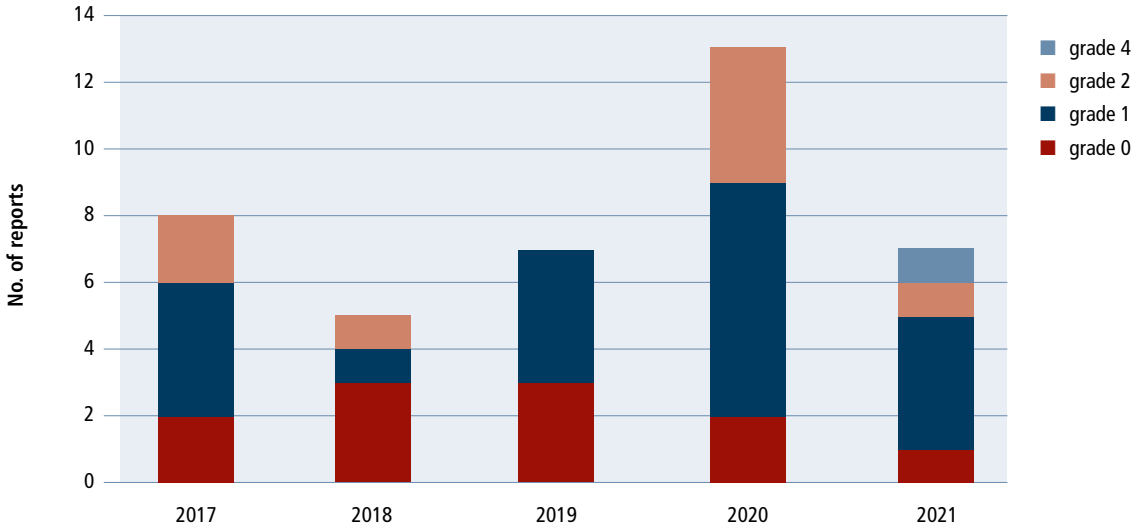

Figure 13 Severity of reports of delayed hemolytic transfusion reactions (main/additional category; imputability definite, probable or possible), 2017-2021

New allo-antibody formation against blood cell antigens

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). As of 2021 cases should only be reported to TRIP in special circumstances, e.g. in combination with a transfusion reaction, (suspected) hemolysis and/or antibody formation due to incorrect blood product selection.

- 14 reports, of which 11 were reported relating to a reaction (5x other reaction; 2x AHTR; 4x DHTR) and two new antibody formations were reported relating to an adverse event (incorrect blood component transplanted). See relevant chapters.
- Four cases report first new antibody formation (then 2x DHTR; 1x IBCT and once antibody formation after platelet transfusion) and one new antibody formation after an adverse event.
- One case concerns antibody formation during transfusion of platelets; female patient < 45 yrs, who formed anti-c and anti-E.

Anaphylactic reaction and other allergic reaction 2021

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 ≥ 20 mm 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 of 111 reports of anaphylactic and other allergic reaction (20 and 91, respectively), compared to 132 reports (46 and 86, respectively) including late reports from 2020.
- Number of reporting hospitals 37 (45%), range 1-19 reports per hospital.
- Number of reports with imputability definite, probable, possible is 102 (92%), anaphylactic reaction 16 (80%) and other allergic reaction 86 (95%).
- The number of reports (N = 11) of severe allergic reactions (grade 2 and higher) with imputability definite, probable or possible is at the 2019 level after a higher number in 2020 (N = 28) and remains within the range of fluctuations in recent years (Figure 15).
- Eight times another allergic reaction was reported as an additional category, 1x for mild NHFR, 1x for non-hemolytic transfusion reaction, 1x for post-transfusion bacteremia/sepsis, 5x for other reaction.
- Information on the reports is summarized in Table 16.

Table 16 Overview of reports of anaphylactic reactions and other allergic reactions with imputability definite, probable or possible

	Anaphylactic reaction (N = 16)	Other allergic reaction (N = 86)
Sex (%)		
Female	3 (19%)	36 (42%)
Male	13 (81%)	50 (58%)
Age (years)	51 (27,5-71)	46 (21-59)
Severity grade (%)		
Severity grade 1	9 (56%)	82 (95%)
Severity grade 2	7 (44%)	4 (5%)
Imputability (%)		
Definite	1 (6%)	5 (6%)
Probable	11 (69%)	47 (55%)
Possible	4 (25%)	34 (40%)
Product (%)		
Red blood cell concentrate	5 (31%)	25 (29%)
Platelet concentrate	7 (44%)	44 (51%)
FFP		1 (1%)
SD plasma		3 (3%)
COVID-19 convalescent plasma	2 (13%)	10 (12%)
Combination of blood components	2 (13%)	3 (3%)
Symptoms (number of reports)		
Itching, urticaria, redness	12	86
Glottal oedema	3	
Increase in temperature 1-2 ˚C	2	9
Increase in temperature ≥ 2 ˚C	2	
Chills	4	2
Unresponsive / less responsive	2	
Dyspnea / decrease in oxygen saturation	11	
Stridor / bronchospasm	5	
Hypotension	9 (5× ≥ 20 mm Hg syst en/of diast)	
Nausea/vomiting/diarrhoea	2	3

