TRIP REPORT 2023

HEMOVIGILANCE

EXTENDED VERSION

TRIP
Hemo- en biovigilantie

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The TRIP 2023 Hemovigilance report, extended version, is published under the responsibility of the TRIP (Transfusion and Transplantation Reactions in Patients) Foundation.

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FOREWORD

Another year has passed, marked by a variety of events across different fields. Hemovigilance, too, has taken another step forward this year. This report provides a clear summary of developments. In short: participation remains very high, and reporting trends are stable. Nothing particularly striking stands out, although individual cases can still be intriguing, insightful, and profound. The stable trends in this field might give the impression that there's little left to improve, and that we've nearly reached our goal. But is that really the case? I don't think so. We can count ourselves fortunate to have a well-functioning system, but there is always room for improvement. Further professional development of hemovigilance staff could yield even deeper insights into transfusion practices in the Netherlands. Continuing to emphasise the importance of hemovigilance in clinical settings and highlighting its relevance to patient safety in this area remains essential. It is crucial to keep the various professional groups involved in transfusion medicine – such as laboratory staff, clinical chemists, transfusion physicians, nurses, physicians prescribing blood components, and staff administering these products – engaged and alert to transfusion-related issues. When I think about it, hemovigilance staff play a pivotal role in this process. And, as TRIP organisation, we are deeply grateful to them! This is starting to sound like a thank-you note, and rightly so: TRIP's success has only been possible through collective effort!

Is there still room for improvement in hemovigilance? Of course! Take a look at page 6 of this report: the recommendations. Hopefully, hospitals will work on these points and share their progress with each other, so we can exchange knowledge and learn from one another!

I hope this report provides everyone with valuable insights and serves as an informative read. I would also like to draw your attention to the new European regulation (2024/1938) on substances of human origin (SoHO). Starting mid-2027, blood components will be subject to the same regulations as tissues and cells. Through TRIP's website, we will share relevant changes affecting the hemovigilance field.

Dr Peter A.W. te Boekhorst
President TRIP Foundation

1 MAIN FINDINGS 2023

1.1 Hemovigilance in 2023

In 2023, TRIP received a total of 1,376 reports before the closing date of this annual report. This includes 1,273 reports of reactions and 120 reports of adverse incidents, with 17 reports describing a combination of an incident and a reaction. The total number of submitted reports showed a slight increase compared to 2022, aligning closely with the figures reported in 2020. As in previous years, hospital participation in hemovigilance remained high, with 79 of the 80 transfusing hospitals (99%) providing information.

The number of reports should be seen in relation to the number of units distributed and transfused (Figures 1 and 2). A downward trend in the number of red blood cell (RBC) units distributed has been observed over the years. After a period of stabilisation from 2017 to 2021, this decline appears to be continuing. Since 2021, this report has used the number of units of SD plasma transfused as provided by the hospitals (solvent/detergent treated plasma; Omniplasma® in the Netherlands), as TRIP does not have access to the number of units of SD plasma distributed.

The number of reported transfusion reactions (excluding reports of new antibody formation) is 2.63 per 1,000 of blood components, slightly above the 2018-2022 average of 2.45. There was a higher absolute number of reports of serious transfusion reactions in 2023 than in previous years. The number of reported serious transfusion reactions with definite, probable, or possible imputability was 0.29 per 1,000 distributed blood components (2018–2022: 0.24). The number of serious transfusion reactions associated with RBC or platelet transfusions showed no significant change compared to 2022.

No transmissions of viral or bacterial infections via contaminated blood components were reported in 2023. There was a notable decrease in reports of post-transfusion bacteremia/sepsis, even as the number of positive culture results after transfusion remained consistent. More culture results may have been considered clinically irrelevant or a contaminated sample, possibly due to the attention given to this topic during the "Meet the Expert" meeting in April 2023 and the corresponding recommendation in last year's report.

In 2023, respiratory symptoms continued to be the type of transfusion reaction associated with the highest morbidity and mortality. Five out of the seven deaths (71%) after a transfusion reaction, in which a link between the transfusion and the reaction was considered as being at least possible, took place after the occurrence of a transfusion-associated circulatory overload (TACO) and/or a transfusion-related acute lung injury (TRALI). The absolute number of TACO reports has increased compared to last year (from 100 to 115), with 94% having a possible, probable, or definite imputability. In the four reports assessed as TRALI in 2023, all with possible imputability, TACO was registered three times as an additional category. In none of the cases responsible leukocyte antibodies were identified.

In 2023, 39 reports of incorrect blood components transfused (IBCT) and 17 reports of near-miss incidents were received, from 21 and 5 healthcare centres, respectively. The number of healthcare centres reporting near misses to TRIP in the last five years (35; 44%) is lower than the number of centres reporting an IBCT (52; 65%). Fewer near misses may be reported to TRIP when a blood group discrepancy is identified in time, as no actual harm is done to the patient in such cases.

In conclusion, this twenty-first annual hemovigilance report shows a stable picture of the blood transfusion chain in the Netherlands in 2023. The high participation of transfusing institutions and the overview of the received reports show that the TRIP reporting system is robust and the transfusion chain in the Netherlands is safe. Fewer incidents, classified as near miss, are reported, while TRIP is keen to receive these reports. These kinds of incidents clearly show that certain protocols work, but also where there are gaps. In both situations, the transfusion community may learn lessons from these events.

1.2 Recommendations

	Recommendation	Who?
1	Annual reporting of some incidents (analysed in detail) per institution to TRIP, including near misses. This allows us to learn from each other and identify possible improvement measures for the future.	Hemovigilance staff and professionals in cooperation with Safe Incident Reporting committees
2	Focus on ensuring the correct patient identification when registering new patients and proper labelling of application forms and blood tubes. Many institutions now digitally monitor the subsequent steps in the transfusion chain.	Hemovigilance professionals in collaboration with all staff members involved in applications, facilitating and conducting research for blood group determination

1.3 Follow-up to previous years

1 Input from clinician and microbiologist in assessing positive bacteriological culture results in the context of transfusion reactions to determine the relevance of the result. In addition, promoting best practices for submitting material for (blood) cultures (see Blood Transfusion Policy Guidelines).

Development:

This recommendation may have contributed to increased attention to the assessment (clinical relevance or potential contamination of sample) of positive culture results when diagnosing and classifying transfusion reactions. While the number of positive culture results remained the same in 2023 compared to 2022, fewer reports were classified as post-transfusion bacteremia. See chapter 3.3, Infectious transfusion complications.

2 OVERVIEW OF 2023 HEMOVIGILANCE DATA

2.1 Overview of 2023 hemovigilance data in comparison with previous years

Of the 1,376 reports received by TRIP before the cut-off date for this report, 1,256 concerned transfusion reactions. A total of 103 incidents were reported, with 17 reports describing a combination of an incident and a reaction. All reported incidents are included in the tables, even if they were registered as an additional category in combination with a reaction, and vice versa.

In 2023, the reporting categories for allergic reactions and other allergic reactions were merged into a single reporting category. The number of reports is comparable to previous years. This new classification simplifies the description of these reactions in the report by focusing on observed symptoms, see the relevant section in Chapter 3 and Table 15.

In 2023, the TRIP reporting system also facilitated hemovigilance surveillance of red blood cell concentrates stored in non-DEHP blood bags, with eight hospitals participating at Sanquin's request.

For several years, Sanquin has been preparing and supplying serum eye drops. This product does not belong tp the 'classic' blood components for transfusion, but it is prepared as a 50% solution from small pools of male AB donor blood. Reports on this product are in principle registered by TRIP and are important because of the need for intensive monitoring of these newly authorised products. In 2023, no reports on this product were received.

Finally, after the termination of Fitrix® distribution (a fibrin glue with two components and derived from donor blood), no applications of this product were reported by the participating hospitals in 2023.

Reported data concerning the reports are presented in the following tables and figures:

* *Additional tables in online appendix to this report*

Table 1 Reported incidents, 2019-2023

Incident	2019	2020	2021	2022	2023	Number of hospitals with reports in 2023
Incorrect Blood Component Transfused	42	44	26	28	39	20
Near miss	70	41	29	34	17	5
Other incident	87	100	74	69	54	19
Calculated risk situation	17	8	8	1	5	5
Other categories of incidentsa	20	10	8	2	5	5
Total	**236**	**203**	**145**	**134**	**120**	**31**

[a] *This includes look-back reports from the producer, previous Incorrect Blood Component Transfused and the reporting or additional category of bacterial contamination of blood component (5 in 2023; see Chapter 3.3).*

Table 2 Reported transfusion reactions, 2019-2023

Reaction	2019	2020	2021	2022	2023	Severity grade ≥ 2[a]	Number of hospitals with reports in 2023
Circulatory overload	91	112	102	100	115	47	44
TRALI	6	2	1	7	4	4	3
Transfusion-associated dyspnea	4	8	5	13	16	3	15
Acute hemolytic transfusion reaction	16	16	9	9	18	7	15
Delayed hemolytic transfusion reaction	3	6	5	6	9	5	7
New antibody formation	724	627	5	3	4	0	4
Anaphylactic reaction[b]	129	134	113	119	117	14	32
Non-hemolytic transfusion reaction	317	304	303	299	284	14	67
Mild non-hemolytic febrile reaction	284	298	327	309	328	5	56
Post-transfusion bacteremia/sepsis	84	74	58	61	47	4	27
Post-transfusion viral infection	0	0	0	0	0	0	0
Other reaction	257	330	245	253	331	39	65
Other categories of transfusion reaction[c]	3	0	0	2	0	0	0
Total transfusion reactions	**1,918**	**1,911**	**1,173**	**1,181**	**1,273**	**142**	**74**
Total severity grade ≥ 2[a]	**104**	**141**	**122**	**115**	**142**		
Total reports	**2,112**	**2,082**	**1,300**	**1,296**	**1,376**		

[a] *Definite, probable or possible imputability.*
[b] *New definition allergic reaction, relates to merging anaphylactic reaction and other allergic reaction into a single category, see § 3.2.*
[c] *Concerns reports of other post-transfusion infections (2019;3, 2022;1), and post-transfusion purpura (2022;1, see § 2.2).*

Table 3 Number of reports per type of blood component in 2023

Type of blood component	No. of blood components in 2023	Transfused in 2023[a]	No. of reports		Reports per 1,000 blood components Distributed	
			All	Serious[b]	All	Serious[b]
Red blood cell concentrate	380,939	370,432	1,124	106	2.95	0.28
Platelet concentrate	53,060	51,851	146	16	2.75	0.30
Fresh frozen plasma	1,599	1,256	0		0.00	
SD plasma[c]		45,515	9	1	0.20	0.02
Fitrix® fibrin glue	0	0	0			
Serum eye drops	1,900	1,583	0			
Anti-COVID-19 plasma	512	448	5	2		
Other blood components			2	0		
Combinations[d]			71	17		
No blood components involved (incidents)			19			
Total	**438,010**	**471,085**	**1,376**	**142**	**2.86[e]**	**0.29[e]**

[a] *Data received from 79/80 hospitals (98.8%).*
[b] *Definite, probable, possible imputability.*
[c] *SD = solvent/detergent treated plasma; Omniplasma® in the Netherlands, only units transfused are reported.*
[d] *Combinations of labile blood components with SD plasma are also included.*
[e] *Reports in relation to total units of red blood cell concentrates, platelet concentrates, fresh frozen plasma, anti-COVID-19 plasma and SD plasma units transfused.*

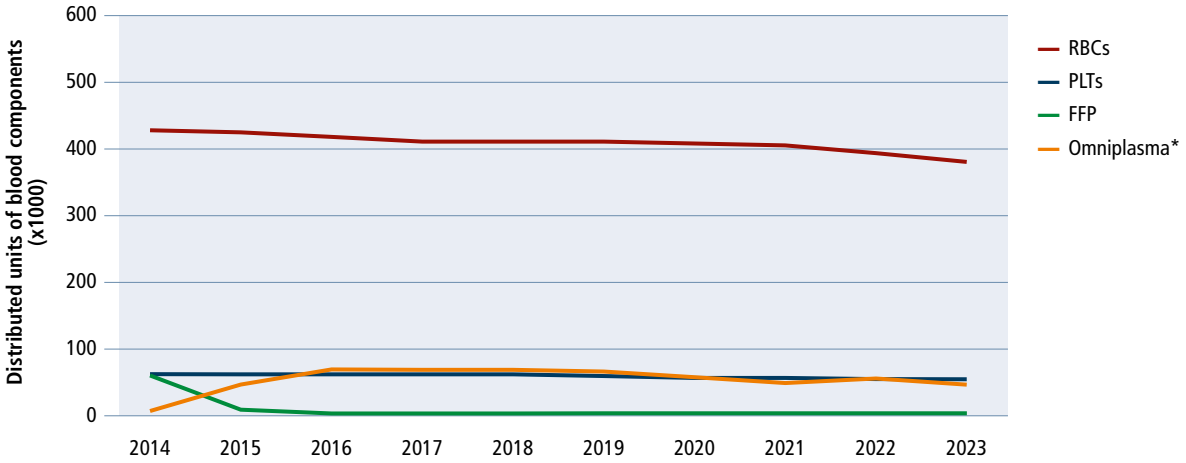

Figure 1 Distributed units of blood components, 2014-2023

* *For SD plasma (Omniplasma®), the units transfused are reported for 2014 and 2015 because of the roll-out phase; the units transfused in 2021-2023 are reported due to the lack of information on distribution.*

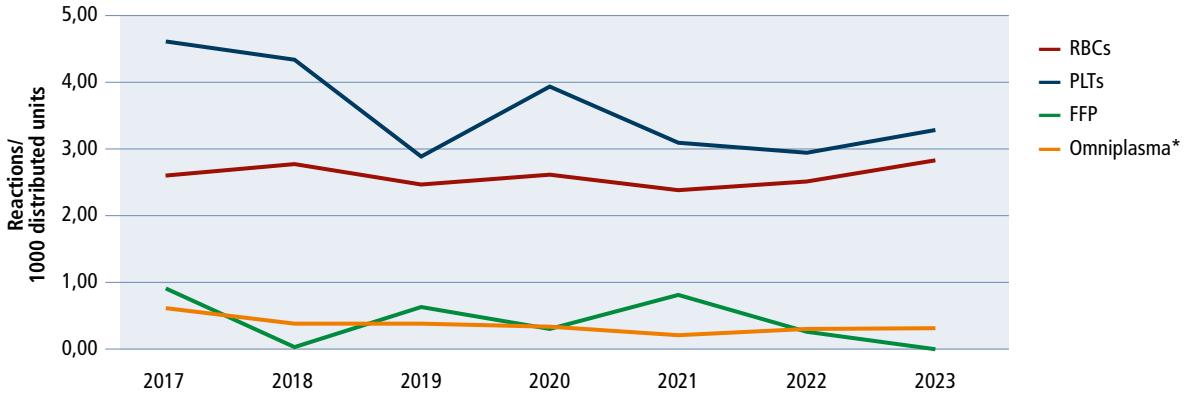

Figure 2 Transfusion reactions per type of blood component, 2017-2023

* *For SD plasma (Omniplasma®), only units actually transfused are reported from 2021*
The graph shows transfusion reactions (all imputabilities) excluding new antibodies, with reactions associated with more than one type of blood component 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 involving platelets and 0.5 reaction involving red blood cells, etc.). This method of analysing has been introduced since reporting year 2017.

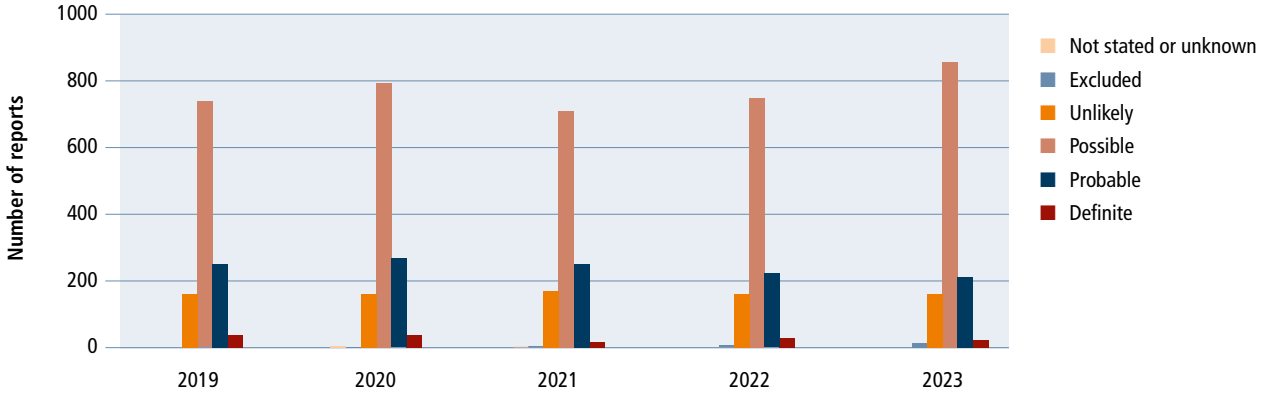

Figure 3 Imputability of transfusion reactions, 2019-2023

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

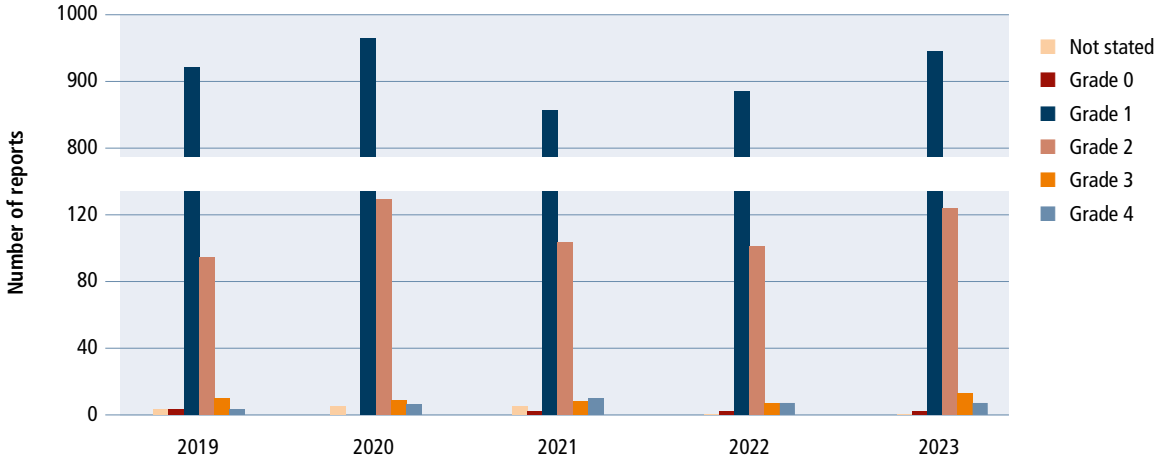

Figure 4 Severity of transfusion reactions (definite, probable, possible imputability), 2019-2023

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

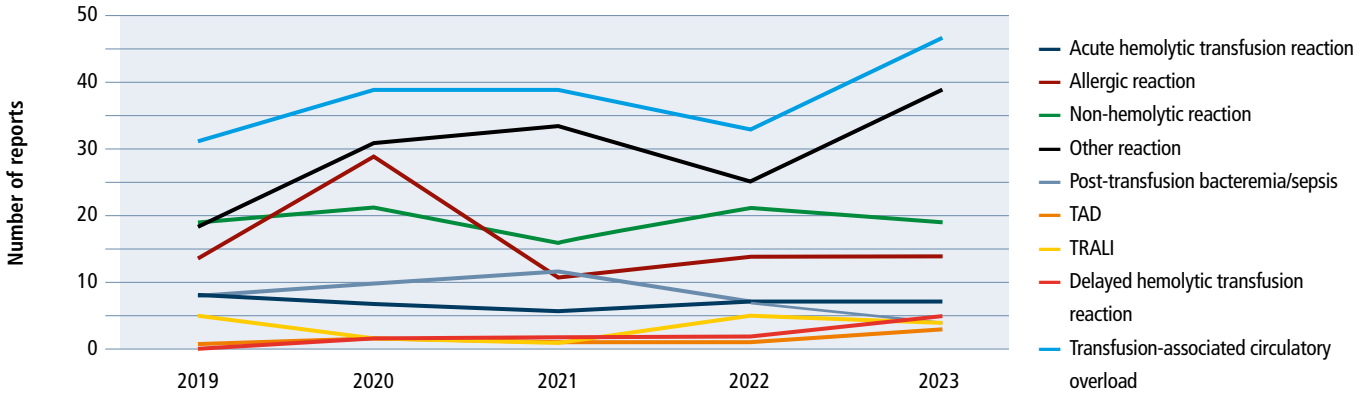

Figure 5 Serious transfusion reactions (definite, probable, possible imputability), 2019-2023