Values are expressed in numbers (%) or medians (IQR)

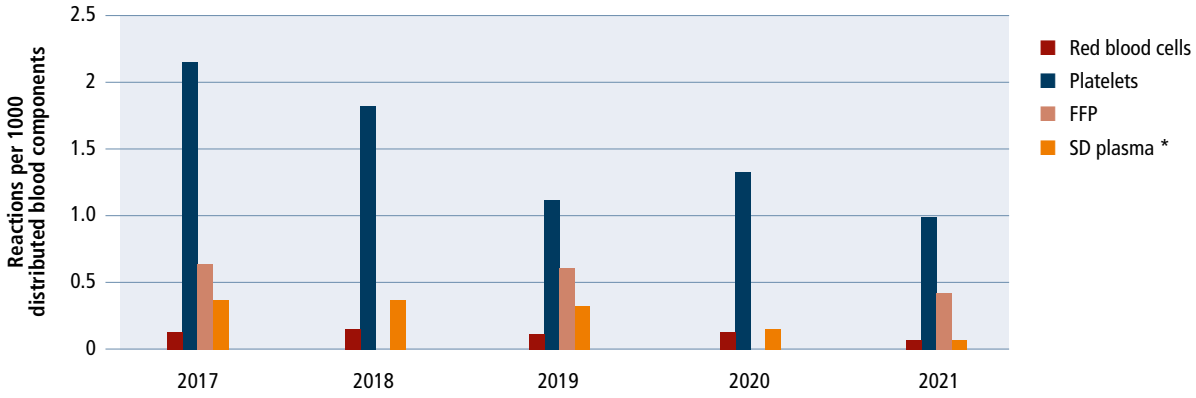

Figure 14 Number of allergic reactions with definite, probable or possible imputability per 1000 blood components distributed

Reactions associated with combinations of blood components have been proportionally attributed to the respective blood component types.
**In the absence of distribution figures for SD plasma in 2021, reactions are shown per 1000 units transfused.*

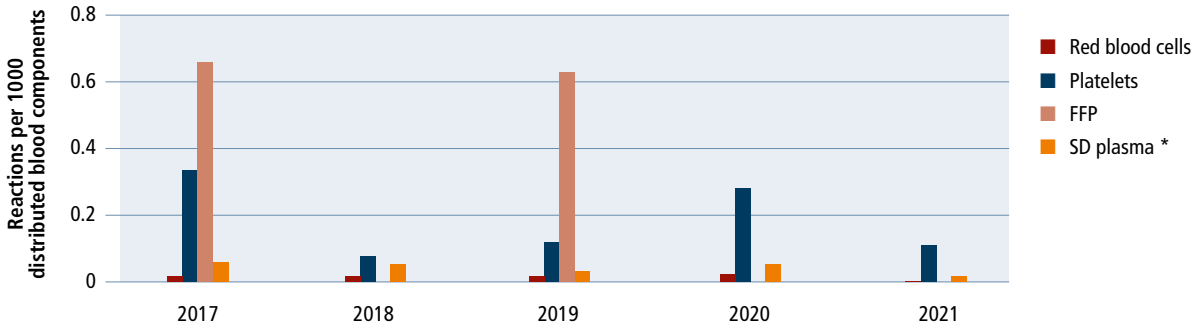

Figure 15 Number of severe allergic reactions with definite, probable or possible imputability per 1000 blood components distributed

Reactions associated with combinations of blood components have been proportionally attributed to the respective blood component types.
**In the absence of distribution figures for SD plasma in 2021, reactions are shown per 1000 units transfused.*

Conclusion on allergic reactions

There appears to be a decreasing trend in the incidence of allergic reactions, particularly visible for reactions associated with platelet transfusions. For reactions after RBC transfusion, the incidence rates are stable. An apparent peak in 2020 for the number of severe allergic reactions after platelet transfusion is partly explained by five repeated reactions in one patient (see Report of the month 2021-6). The decreasing trend can possibly be partly explained by the introduction of the platelet storage solution PAS-E (platelet additive solution-E) containing acetate, potassium, magnesium and phosphate). Since April 2018, 65% PAS-E with 35% plasma has been used for pooled platelets instead of 100% plasma, and since March 2019 also for apheresis platelets.

Non-hemolytic reactions

Non-hemolytic transfusion reaction (NHTR)

Rise in temperature of ≥ 2oC (with or without rigors/chills) during or in the first two hours after a transfusion, with normalisation within 24 hours after the transfusion, OR rigors/chills within the same time limits, without other relevant symptoms or signs.

Mild non-hemolytic febrile reaction (mild NHFR)

Rise in temperature ≥1°C (<2°C) during or in the first two hours after a transfusion with normalisation within 24 hours after the transfusion, without other relevant symptoms or signs.

Total of 622 reports of non-hemolytic reactions, non-hemolytic transfusion reactions and mild non-hemolytic febrile reactions (299 and 323, respectively), compared to 602 reports (304 and 298, respectively) including late reports from 2020.

- Number of reporting hospitals 70 (85%), range 1-69 reports per hospital
- Number of reports with definite, probable or possible imputability is 524 (84%), NHTR 256 (86%) and mild NHFR 268 (83%).
- The number of reports (N = 16) of severe non-hemolytic reactions (grade 2 or higher) with definite, probable or possible imputability is similar to that in 2020 (N = 21) including late reports.
- Two cases of mild NHFR were reported as an additional category in association with TACO.
- Three times an NHTR was reported in the additional category, once for TACO, once for transfusion-associated dyspnea and once for other reaction.
- Information on the reports is summarized in Table 17.

Table 17 Overview of reports of non-hemolytic reactions with definite, probable or possible imputability

	NHTR (N = 256)	Mild NHFR (N = 268)
Sex (%)		
Female	113 (44%)	125 (47%)
Male	143 (56%)	143 (53%)
Age (years)	66.5 (53-75)	68 (56-77)
Severity grade (%)		
Severity grade 1	241 (94%)	267 (100%)
Severity grade 2	15 (6%)	1 (0%)
Imputability (%)		
Definite	3 (1%)	
Probable	44 (17%)	45 (17%)
Possible	209 (82%)	223 (83%)
Product (%)		
Red blood cell concentrate	212 (83%)	246 (92%)
Platelet concentrate	36 (14%)	13 (5%)
COVID-19 convalescent plasma	2 (1%)	
Combination of blood components	6 (2%)	9 (3%)
Symptoms (number of reports):		
Increase in temperature < 1 ˚C	13	17
Increase in temperature 1-2 ˚C	96	251
Increase in temperature ≥ 2 ˚C	116	
Chills	182	
Tachycardia	38	19
Hypertension	19 (7x ≥ 20 mm Hg syst en/of diast)	9 (6x ≥ 20 mm Hg syst en/of diast)
Hypotension	12 (7x ≥ 20 mm Hg syst en/of diast)	6 (1x ≥ 20 mm Hg syst en/of diast)
Dyspnea/tachypnoea	10	10
Nausea/vomiting/diarrhoea	13	10

Values are expressed in numbers (%) or medians (IQR)

Other reaction

Transfusion reaction which does not fit into the categories above.

237 reports in 2021.
Decrease compared to 2020 (330 including late reports).
Whereas the number of other reactions characterized by dyspnea had increased in 2020, it is lower in 2021 (35 with definite, probable or possible imputability) and more similar to 2019 (23) and 2018 (27).

- The numbers of reactions with hypotension and with hypertension are lower in 2021 than in 2020.
- Since 2010, the other reaction category has been one of the three largest categories of reports with severity grade 2 or higher and definite, probable or possible imputability each year.
- Other reaction was recorded as an additional category for four reported reactions: one mild non-hemolytic febrile reaction indicating fluctuations in blood pressure, two NHTR indicating inadequate yield of a platelet transfusion, and 1 TACO in which a contribution of antibody to low-frequency antigen could not be excluded.

Other reaction: what reactions are they?

If a transfusion reaction is recorded as an other reaction, it should be clear why this category was chosen. For several years TRIP has used a subdivision into certain subgroups (Table 18), which will be explained this year using case histories. However, the breakdown does not provide information on possible (transfusion-related) pathophysiology or points of intervention to reduce risks of other reactions, and research remains necessary.

Table 18 Types of reactions that are registered as other reactions (broken down as in previous TRIP reports)

Type of reaction	2020	2021	2021 Imputability definite, probable	2021 Imputability possible	2021 ≥ gr 2*
Reactions with hypotension	57	51	7	36	1 (10)
Subgroup hypotensive reaction (ISBT)#	14	5	0	4	0 (7)
Reactions with dyspnea	68	41	10	25	11 (6)
Hypertension	31	12	3	8	1 (1)
(possibly) cardiac	19	12	0	9	1 (3)
Did not fully meet TRIP definitions of standard categories	99	64	10	38	7 (5)
Other features	56	57	6	38	11 (5)
Total	**330**	**237**	**36**	**154**	**32 (30)**

* *Imputability definite, probable or possible; number in 2021 (number in 2020)*
\# *For this, systolic blood pressure must be ≤ 80 mm Hg and drop by ≥ 30 mm Hg*

Case description

Reaction with dyspnea: symptoms of dyspnea that led to additional investigation or clinical intervention e.g. by administration of oxygen or nebulization, and/or measured drop in oxygen saturation (≥ 5%) whether or not in combination with an increase in temperature, where the reaction did not meet the criteria of the reporting categories of TRALI, TACO, TAD or allergic reaction.

- Male patient, age group 40-49 years, receives RBC concentrate in day care in one-and-a-half hours after his first chemotherapy treatment for Hodgkin lymphoma; after termination, he has an increased body temperature (before Tf: 36, during reaction: 39.5 °C) and chills, his blood pressure has risen from 107/66 to 160/80. There are dyspnea symptoms and oxygen saturation drops from 99% (before

Tf) to 83%. Clemastine 2mg and paracetamol 1000 mg are administered intravenously, and oxygen is given (5L/min), on which saturation recovers. Blood group serology and hemolysis parameters show no abnormalities, there are no abnormalities on auscultation of the lungs, and chest X-ray shows normal air-filled lungs without increased vascularity. Oxygen support can be tapered in half an hour. Report of other reaction, type with dyspnea, severity grade 2 (due to admission for observation) and imputability possible.