Table 4 Severity grade 4 reports in 2023

Reaction	Blood component	Sex, age group (years)	Imputability	Symptomatology
TRALI	RBC	F, 80-90	Possible	Pneumosepsis and ECG abnormalities in a patient with anemia. During transfusion (Tf), the patient experienced a drop in blood pressure and oxygen saturation to 80%. A CT-thorax showed bilateral ground-glass opacities and signs of circulatory overload. Despite diuretic treatment, there was no improvement and an ultrasound suggested underload. The patient passed away within 24 hours.
Circulatory overload	RBC	M, 80-90	Possible	Patient with heart failure and multiple myeloma (MM) for whom palliative care measures were in place. During transfusion, oxygen saturation dropped to 72%. Comfort care was given and patient passed away later that day.
Circulatory overload	RBC	M, 60-70	Possible	Patient with MM and neutropenic sepsis with dyspnea during chemotherapy. During Tf, blood pressure increased, and oxygen saturation dropped to 63%. Chest X-ray revealed signs of fluid overload. Patient was intubated, but passed away later that day.
Circulatory overload	RBC	M, 70-80	Possible	Patient with pneumonia with metastatic lung carcinoma. During Tf dyspnea and drop in blood pressure. Acute respiratory impairment, leading to death shortly thereafter.
Circulatory overload	RBC	F, 70-80	Possible	Patient with kidney transplant, cardiac history and stoma bleeding developed dyspnea and increased blood pressure after Tf. Chest X-ray, cardiomegaly, pleural fluid and increased markings on both sides. Patient died two days later.
Other reaction	RBC	M, 80-90	Possible	Patient with extensive cardiac history, admitted via ED for collapsible iron-deficiency anemia. During Tf, patient developed sudden snoring respiration and died, possibly due to a rhythm disorder in the context of underlying conditions.
Other reaction	PLT	M, 60-70	Possible	Patient with MDS developed fever, dyspnea and chills following Tf. Clinical signs of extensive cell decay and hyperkalemia. Patient died within 24 hours under palliative care.
Post-transfusion	RBC	M, 40-50	Unlikely	Patient developed drop in blood pressure, oxygen saturation and temperature drop following Tf. Blood cultures bacteremia/sepsis revealed a Staphylococcus aureus. Comfort measures were taken due to hopeless pre-Tf situation, deceased within 24 hours.
Delayed hemolytic	RBC	M, 80-90	Unlikely	Patient with AIHA and CLL admitted due to jaundice 2 days after Tf. No evidence transfusion Reaction of allo-incompatibility. With rapid progression of underlying disease, limited care was given. Patient died two days later.
Circulatory overload	RBC	M, 80-90	Unlikely	Patient with MDS develops myocardial infarction and pneumonia. Immediately after the start of Tf, A drop in blood pressure occurs, followed by dyspnea. He died the same night due to underlying condition.
Other reaction	RBC	M, 50-60	Unlikely	Patient with decompensated liver cirrhosis is found dead during Tf. Death due to underlying condition.
Other reaction	RBC	F, 60-70	Unlikely	Patient with extensively metastatic malignancy. Died four days after Tf due to a paraneoplastic syndrome.
Other reaction	RBC	M, 70-80	Unlikely	Patient with chest pain and dyspnea during Tf, showing pan-ischemia and tachycardia on ECG. Ventilation, but despite this rapid decline and patient died from myocardial ischemia (due to anemia) and shock.
Other reaction	PLT	F, 20-30	Unlikely	Patient with AML developed fever, dyspnea and tachycardia after Tf, with the same symptoms before Tf. Respiratory failure, ventilation administered, nevertheless died that same day.

Table 5 Severity grade 4 reports (with definite, probable or possible imputability), 2014-2023

Reaction	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	Total
Acute hemolytic transfusion reaction		2						1			3
Other reaction		1	1	1	2			2	1	1	9
Post-transfusion bacteremia/sepsis	2							1		1	4
Post-transfusion purpura	1										1
TRALI		2	1	1	1	1			1	1	8
Delayed hemolytic transfusion reaction								1			1
Circulatory overload	3	2	3	6	2	2	6	5	5	4	38
Total	**6**	**7**	**5**	**8**	**5**	**3**	**6**	**10**	**7**	**7**	**64**

2.2 Late reports

After the cut-off date for submitting reports for the 2022 reporting year, 15 late reports were still received from that year and, in addition, one report from 2020 was completed (Table 6). The late 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, four serious reactions were recorded with a severity grade of 2 or higher. These included three anaphylactic reactions (severity grade 2, imputability definite) and once acute hemolytic transfusion reaction (severity grade 2, imputability possible). In accordance with the mandatory procedure, these four reports have been added to the overview for the European Commission for 2023, see Section 2.3.

Table 6 Late reports from 2022 and 2020 in the 2023 report (N = 15 + 1)

Reporting category	Severity grade		
	n/a	1	2
Anaphylactic reaction			3
Other allergic reaction		2	
Acute hemolytic transfusion reaction			1
Mild non-hemolytic febrile reaction		3	
Non-hemolytic transfusion reaction		3	
Other reaction		1	
Post-transfusion purpura		1	
Post-transfusion bacteremia/sepsis		1	
Other incident	1		

Post-transfusion purpura (PTP)
Serious transient thrombocytopenia with or without bleeding, occurring 1 to 24 days after a transfusion of red blood cells and/or platelet concentrate.

- One late report related to a report of post-transfusion purpura with severity grade 1 and likely imputability. The patient, aged 40-50 years, with extensive cardiac history receives several units of platelets, red blood cells and plasma during surgery. After the transfusion, a sudden sharp reduction in platelet count was observed, which spontaneously recovered after a few days. No clinical symptoms, such as bleeding, occurred. Further investigation revealed the presence of highly reactive platelet-specific allo-antibodies against Human Platelet Antigen-5a (HPA-5a) in the recipient. The presence of the anti-HPA-5a and the episode of thrombocytopenia are consistent with post-transfusion purpura, and the recipient was subsequently recommended HPA-5a negative platelets for future transfusions.

2.3 Overview of mandatory reports to the European Commission

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

- Reactions with definite, probable or possible imputability are reported; late reports from the previous year should be included.
- Reactions that occurred after transfusion of an incorrect blood component or other incident are taken into account in the relevant category.
- Hemolytic reactions are subdivided into immunological (ABO), immunological (non-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) hospitalisation (Table 7).

Table 7 Number and imputability of reports of severity grade 2 or higher in 2023 or late reports from 2022, in accordance with EU overview

Severity grade	2 or 3			4	
Imputability	Definite	Probable	Possible	Possible	Total
Hemolytic transfusion reaction (ABO)	2				2
Hemolytic transfusion reaction (immunological, non-ABO)	1	3	1		5
Hemolytic transfusion reaction (non-immunological)		3	3		6
Allergic reaction	3	6	8		17
Febrile reaction	1	3	10		14
Other reaction		10	26	2	38
TAD		1	2		3
TRALI			3	1	4
Circulatory overload	3	18	22	4	47
Total	**10**	**44**	**75**	**7**	**136**

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 effectiveness have been carried out and published both in the Netherlands and internationally. In 2023, CCP was mainly used in immuno-compromised patients. A total of 512 units were distributed (445 in 2022) and 448 units were reported as applied (433 in 2022).

Table 8 shows the five reactions reported to TRIP from five hospitals in 2023 after the application of CCP. Due to the small number of reports, no sub-analysis of these reactions was performed, consistent with 2022.

Table 8 Reports regarding CCP in this report (N = 5)

Reaction	Additional category	Sex, age group (years)	Severity	Imputability
TRALI	Circulatory overload	M, 70-80	3	Possible
Circulatory overload		M, 70-80	2	Probable
Allergic reaction		M, 30-40	1	Probable
Allergic reaction		F, 70-80	1	Possible
Non-hemolytic transfusion reaction overload		M, 60-70	1	Possible

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 given a blood component that did not fulfil all the requirements of a suitable component for that patient, or that was intended for a different patient.

39 reports (28 reports in 2022)
Reports were submitted by 21 different hospitals (26%), range 1-7 reports per hospital

- Of the seven cases in which there was a chance that ABO-incompatible blood was transfused (ABO risk), all seven cases involved an identification error, a mix-up of blood bags, patients or patient data. These included one case that caused an acute hemolytic transfusion reaction (AHTR) and another that led to a different type of reaction. For further details on these reactions, see Report of the Month 2024 - 1 and Report of the Month 2024 - 2.
- Preventive policy to avoid the formation of irregular antibodies was not followed 11 times. In two cases, this led to the formation of a new antibody (1 case of anti-c in AIHA patient and 1 case of anti-K in a woman < 45 years).
- Eight reports of an incorrect blood component transfused concerns a patient with previously found irregular antibodies. This has once led to an AHTR, severity grade 1 (see case description below) and once to an AHTR severity grade 2.
- In one case, a transplant was incorrectly not taken into account in the patient's history and units were issued based on type & screen instead of performing cross-matching. This oversight resulted in undetected anti-A1 in the patient. Consequently, transfusion of red blood cells of blood group A (instead of O) caused an AHTR.

TRIP risk classification
As in previous years, TRIP assessed all reports of Incorrect Blood Component Transfused (IBCT) to determine the worst potential risk which a patient was exposed to as a result of transfusion of an incorrect blood component. The risk classification used by TRIP is detailed on the website.