Reactions can also be registered in this subgroup if dyspnea was the most prominent symptom but they cannot be classified as TRALI, TACO or TAD due to a combination of symptoms and/or underlying clinical picture.

Reaction with hypotension: relevant hypotension (e.g. ≥ 20 mm Hg systolic and/or diastolic) whether or not in combination with increase in temperature

- Female patient (age group 60-69 years) with malignancy and profound anemia is given one unit of RBC concentrate which is discontinued after 50 minutes because of hypotension (123/77 to 76/47 mm Hg) without increase in temperature. A switch to 0.9% NaCl is made; after laboratory tests ruling out blood group serological problems, two RBC units are administered without problems. Blood culture and unit culture remained negative. Report of other reaction with hypotension, severity grade 1, imputability possible.

Hypotensive reactions constitute a separate reporting category in some hemovigilance systems. Only a small minority meet the ISBT definition for hypotensive reaction, which requires a drop in systolic blood pressure ≥ 30 mm Hg and ≤ 80 mm Hg. The Advisory Board has advised against introducing a separate reporting category for this, as timely intervention prevents such a drop in BP.

Reaction with hypertension: relevant increase in BP (e.g. ≥ 20 mm Hg systolic and/or diastolic) whether or not in combination with increase in temperature.

- Male patient (age group 80-89 years) with normocytic anemia and Hb 5.9 mmol/L prior to orthopaedic surgery after fall, was scheduled for two RBC units. The first unit was transfused in 4 hrs, followed by increase in BP (103/65 at pulse 121 to 163/94 at pulse 94), headache, nausea and vomiting. After administration of 20 mg furosemide IV, he was stable, blood pressure 145/81; based on his Hb result after transfusion of 6.1 mmol/L the second unit is cancelled.

(Potentially) cardiac: occurrence of symptoms during or immediately after a blood transfusion that are or may be of cardiac origin, such as chest pain, tachycardia or arrhythmia, which were not present at the start of transfusion; whether or not in combination with an increase in temperature.

- Male patient (age group 50-59 years) with a history of atrial fibrillation, RBC unit ordered by pulmonologist (5 weeks after hip surgery) was discontinued after 15 minutes due to pulse acceleration from 78 to 151 per minute without change in temperature or blood pressure; recovery after administration of metoprolol. No additional laboratory investigations performed. Report of other reaction, severity grade 1 with imputability possible.
- Male patient (age group 60-69 years) admitted to gastroenterology department for transfusion for symptomatic anemia without bleeding focus (Hb 4.7 mmol/L), chest tightness during administration of first of two RBC units with stable vital parameters. Cardiology opinion, ECG showed slightly more pronounced repolarization disturbances than before. Symptoms subsided and transfusion was continued. Report of other reaction severity grade 1, imputability possible.

In transfusion reactions which do not fully meet TRIP definitions of standard categories, the most common types are:

— Reactions with an increase in temperature but the temperature does is not normalise within 24 hrs, or it occurs more than 2 hrs after the end of transfusion or the increase was less than 1 degree Celsius; N = 26.
— Reactions with an increase in temperature and a positive blood culture taken within the context of the transfusion reaction, whilst the same bacterial species has previously been found in a blood culture of the patient; N = 17.
— Reactions with an increase in temperature but there was also proven or possible blood group incompatibility, and hemolysis was not demonstrated or plausible; N = 7.

Other symptoms: there were new or worsened symptoms, not fitting a specific type of transfusion reaction and possibly (partly) related to underlying condition; or more than one of the above reasons why a reaction falls outside the definition of the standard category.
Among other things, reduced conscious level or confusion may be a secondary symptom leading to registration as other reaction. This subgroup also includes acute pain reactions, which are distinguished as a separate type of transfusion reaction in some hemovigilance systems. In this group, as well as in the groups of hypertension and dyspnea, there are reports that were suspicious for TACO but showed fewer characteristics required by in the definition or were insufficiently substantiated for reporting in that category. Finally, a new type of transfusion reaction could fall into this subgroup and be reported on.

Conclusion on other reactions

The number of other reactions, after increasing in 2020, is similar to that in 2017 up to and including 2019. The largest groups are reactions with hypotension, reactions with dyspnea and reactions that fell outside the definitions for standard categories for other/multiple reasons. In the group of reactions with dyspnea, there were some reactions that were suspicious for TRALI but were registered as other reactions after expert assessment.

3.3 Infectious transfusion complications

Bacterial problems in blood transfusion

Post-transfusion bacteremia/sepsis

Clinical symptoms of bacteremia/sepsis arising during, directly after or some time subsequent to a blood transfusion, with a relevant positive patient blood culture result; a causal link to a transfused blood 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 in the approved way with laboratory techniques, preferably including typing of the bacterial strain or strains.

Total of 56 reports of post-transfusion bacteremia/sepsis, up from 74 in 2020, including late reports (Table 19). Number of reporting hospitals: 30 (37%), range: 1-8 reports per hospital.

- The number of reports with definite, probable or possible imputability is 34 (61%) (Table 20).
- The number of serious reports of post-transfusion bacteremia/sepsis (grade 2 or higher) with definite, probable or possible imputability is 12, in comparison to 10 in 2020.
- One of the reports of post-transfusion bacteremia/sepsis met the criteria for TTBI in 2021 (Table 21 and Figure 16).
- Eight reports of bacterial contamination of blood component were made: two in conjunction with post-transfusion bacteremia/sepsis, one with mild non-hemolytic febrile reaction, one with a non-hemolytic transfusion reaction, one with an other allergic reaction and two with other reaction. One report involved a positive screening result obtained at the blood bank, a Fusobacterium species was cultured, while the unit of platelets had already been transfused. The patient, who already had an unfavourable prognosis, showed no symptoms of infection, was treated with antibiotics and died two days after transfusion from the underlying pathology.

Table 19 Overview of reports from hospitals relating to bacterial problems, 2017-2021

	2017	2018	2019	2020	2021
Post-transfusion bacteremia/sepsis	72	72	84	74	56
(cases of TTBI, as assessed by experts)	(2)	(1)	(1)	(0)	(1)
Post-transfusion bacteremia/sepsis as additional category (not TTBI)	5	1	0	5	0
Bacterial contamination of blood component (including reports of positive bacteriological screening)*	4	0	1	0	1
Bacterial contamination of blood component (including reports of positive bacterial screening) as additional category	19	11	12	9	7

* *Cases in which the patient exhibited symptoms or experienced adverse consequences, such as postponement of surgery or prophylactic administration of medication*

Table 20 Overview of reports of post-transfusion bacteremia / sepsis with definite, probable or possible imputability.

	Post-transfusion bacteremia/sepsis N = 34
Sex (%)	
Female	10 (29%)
Man	24 (71%)
Age (years)	69 (15-76)
Severity grade (%)	
Severity grade 1	22 (65%)
Severity grade 2	11 (32%)
Severity grade 3	0
Severity grade 4	1 (3%)
Imputability (%)	
Definite	1 (3%)
Probable	3 (9%)
Possible	30 (88%)
Product (%	
Red blood cell concentrate	29 (85%)
Platelet concentrate	4 (12%)
Combination of blood components	1 (3%)
Signs and symptoms (number of reports):	
Increase in temperature 1-2 ˚C	12
Increase in temperature ≥ 2 ˚C	18
Chills	19
Dyspnoa / decrease in oxygen saturation / tachypnoea	9
Hypotension (≥ 20 mm Hg syst and/or diast)	8
Hypertension (≥ 20 mm Hg syst and/or diast)	6
Tachycardia	13

Values are expressed in numbers (%) or medians (IQR)