Figure 6 shows a breakdown of IBCT risks over the past five years.
Also in 2023, the Irrab prevention policy represented the largest risk group, with 11 reports. At the time of product application, the technician or physician overlooked that the patient required typed products; These cases included four patients with MDS, one with AIHA, three undergoing daratumumab treatment, one female < 45 years, one with thalassemia and one with sickle cell anemia. Eight reports were recorded in the Irrab risk group, including: One case where a patient with known irregular antibodies received an incompatible transfusion. Errors in the lab: three selection errors, two procedural errors, two assessment errors and one communication error.

Acute Hemolytic Transfusion Reaction (AHTR) due to incorrect blood component transfused (Irrab risk)

- During transfusion, the patient experienced worsening shortness of breath, oxygen saturation dropped from 95% to 90%, and oxygen needs increased. One day later, haptoglobin levels dropped sharply and Hb did not rise. Further investigation revealed that the laboratory had incorrectly interpreted a positive result of the indirect antiglobulin test (IAGT) as negative, leading to the selection of a K-positive unit for a patient with anti-K antibodies. The reaction is classified as AHTR severity grade 1, with likely imputability. Patient recovered completely.

Three reports relate to an IBCT with TA-GVHD risk, non-irradiated products were transfused despite the requirement for irradiated products to prevent transfusion-associated graft-versus-host disease. In two cases, the indication for irradiated products was missed by the physician. In a third case, the applicant failed to complete the form, overlooking that the patient had recently undergone an autologous stem cell transplant at another hospital. A (possible) transfusion reaction prompted the laboratory to identify the need for irradiated units in this patient.

In 2023, eight hospitals participated in the non-DEHP blood bag study in 2023, including patients who did not meet the inclusion criteria. Due to a communication/organisational error, the study conditions were not processed in time in the hospital system and units were administered to the wrong patient group (a total of 6 cases were reported across two hospitals). As this study involved two different blood bags, both considered standard (safe) products, no adverse effects were to be expected; the patients involved did not show any transfusion reactions.

Two reports fall into the category of undertransfusion; one product intended for exchange transfusion – but no longer required – was administered to an adult, and one platelet product with insufficient platelets was distributed.
Furthermore, one report involved the administration of one unit of red blood cells without adherence to the preventive policy for parvovirus B19; this did not affect the pregnant patient involved.

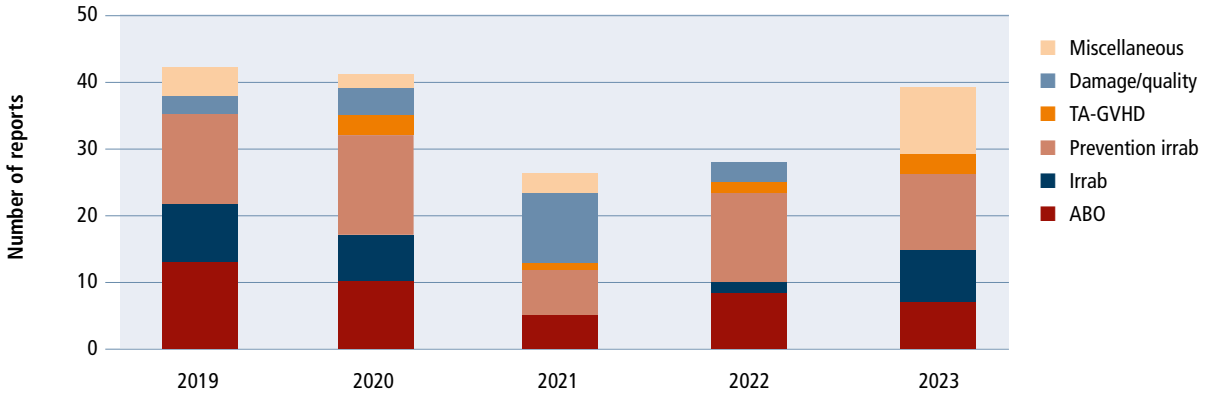

Figure 6 Incorrect Blood Component Transfused 2019-2023: subdivided according to risk group
ABO = Risk of an ABO-incompatible blood transfusion
Irrab = Risk of an irregular antibody-incompatible transfusion
Prevention Irrab = Risk of alloimmunisation due to non-compliance with preventive selection criteria
TA-GVHD = Risk of transfusion-associated graft-versus-host disease (after transfusion of non-irradiated blood)
Damage = Risk of (potentially) reduced quality of a blood product due to damage
Miscellaneous = other risks (not meeting preventive policy parvovirus B19-tested product (N=1), transplantation (N=1), other composition product (N=2), other (6x not meeting inclusion criteria))

Near miss (NM)

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

In total, 17 reports were submitted by five different hospitals (6.3%), range 1-5 reports per hospital.

- In 15 reports, there was potential ABO risk and an identification error. In one case, there was a risk of administering a blood component whose quality could no longer be guaranteed, and in one case, a Rhesus D-positive product was selected. There was a deviation from the policy to prevent irregular antibody formation.
- Eight near misses were detected in time due to blood group discrepancy (in 2022, this was 15 cases out of 29 reports with potential ABO risk). In one report, the error was detected because the Hb results were incorrect (reported as 7.8 instead of 4).
- In one report, it was only later discovered, during invoicing, that the lab results belonged to another patient. The treatment of the patient in question (based on the data of someone else) had no negative consequences.
- One report concerns the transfusion of a Rhesus positive unit (A pos) to a patient with blood type A neg, a selection error. A warning from the Laboratory Information System was unintentionally ignored and also not noticed during the second lab check. This error was eventually identified by the nurse on the ward.
- In one case, a bag was returned to stock but was not properly labelled (it should have been quarantined), a storage error. The notifications from the digital system were not seen by the analyst.

Table 9 Near miss reporting

Occurrence*	N	Where detected	N	How detected	N
Investigation prior to transfusion (request)	16	Planned check	9	Blood group discrepancy	8
				Discrepancy with previous Hb results	1
		Alertness of ward staff	2	ED finds out it concerns wrong patient	1
				Analyst selected Rhesus D post unit. Nurse saw in time that the Rhesus unit was incompatible	1
		By lab	4	By chance by inquiry operation room time	1
				Another patient arrives at the lab	1
				Form/tube discrepancy	2
		By hospital admin	1	Other date on declaration form	1
Stock management	1	Planned check on ward	1	When scanning error message	1

** Place in the transfusion chain. Where in the transfusion chain did the incident occur? See TRIP website.*

Causes of identification errors:

- Incorrect sticker on tube due to labelling the tubes at a different time/different location (9x)
- Incomplete check of patient's name/date of birth (3x)
- No identifiable cause (3x)

Scanning bar codes appears to be an effective method to reduce the number of mix-ups. However, it is not always possible at the initial stages, such as when entering data for a new patient or applying the correct labels to blood tubes and application forms. Continued attention to these processes is essential, as is the reporting of near misses, to facilitate learning and identify methods that can further reduce the risk of identification errors.

Case studies (in Dutch) in the category near miss cases can be found at www.tripnet.nl in the Report of the Month section (Melding van de maand): Report of the Month 2023 - 3: Digitisation in the blood transfusion chain

Other incident (OI)
Error or incident in the transfusion chain that does not fit into any of the categories above, 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.

In total, 54 reports were submitted by 21 different hospitals (26%), range 1-14 reports per hospital.

- Three reports were categorised as 'other incident' including one reaction with severity grade 1 (1x other reaction; 1x mild NHFR, 1x TACO).
- In the case of TACO, the unit was administered within 2 hours instead of the prescribed 4 hours. This resulted in circulatory overload with severity grade 1.
- No investigation was conducted, even though there may have been a transfusion reaction. The patient died during the transfusion, and it was assumed that the cause was likely the underlying condition.
- One patient was mistakenly transfused with two units of red blood cells based on a one-month-old Hb measurement. At the time of the transfusion, the Hb was 6.8, as later revealed from a sample taken after the transfusion reaction. The patient developed a high fever during the transfusion, was briefly admitted to the ICU, and had a positive blood culture. The reaction was classified as post-transfusion bacteremia/sepsis, severity grade 2, with possible imputability. The culture of the blood component remained negative.
- 36 units were (partially) lost, of which 28 were not 'errors' (see below).

Classification by type of error
Like last year, categorisation of 'other incidents' is again based on the type of error and whether the product was (partially) lost. As reported above, 36 incidents resulted in the loss or partial loss of blood components. These are categorised as 'lost' when the blood bag could not be returned to stock or could not be fully transfused because of an incident.
The largest group of other incidents are classified as error category 'other' (31). In this category, it turns out that in ten cases, the unit still runs subcutaneously despite the formal checks (e.g. after 10 minutes) or the unit is accidentally punctured (9x). These were also the most common reasons for unit losses.
A number of reports involved the incorrect administration of red blood cells due to an inaccurate Hb measurement (9x). The underlying causes varied, an error in blood collection (4x), a retrospective mix-up or measurement error. In three reports, the cause could not be identified.

Table 10 Reports of other incidents in 2023, subdivided according to type of error

Type of error	N	Loss (or partially loss)	N	Description	N
Administration error	1	No	1	— The patient was known to have anti-K (from 1991) in paper records, but this information was not transferred during the implementation of new digital system (cause unknown). IRA was negative before administration, but anti-K was found in the serum afterwards. Hb increased slightly, hemolysis parameters unknown.	1
Execution of test error	1	No	1	— Two units of RBC administered based on an incorrectly measured Hb of 4.8 (in blood gas). Hb was actually 8.1 in another sample, taken after transfusion.	1
Assessment error	8	Yes	5	— A unit of RBC was sent via the pneumatic tube to the wrong department, and remained there for one day. Naming of recipient on tube not unambiguous	1
				— 2 units of RBC were not removed from tube post system when they proved unnecessary and therefore, they were returned to the lab too late.	1
				— The unit of RBC was already spiked when it turned out that the infusion watch needle was, leaking NaCl, which should have been checked first.	1
				— The unit of RBC was already spiked, and the physician later called, stating that on closer examination, the transfusion should be abandoned due to risk of circulatory overload (consultation took place after the order was given)	1
				— The unit of RBC was picked up too early and stored under the wrong conditions	1
		No	3	— Initial indication from nephrology was no blood transfusion due to potential kidney transplant, as indicated in the medical file. The patient received EPO. The anesthesiologist administered 2 units of RBC without consulting the nephrologist due to low Hb.	1
				— In citrate tube low platelet number measured of 11, aggregates missed. Unnecessary platelets administered	1
				— The patient died during the transfusion of the first unit of RBC, related to cardiac arrhythmia, which was not recognised as a possible transfusion reaction. No investigation was initiated.	1
Storage error	1	Yes	1	— Unit was stored for too long/wrongly because of high work load	1
Blood sampling name error	4	No	4	— Transfusion based on Hb determination from infusion arm, blood gas, diluted sample	2
				— Transfusion of 2 units, POCT 1st Hb incorrect, Hb at 2nd measurement higher. No adverse effects on the patient	2
Identification error	1	No	1	— Hb measurements are incorrect, too high. Conduct of test correctly, measurement that served as the indication for transfusion was likely based on blood sample from another patient.	1
Technical error	2	Yes	2	— Ordered unit of RBC does not arrive. Hours later, cause was discovered as failure of the tube post system.The unit of RBC remained outside the required storage conditions for too long.	2
Administration error	5	Yes	2	— Checks of transfusion system were either not performed or not performed properly (e.g. infusion not properly connected, transfusion not started, running subcutaneously)	2
		No	3	— Check of transfusion system was performed after 10 minutes, but after 35 minutes, the Tf ran subcutaneously. It was reconnected using a new venflon (deviation from hospital protocol).	1
				— During the 1st unit of RBC, the venflon leaked, was decoupled and restarted with new venflon. (deviation from hospital protocol), mild NHFR.	1
				— Unit of RBC was administered over 2 h instead of the prescribed 4 h. This resulted in a transfusion reaction, TACO, severity grade 1, complete recovery.	1
Other	31	Yes	26	— Venflon/transfusion system malfunctioned after > 10 min	4
				— Checks transfusion (system) performed, but ran subcutaneously (at later stage)	10
				— Unit of RBC punctured during connection	9
				— Failure to (re)connect the IV resulted in the unit of RBC being returned to the lab too late.	2
				— One unit of RBC was sent to the wrong department and only discovered after a delay	1
		No	5	— Blood components were delayed with reaching the patient. The doctor was insufficiently aware of the protocol for massive blood loss, for example, PLTs not included in the package and should have been ordered separately.	1
				— Transfusion (2 RBC) was performed on a Hb taken one month earlier. This measurement turned out to be incorrect, a T&S later showed that Hb was not actually too low. During Tf, the patient developed a high fever, and a blood culture taken afterwards tested positive.	1
				— Hb measurement error causing unnecessary transfusion, cause unknown	3

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 as mentioned in the literature and where the intended benefit from transfusion is deemed to justify the risk of harm and its possible severity.

Five reports have been received from five different hospitals.

- All five reports involved emergency situations. In four cases, pre-existing antibodies in the patient could not be considered (Irrab risk).
- In one case, the preventive policy for women < 45 years could not be followed. The patient, who should have received c-negative RBC, was transfused with c-positive units.
- None of the five cases resulted in a transfusion reaction.

Conclusion on incidents in the transfusion chain

The total number of reported incidents in 2023 (120) is slightly lower than in 2022 (134). In 2023, 39 reports were classified as incorrect blood component administered (2022: 28 reports). Notably, there were significantly fewer near misses reported this year (17 versus 34 last year), and these were submitted by only a small number of hospitals (5 versus 14 last year), see Figure 7.

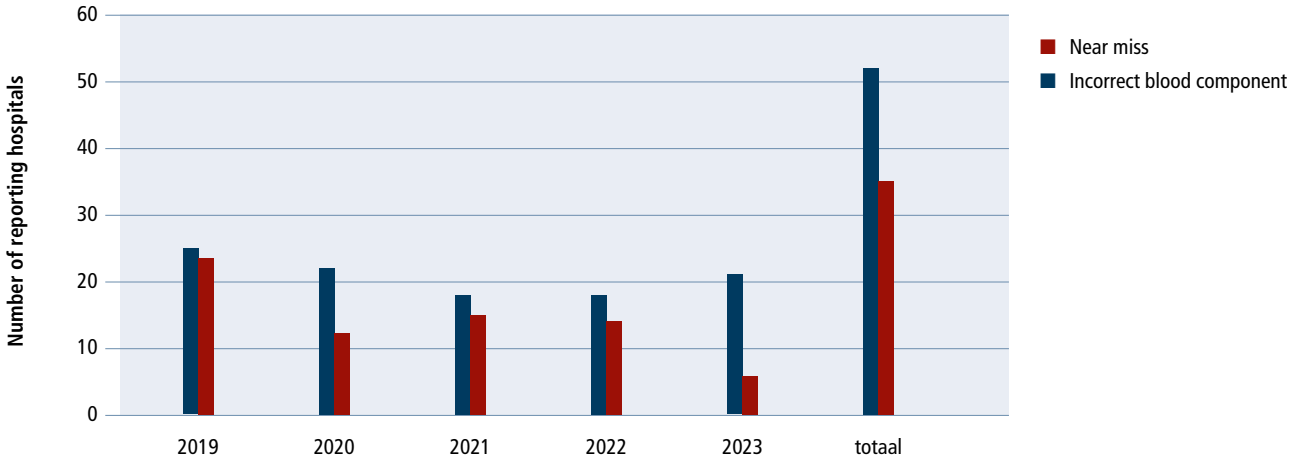

Figure 7 Number of different hospitals reporting a IBCT or NM

It is worth noting that not all identification errors detected in time through blood group discrepancies may be reported to TRIP. However, TRIP strongly encourages continued reporting of identification incidents, even those identified in time, as these incidents can highlight areas for improvement and provide valuable learning opportunities for other institutions. See recommendations.

3.2 Non-infectious transfusion complications

Respiratory transfusion reactions

Circulatory overload, Transfusion Associated Circulatory Overload (TACO)

Respiratory problems during or within 12 hours after blood transfusion, manifesting as at least one pulmonary feature (criterion A or B). In all, at least 3 of the criteria below must be met. See also notes 1 to 6 on www.tripnet.nl.

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

In 2023, 115 reports of TACO were reported by 44 hospitals (55%), with a range of 1 to 7 reports per hospital.

- TACO was reported five times as a additional category of another type of transfusion reaction.
- 108 (94%) reports of TACO with definite, probable or possible imputability.

Definite, probable, possible TACO (Table 11):

- Cases of TACO concerned 10% of the total number of transfusion reactions and 33% of the total number of serious reactions. TACO is the transfusion reaction with the highest number of serious reports.
- In four cases, the patient died after transfusion.
- Twenty-one times, TACO was reported as a additional category of another type of transfusion reaction, due to additional findings that were inconsistent with TACO. TACO was reported twice in combination with an incident, where in one case the infusion rate was set too high, and in the other case the reaction was unrelated to the incident.
- TACO is most often seen after transfusion of red blood cells (Figure 8).

Table 11 Overview of TACO reports in 2023 with definite, probable or possible imputability

	TACO N = 108
Sex (%)	
Female	54 (50%)
Male	54 (50%)
Age (years)	74 (64-82)
Time interval between start of transfusion and occurrence of transfusion reaction (hrs:min)	2:55 (1:27 – 4:31)
Severity grade of transfusion reaction (%)	
Severity grade 1	61 (56%)
Severity grade 2	34 (31%)
Severity grade 3	9 (8%)
Severity grade 4	4 (4%)
Imputability (%)	
Definite	5 (5%)
Probable	47 (44%)
Possible	56 (52%)

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

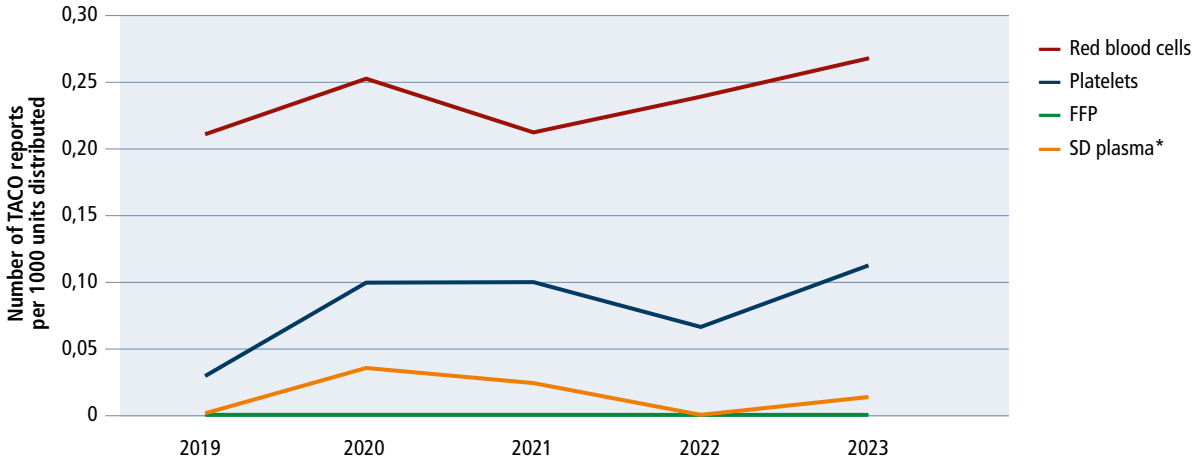

Figure 8 Number of TACO reports with definite, probable, possible imputability per 1,000 blood components distributed, 2019-2023

The reactions associated with more than one type of blood component were proportionally attributed to the respective blood component types.
** In the absence of distribution figures for SD plasma from 2021 onwards, reactions for the years from 2021 onwards are shown per 1,000 units transfused.*

Transfusion-related acute lung injury (TRALI)

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

In 2023, four TRALI reports were registered, reported by three different hospitals.