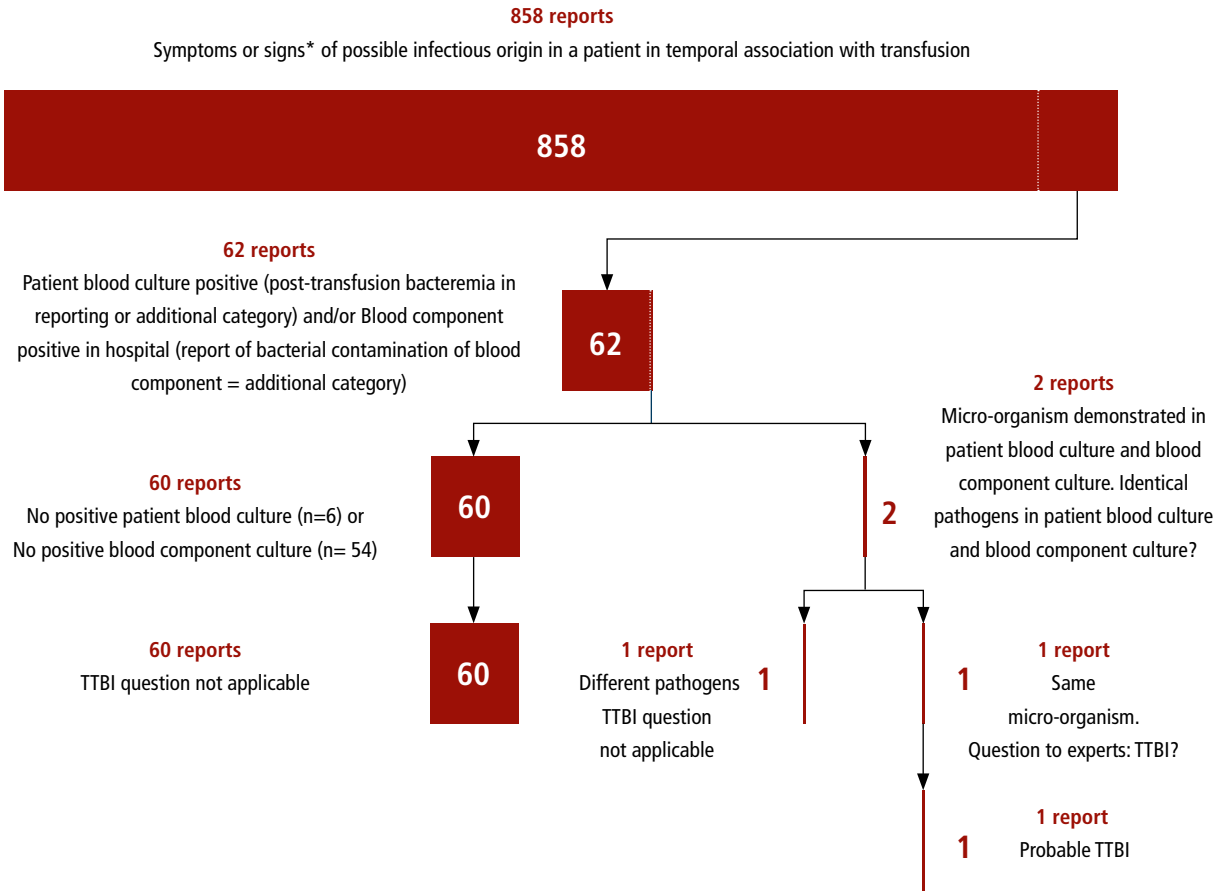

Figure 16 Is it a case of transfusion-transmitted bacterial infection (TTBI)?

** Reactions in 2021 with rise in temperature, decrease in temperature >1 °C and/or chills, all imputabilities*

Table 21 Assessment of transfusion-transmitted bacterial infections (TTBIs) in 2021 (N = 1, discussed with Expert Committee)

Patient blood culture	Component culture result in hospital	Blood component	BacTAlert / culture from Sanquin	Reporting category	Severity grade	Imputability of reaction	Imputability of TTBI
Bacillus cereus	*Bacillus cereus*	Platelets (pool)	Remained negative	Post-transfusion bacteremia / sepsis	4	definite	probable

Table 22 Overview of bacterial screening of platelet concentrates by Sanquin

Total reported by Sanquin	2017	2018	2019	2020	2021
PLTs with initial positive result	188	185	185	183	203
Number already transfused (PLTs and associated RBCs)	96	100	81	84	73*

** In all cases Sanquin asked the treating physicians whether a transfusion reaction had been observed: in 68 cases no transfusion reactions had occurred, in one case the hospital did not know whether a reaction had occurred. In four cases Sanquin did not receive a response from the hospital.*

Post-transfusion viral infection

Demonstration of a viral infection in a transfused patient within a period corresponding to the incubation period of that infection, leading to investigation of a possible causal link to a transfused unit.

Information from hospitals

In 2021, there were no reports of post-transfusion viral infection.

Look-back by the supplier

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

Information from hospitals

As of 2020, hospitals are requested to only report a look-back to TRIP if there were consequences for the patient (a reaction, longer hospital stay, additional treatment, etc.). In 2021, no reports of look-back were received from hospitals.

Information from Sanquin

In 2021, lookback was performed according to protocol after 5 seroconversions (4x HBV, 1x *Treponema pallidum*). Hospitals were asked to trace recipients with the aim of informing them (look-back); no transmissions were found.

Conclusion on infectious transfusion complications

There were no reports of viral infections transmitted in 2021. In 2021, there was one report of post-transfusion bacteremia/sepsis, associated with a finding of *Bacillus cereus* in both patient's blood culture and the culture of the residual blood component, which can be presumed to be a transfusion-transmitted bacterial infection, TTBI. This infection probably contributed to the earlier death of the patient. Overall, the collected data show a very low incidence of infections transmitted by blood transfusion; 1 in about 489,000 units transfused. Alertness and timely investigation remain necessary to properly treat patients with signs that may indicate sepsis and to recall any related blood components from circulation.

3.4 Blood management techniques (BMT)

In 2021, one report related to a transfusion reaction following administration of cell saver blood followed by SD-plasma (four units), all within a one-and-a-half-hour window during recovery of a patient after neurosurgical surgery. This was an anaphylactic reaction (severity grade 2, imputability likely); there is no clarity on the contribution of the cell saver blood versus that of the SD-plasma or surgery.

TRIP drew attention to the various forms of autologous transfusions in 2007 through a board paper on Blood Management Techniques and expressed the view that these applications should fall under the remit of blood transfusion committees. TRIP included the different types of autologous transfusions in its inventory of blood use from 2009 to 2015 (see 2015 report). Reports associated with BMT have been sporadic since 2015.

In recent years, blood management techniques are mostly seen in a broader context of Patient Blood Management, which also pays attention to preoperative optimization of hemoglobin levels. In response to a query from TRIP about the current status of these techniques and the relevance of monitoring theirf safety, the Dutch Orthopaedic Association will repeat an inventory of their use in 2022.

Table 23 Reports relating to blood-saving techniques, 2017-2021

Year	Type	Reporting category	Severity grade
2017	Drain blood	Mild non-hemolytic febrile reaction	1
2018	Drain blood	Non-hemolytic reaction	1
2021	Cell saver, also SD plasma	Anaphylactic reaction	2

3.5 Reports relating to SD plasma (Omniplasma®) in 2021

Use of SD plasma in the Netherlands

SD stands for solvent-detergent, a pharmaceutical virus-reducing treatment on pooled donor units of plasma. In 2014-2016, Omniplasma®, an SD plasma produced from Dutch plasma donations at Sanquin, was rolled out by Sanquin as a standard plasma product for transfusion. FFP is still supplied by Sanquin for pediatric use and other special indications. Figure 1 (Page 9) shows the progression of SD plasma use.

As this is a product subject to the Medicines Act, a contract is drawn up at the hospital between the hospital pharmacy and the blood transfusion laboratory. In accordance with agreements made between TRIP and Lareb, the TRIP route is used for reports of transfusion reactions or incidents. Since 2018, reactions are reported by TRIP to Lareb, with the exception of new antibody formation where cellular products have also been administered and incidents unrelated to product quality. (Forwarding also applies if labile blood components have also been transfused). After coding according to the pharmacovigilance system, reports are entered into the European Eudravigilance database. Through the TRIP hemovigilance reporting, a complete picture of the transfusion chain is maintained at the same time.

Besides two incidents, a total of 14 reactions related to SD plasma were received by TRIP in 2021 (Table 24); a lower number than the 30 reports in 2020. Six reports also involved the transfusion of RBC concentrates and one involved cell saver blood (cited in the previous chapter). The largest numbers of reactions, as before with FFP, are allergic reactions (anaphylactic and other allergic reactions). The picture is similar to that when FFP was the standard product.

Table 24 Reports relating to SD Plasma in 2021 (N = 16)

	Non-serious reactions		Serious reactions	
Type of reaction	SD only	SD and other BC	SD only	SD and other BC
Anaphylactic reaction				1
Other allergic reaction	2	1	1	
Other reaction	2	1	1	1
Transfusion-associated circulatory overload (TACO)				3
TRALI			1	
Incidents				
Other incident*	1			
Calculated risk#	1			

** Too few units ordered for therapeutic plasmapheresis*
 # Group O (vs AB) Omniplasma administered to trauma patient in emergency situation on a named patient basis; see 3.1.

4 GENERAL

4.1 TRIP working method and participation

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.

The 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 and voluntary in principle. Nevertheless it is regarded as the professional standard by the Healthcare Inspectorate (IGJ) and the national Blood Transfusion Policy Guideline 2020. Reporting to TRIP is separate from the hospitals' responsibility to provide care.

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 act implementating the Quality, Complaints and Disputes in Healthcare Act (WKKGZ; Wet kwaliteit, klachten en geschillen zorg), under "hospital blood banks" (ziekenhuisbloedbanken), section 5.1, paragraph 3. The hospitals can send serious reports (severity grade 2 or higher) to the healthcare inspectorate and Sanquin using the TRIP online reporting system. TRIP performs the analysis of these reports 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. 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 2021, TRIP received reports from 76 hospitals. Three hospitals indicated that there had been no reports of incidents or reactions in the TRIP reporting categories in 2021. Two hospitals had not provided any information about reports or numbers of transfusions. One of the hospitals submitted its reports after the closing date and is therefore not included in the participation figure for reports. The rate of participation by hospitals in 2021 was 79/82=96% as regards reports and 80/82=98% for provision of transfusion activity data..

In addition to the hospitals, there are eight 'designated institutions' which have been licensed by the Ministry of Health, Welfare and Sport to receive and transfuse blood components to their patients. Five of the licensed institutions submitted data in 2021, of which three reported that they had not administered any blood products in 2021, one institution had administered two units to one patient in 2021 and one had administered a single unit to a patient. Three institutions informed TRIP that the blood component figures and reports of any reactions would be providec by the transfusion labs with which they have contracts for the provision of blood components.