- TRALI was twice registered as an additional category together with a TACO report.
- All reports were assessed as at least possibly related to the transfusion (Table 12).
- Three of the four TRALI reports were recorded in combination with the transfusion reaction TACO in the additional category. This occurs when the clinical findings are consistent with both TRALI and TACO, and/or in the absence of data to determine whether or not a relevant increase in left atrial pressure is present.
- TRALI occurred twice after administration of RBC units, once after administration of platelets and once after administration of convalescent anti-COVID-19 plasma (Figure 9).
- In two TRALI cases known to TRIP, Sanquin investigated the presence of leukocyte antibodies in the serum of the patient and the donors: In both cases, no HLA antibodies were detected in the serum of both patients and donors. The serological examination did not provide any explanation for the clinical picture.

Table 12 Overview of TRALI reports in 2023

	TRALI N = 4
Sex (%)	
Female	1 (25%)
Male	3 (75%)
Age (years)	47-82
Time interval between start of Tf and occurrence of transfusion reaction (hrs:min)	1:25 – 4:29
Severity grade of transfusion reaction (%)	
Severity grade 3	3 (75%)
Severity grade 4	1 (25%)
Imputability (%)	
Possible	4 (100%)

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

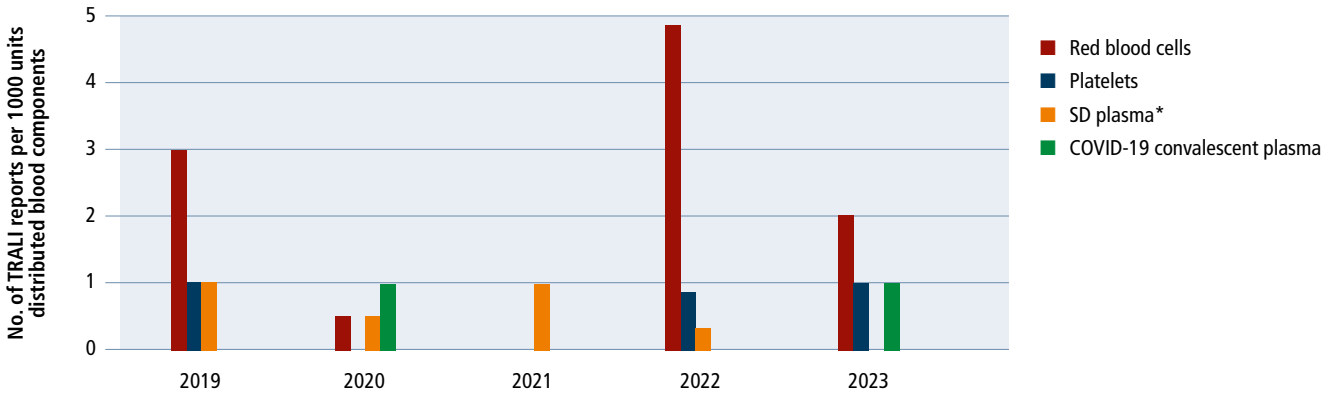

Figure 9 TRALI case per type of blood component (definite, probable or possible imputability), 2019-2023

The reactions associated with more than one type of blood component were proportionally attributed to the respective blood component types.

Transfusion-associated dyspnea (TAD)

Shortness of breath or hypoxia during or up to 24 hours after transfusion, but the criteria for TRALI, TACO and allergic (anaphylactic) reaction are not met. Respiratory problems are the most prominent symptom and they cannot be explained by the patient's underlying medical condition or another known medical cause.

TRIP registered 16 reports of TAD, of which 15 with definite, probable or possible imputability.

- TAD was twice registered as an additional category together with another type of transfusion reaction.

Although there are ongoing international studies into respiratory transfusion reactions, the pathology of TAD is still unresolved. It therefore remains an exclusion diagnosis.

Table 13 Overview of TAD reports in 2023 with definite, probable or possible imputability

	TAD N = 15
Sex (%)	
Female	9 (60%)
Male	6 (40%)
Age (years)	80 (31-91)
Time interval between start of Tf and occurrence of transfusion reaction (hrs:min)	2:00 (0:35 - 4:36)
Severity grade of transfusion reaction (%)	
Severity grade 1	12 (80%)
Severity grade 2	3 (20%)
Imputability (%)	
Probable	2 (13%)
Possible	13 (87%)

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

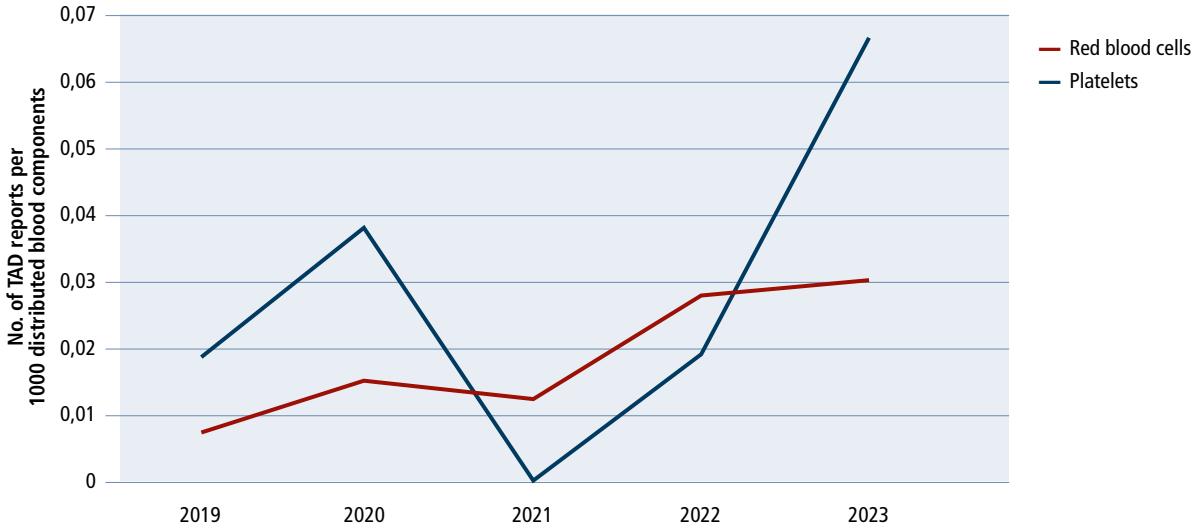

Figure 10 Number of TAD reports with definite, probable, possible imputability per 1,000 blood components distributed, 2019-2023

The reactions associated with more than one type of blood component were proportionally attributed to the respective blood component types.

Acute hemolytic transfusion reaction (AHTR)

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

A total of 18 AHTR reports were received (up from 9 in 2022), all occurring during or after administration of units of RBC. Number of reporting hospitals: 15 (19%), range: 1-2 reports per hospital.

- Seventeen reports (94%) with definite, probable or possible imputability, see Table 14.
- Seven reports of serious reactions (severity grade 2 and higher) with imputability definite, probable or possible.
- Four reports of AHTR in combination with an incident of incorrect blood component transfused.
  - One reaction of severity grade 2 resulted from an ABO incompatible transfusion during surgery with massive bleeding, IBCT is the reporting category and is described in the Report of the Month 2024 - 1.
  - One reaction of severity grade 1 involved an antibody incompatible transfusion, a patient with anti-K received K+ units because the screening was incorrectly interpreted as negative.
  - In one case, the patient's transplant status was unknown to the lab, and units were incorrectly issued after Type and Screen test. At a later stage, following a hemolytic transfusion reaction of severity grade 2, anti-A1 was detected.
  - In one case, units with positive cross matches were intentionally issued but not in the correct order. The 2+ bags were transfused first, leading to transfusion reaction (severity grade 2). The plan had been to administer the 1+ bags first.
- Three reports concern patients with previously undetected irregular antibodies. In all cases, the administered units were antigen-positive for the newly identified antibody in the patient. In one report, the antibody (anti-Wra) had likely already developed in the patient but was undetectable. Hemolysis was present alongside auto-antibodies, and may have worsened during transfusion.

Table 14 Overview of reports of acute hemolytic transfusion reactions with definite, probable or possible imputability

	AHTR N = 17
Sex (%)	
Female	9 (53%)
Male	8 (47%)
Age (years)	68 (0-84)
Time interval between start of Tf and occurrence of transfusion reaction (hrs:min)*	02:30 (00:30-06:48)
Severity grade of transfusion reaction (%)	
Severity grade 1	10 (59%)
Severity grade 2	7 (41%)
Imputability (%)	
Definite	4 (24%)
Probable	9 (53%)
Possible	4 (24%)
Cause	
ABO incompatibility (reporting category IBCT)	1
Irregular antibodies incompatibility (additional category IBCT)	1
Irregular antibodies not previously detected (anti-Fy(a); anti-Jk(a); 1 x anti-Wr(a))	3
Presence of other antibodies with IBCT (anti-A1; anti-Yt(a))	2
Presence of other antibodies (HLA; cold-reactive)	2
Autoimmune hemolytic anemia, worsening during transfusion	1
No clear cause was demonstrated	7

Values are expressed in numbers (%) or medians (ranges)
** in one case, interval unknown (within 24 hours of transfusion start)*

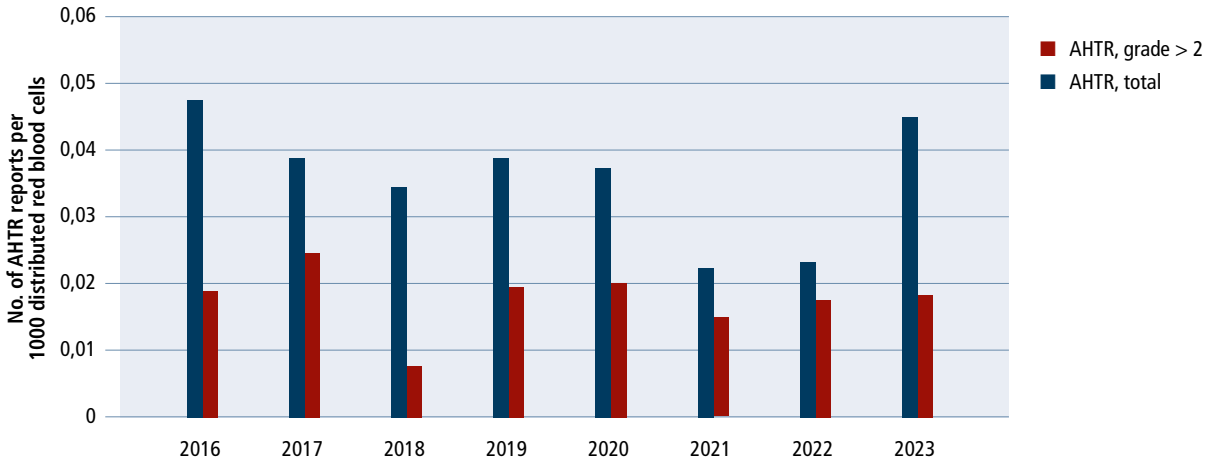

Figure 11 Number of acute hemolytic transfusion reaction reports with definite, probable, possible imputability per 1,000 RBC concentrates distributed, 2016-2023
Including hemolytic reactions when incorrect blood component transfused or new antibody formation is detected

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.