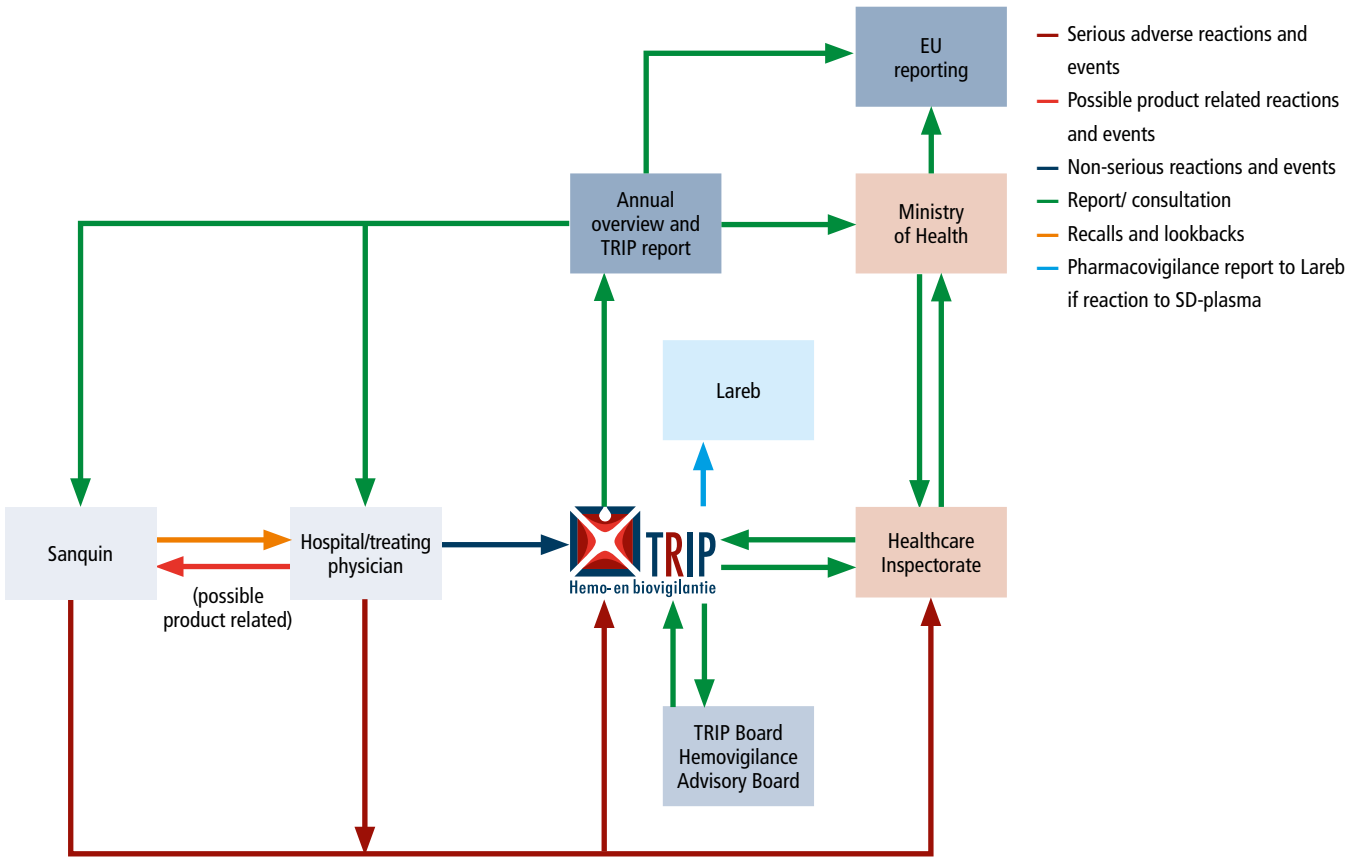

Figure 17 Flow of hemovigilance information and outputs in the Netherlands

LIST OF TERMS AND ABBREVIATIONS

AF	Atrial fibrillation
AHTR	Acute hemolytic transfusion reaction
AML	Acute myeloid leukemia
BMT	Blood management technique
BNP	Brain-type natriuretic peptide
BC	Blood component
CCP	COVID-19 convalescent plasma
CML	Chronic myeloid leukemia
COVID-19	Coronavirus disease 2019
CT	Computed tomography (imaging)
DEHP	Di(2-ethylhexyl)phthalate, plasticiser used in the production of PVC
DHTR	Delayed hemolytic transfusion reaction
ECG	Electrocardiogram
EU	European Union
FFP	Fresh frozen plasma
Hb	Hemoglobin
HLA	Human leucocyte antigen
IBCT	Incorrect blood component transfused
ICU	Intensive care unit
IGJ	Inspectorate for Healthcare and Youth
IQR	Interquartile range
Irrab	Irregular antibodies
IV	Intravenous
IVIg	Intravenous immunoglobulin
Mild NHFR	Mild non-hemolytic febrile reaction
Non-STEMI	Myocardial infarction without ST elevation on ECG
NHTR	Non-hemolytic transfusion reaction
NM	Near Miss
NVB	Netherlands Blood Transfusion Association
OR	Operation room, may also refer to surgery
PAS-E	Platelet additive solution-E, platelet preservation solution containing acetate, potassium, magnesium and phosphate
PLT	Platelet concentrate
Pt	Patient
RBC	Red blood cell concentrate
Sanquin	National not-for-profit blood supply organisation
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SD plasma	Solvent-detergent plasma; in the Netherlands: Omniplasma®
TA-GvHD	Transfusion-associated graft versus host disease
TACO	Transfusion-associated circulatory overload, volume overload associated with administration of blood transfusion
TAD	Transfusion-associated dyspnea
Tf	Transfusion
TR	Transfusion reaction
TRALI	Transfusion-related acute lung injury
TRIP	Transfusion and Transplantation Reactions In Patients
TRIX	Transfusion Register of Irregular antibodies and X(cross-match) problems
TTBI	Transfusion-transmitted bacterial infection
VWS	Dutch Ministry of Health, Welfare and Sport
WKKGZ	Wet kwaliteit, klachten en geschillen zorg (Healthcare Quality, Complaints and Disputes Act)