Nine reports (all in units of RBC) received from seven hospitals.

- Eight reports with definite, probable or possible imputability, see Table 12.
- The formation of new antibodies was demonstrated in four cases:
  - anti-Fy(a)
  - anti-Jk(b) + anti-S
  - anti-c + anti-Jk(a)
  - anti-Jk(b), likely due to the boosting of pre-existing but previously undetected antibodies.
- Hemolysis occurred post-transfusion in three cases with pre-existing hemolysis, two patients with sickle cell anemia and one patient with autoimmune hemolytic anemia.
- In one case, no cause of hemolysis was identified. The patient experienced a Hb decrease two weeks post-transfusion, which was faster than expected given the underlying disease.

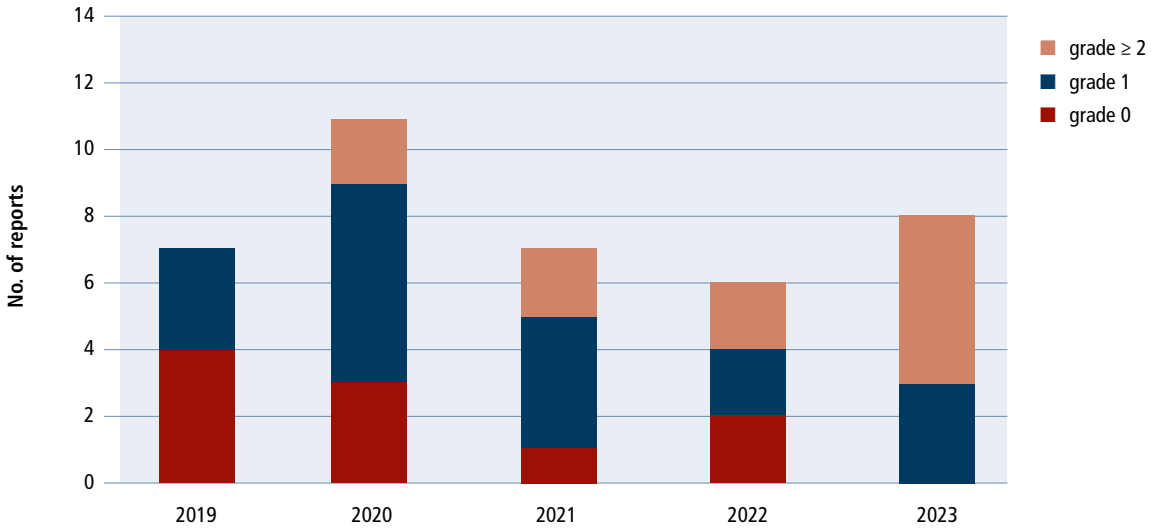

Figure 12 Severity of reports of delayed hemolytic transfusion reactions (definite, probable, possible imputability), 2019-2023

New 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.

Four reports of new antibody formation were received from four different hospitals.

- Two reports of antibody formation (anti-c; anti-K) due to incorrect product selection, these were reported as incorrect blood component transfused and are described in § 3.1.
- Two reports of antibody formation (anti-c; anti-E) following administration of platelet concentrates to patients subject to preventive product selection for Rhesus phenotype in case of RBC transfusion.

Allergic reaction – 2023: new, combined definition

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

A total of 117 reports of allergic reactions were submitted in 2023, compared to 119 reports in 2022, which includes late reports from that year (33 anaphylactic reactions and 86 other allergic reactions). Number of reporting hospitals: 32 hospitals (40%), range: 1-35 reports per hospital.

- 116 reports (99%) were classified with definite, probable or possible imputability, see Table 15.
- The number of reports (N = 14) of serious allergic reactions (grade 2 and higher) with definite, probable or possible imputability has remained stable since 2018 except for a peak in 2020 (N = 28).
- Five allergic reactions were reported in the additional category, 1 case of mild NHFR,1 case of post-transfusion bacteremia/sepsis and 3 cases of other reactions.
- In 2023, a new combined definition for allergic reaction was introduced, merging the previous definitions of anaphylactic reaction and other allergic reaction.
- 50 reports of reactions with local skin or mucosal manifestations, without further symptoms.
- 34 reports of reactions with generalised manifestations, without further symptoms.
- 16 reports of local skin reactions and 4 reports of generalised skin reactions accompanied by other symptoms, such as dyspnea, low blood pressure and/or gastrointestinal complaints.
- Twelve reactions presented symptoms of an allergic reaction without skin involvement.
- Of the 14 serious allergic reactions, 7 occurred without skin symptoms.
- In six cases, further research for IgA deficiency was conducted; one patient was found to have an IgA deficiency without the presence of anti-IgA antibodies. In one case, the patient had anti-IgA antibodies, providing an explanation for the serious systemic allergic reaction.

Table 15 Overview of reports of allergic reactions with definite, probable or possible imputability

	Allergic reaction (N = 116)
Sex (%)	
Female	56 (48%)
Male	60 (52%)
Age (years)	49 (IQR 15-69)
Time interval between start of Tf and occurrence of transfusion reaction (hrs:min)	01:05 (00:39-02:04)
Severity grade (%)	
Severity grade 1	102 (88%)
Severity grade 2	14 (12%)
Imputability (%)	
Definite	6 (5%)
Probable	65 (56%)
Possible	45 (39%)
Component (%)	
Red blood cell concentrate	45 (39%)
Platelet concentrate	53 (46%)
SD plasma	7 (6%)
COVID-19 convalescent plasma	2 (2%)
Combination of blood components	9 (8%)
Symptoms (number of reports)	
Itching, urticaria, redness -local	63 (55%)
Itching, urticaria, redness -generalised	38 (33%)
Swelling of tongue, lips, eyelids	10 (9%)
Glottal edema	1 (1%)
Increase in temperature 1-2°C	16 (14%)
Rise in temperature ≥ 2°C	4 (3%)
Chills	16 (14%)
Unresponsive / less responsive	1 (1%)
Dyspnea / saturation drop	20 (17%)
Hypotension	11 (9%)
Nausea/vomiting/diarrhea	10 (9%)

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

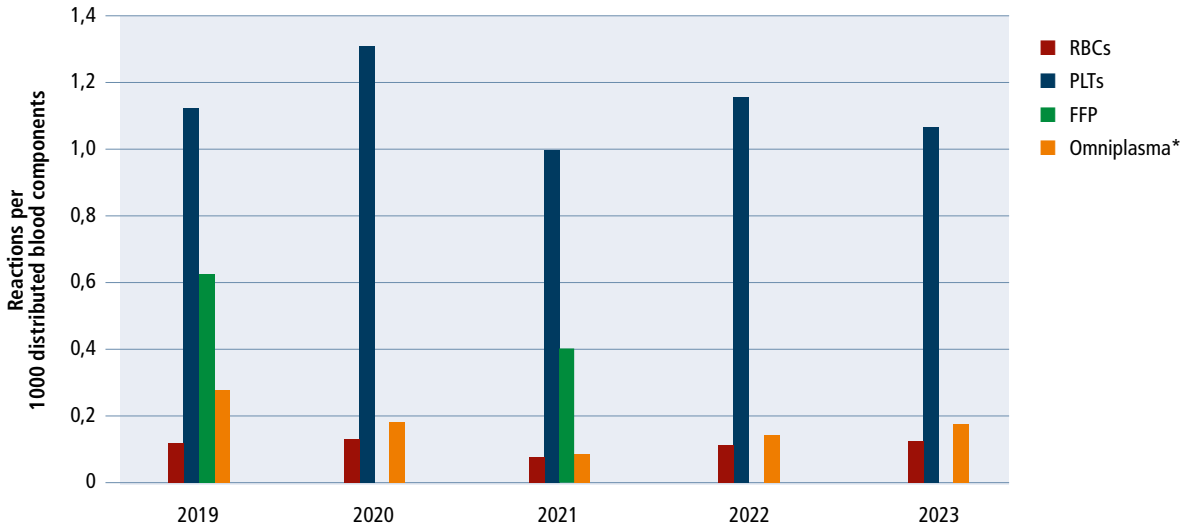

Figure 13 Number of allergic reactions with definite, probable or possible imputability per 1,000 blood components distributed

Reactions associated with more than one type of blood component were proportionally attributed to the respective blood component types.
Two reactions after convalescent anti-COVID plasma (3.9/1,000 distributed units CCP).
** For SD plasma (Omniplasma®), only units transfused were reported in 2021-2023.*

Non-hemolytic reactions

Non-hemolytic transfusion reaction (NHTR)

Increase in temperature of ≥ 2°C (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)

Increase 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 612 reports of non-hemolytic reactions, non-hemolytic transfusion reactions and mild non-hemolytic febrile reactions (284 and 328, respectively), compared to 608 reports (299 and 309, respectively), including late reports from 2022. Number of reporting hospitals: 70 hospitals (88%), range: 1-45 reports per hospital.

- Number of reports with definite, probable, possible imputability is 533 (87%), NHTR 242 (85%) and mild NHFR 291 (89%).
- The number of reports (N = 19) of serious non-hemolytic transfusion reactions (grade 2 or higher) with definite, probable or possible imputability is similar to that in 2022 (N = 21).
- Seventeen times, a mild NHFR or an NHTR were reported as the additional category in combination with an other type of transfusion reaction: 9x with an allergic reaction, 6x circulatory overload and 2x other reaction.
- Information on the reports is summarised in Table 16.

Table 16 Overview of reports of non-hemolytic reactions with definite, probable or possible imputability

	NHTR (N = 242)	Mild NHFR (N = 291)
Sex (%)		
Female	125 (52%)	138 (47%)
Male	117 (48%)	153 (53%)
Age (years)	66 (54-76)	70 (58-78)
Severity grade (%)		
Severity grade 1	227 (94%)	286 (98%)
Severity grade 2	14 (6%)	5 (2%)
Unknown	1 (0%)	
Imputability (%)		
Definite	4 (2%)	1 (0%)
Probable	26 (11%)	30 (10%)
Possible	212 (88%)	260 (89%)
Component (%)		
RBC	195 (81%)	268 (92%)
PLT	22 (9%)	12 (4%)
Anti-COVID-19 plasma	1 (0%)	0
Combination of blood components	24 (10%)	11 (4%)
Symptoms (number of reports)		
Rise in temperature < 1˚C		19 (7%)
Rise in temperature of 1-2˚C	93 (38%)	272 (93%)
Rise in temperature ≥ 2˚C	125 (52%)	
Chills	173 (71%)	
Tachycardia	45 (19%)	23 (8%)
Hypertension	19 (8%)	15 (5%)
Hypotension	7 (3%)	11 (4%)
Dyspnea/tachypnea	21 (9%)	5 (2%)
Nausea/vomiting/diarrhea	11 (5%)	6 (2%)

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

Other reactions

Transfusion reaction which does not fit into the categories above.

331 reports in 2023 (252 reports in 2022).

- In 2023, 253 reports of 'other reaction' had an imputability of definite, probable or possible (Table 17).
- The number of 'other reactions' characterised by dyspnea decreased to 34 in 2023, versus 49 in 2022. This may reflect a shift toward classification under the TAD and TACO categories.
- Over the past four years, the reaction category 'other reaction' has consistently been one of the second largest categories for reports with severity grade 2 or higher and definite, probable or possible imputability.
- Notable is the type of 'other reaction' where an increase in tension is the primary feature. In 2023, this was reported 46 times as definite, probable or possible as a result of the transfusion, compared to 11 reports in 2022.

Other reactions: what reactions are they?

If a transfusion reaction is recorded as an 'other' reaction, it must be clear why this category was chosen. TRIP has been using a breakdown into certain subgroups for several years (Table 17). 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 17 Overview of reports of 'other reactions' with definite, probable or possible imputability

Type of reaction	2022	2023 Imputability definite, probable	2023 Imputability possible	2023 Severity grade ≥ 2[a]
Reactions with hypotension	44	3	58	7 (4)
Subgroup hypotensive reaction (ISBT)[b]	4	0	6	1 (0)
Reactions met dyspnea	49	3	31	4 (13)
Hypertension	11	7	39	3 (1)
(Possibly) cardiac	15	1	5	2 (3)
Did not fully meet TRIP definitions of standard categories	29	6	33	7 (0)
Other symptoms/signs	40	9	58	16 (4)
Total	**188**	**29**	**224**	**39 (25)**

[a] *Number in 2023 (number in 2022)*
[b] *Drop in systolic blood pressure of ≥ 30 mm Hg and a systolic blood pressure < 80 mm Hg*

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.

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 47 reports of post-transfusion bacteremia/sepsis, up from 61 in 2022, including late reports (Table 18). Number of reporting hospitals: 27 hospitals (34%), range: 1-7 reports per hospital.

- 31 reports (66%) were classified with definite, probable or possible imputability, see Table 19.
- 4 serious reactions with reporting category of post-transfusion bacteremia/sepsis (grade 2 or higher) with definite, probable or possible imputability, in comparison to 7 in 2022.
- None of the post-transfusion bacteremia/sepsis reports in 2023 met the criteria for Transfusion-Transmitted Bacterial Infection (TTBI), see Figure 14.
- According to the TRIP definition, TTBI is diagnosed when identical micro-organisms are identified in both the recipient's blood culture and the blood component's culture, with transmission deemed definite, probable, or possible after evaluation by TRIP experts. If a positive blood culture is not obtained from the patient and/or no positive culture is detected in the blood component, TTBI is excluded (Figure 14).
- Five reports were made of bacterial contamination in blood components. In all cases, there was a positive culture result from the unit, often accompanied by another reaction, such as an increase in temperature.

Table 18 Overview of reports from hospitals relating to bacterial problems, 2019-2023

	2019	2020	2021	2022	2023
Post-transfusion bacteremia/sepsis	84	74	58	61	47
(assessed as TTBI)	(1)	(0)	(1)	(1)	(0)
Post-transfusion bacteremia/sepsis as additional category (not TTBI)	0	5	0	8	11
Bacterial contamination of blood component (including reports of positive bacteriological screening*)	1	0	1	0	0
Bacterial contamination of blood component (including reports of positive bacteriological screening) as additional category	12	9	7	2	5

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

Table 19 Overview of reports of post-transfusion bacteremia/sepsis with definite, probable or possible imputability

	Post-transfusion bacteremia/sepsis N = 31
Sex (%)	
Female	11 (35%)
Male	20 (65%)
Age (years)	68 (62-77)
Severity grade (%)	
Severity grade 1	27 (87%)
Severity grade 2	4 (13%)
Imputability (%)	
Probable	1 (3%)
Possible	30 (97%)
Component (%)	
Red blood cell concentrate	27 (87%)
Platelet concentrate	2 (6%)
Combination of blood components	2 (6%)
Symptoms (number of reports)	
Increase in temperature ≥ 1 < 2˚C	12 (39%)
Increase in temperature ≥ 2˚C	16 (52%)
Chills	19 (61%)
Dyspnea/saturation drop/tachypnea	9 (29%)
Hypotension (≥ 20 mm Hg syst and/or diast)	3 (10%)
Hypertension (≥ 20 mm Hg syst and/or diast)	15 (48%)
Tachycardia	12 (39%)

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

Post-transfusion other infection

In 2023, no report has been registered in the reporting category other post-transfusion infection.

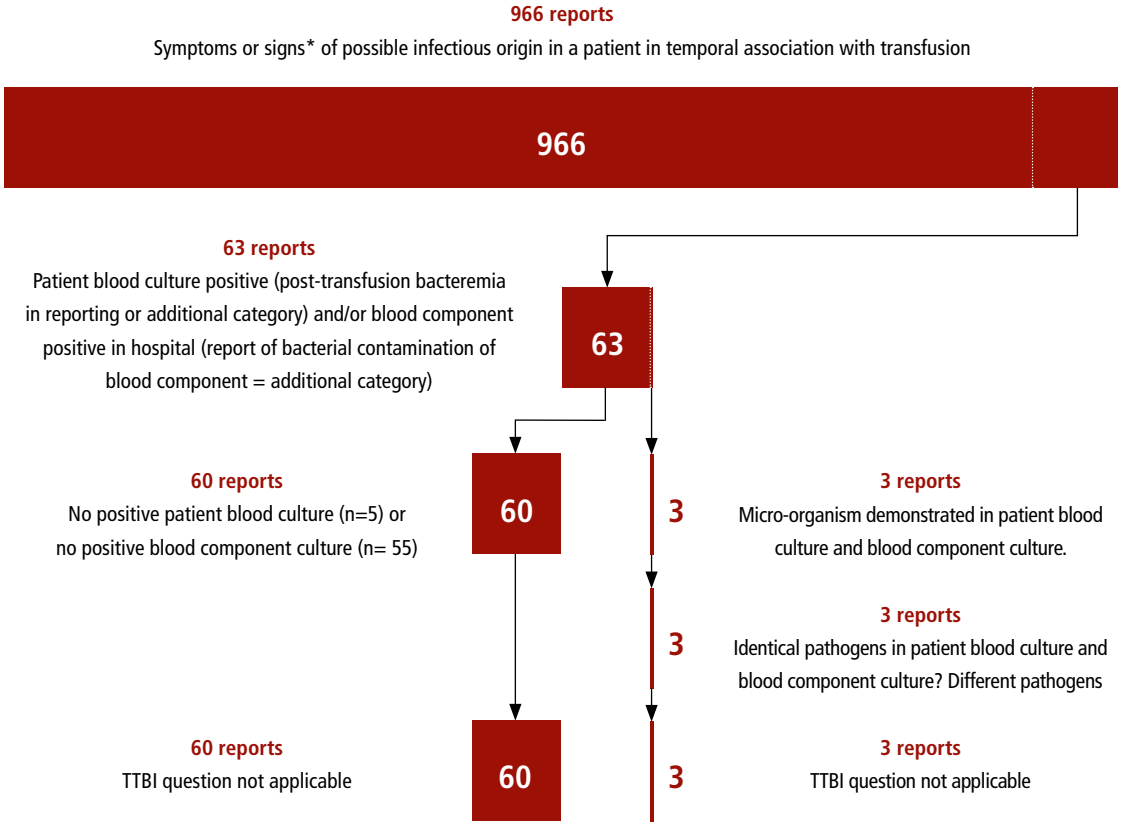

Figure 14 Did transfusion-transmitted bacterial infection (TTBI) occur?
** reactions in 2023 with increase or decrease in temperature > 1°C and/or chills, all imputabilities*

Table 20 Overview of positive bacteriological screening of platelets from units already issued by Sanquin

Total reported by Sanquin	2019	2020	2021	2022	2023
Number already administered (PLT concentrates and associated RBC)	81	84	73	63	74*

** in all cases a recall was issued, no serious reactions were reported.*

Post-transfusion viral infection

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

Information from hospitals

In 2023, there were no reports of post-transfusion viral infections..

Look-back/recall by the supplier

Retrospective notification of a possibly infectious donation (not being a bacterial contamination of a blood component) leading to testing of the recipient for that infection or possible consequences.

Information from hospitals

Hospitals only report a look-back to TRIP if there were consequences for the patient (a reaction, prolonged hospital stay, additional treatment, etc.). In 2023, no reports of look-backs/recalls were received from hospitals.

Information from Sanquin

In 2023, Sanquin performed a look-back procedure eleven times. In all cases, the look-back did not show that transmission of the infection took place.

Conclusion on infectious transfusion complications

No reports of transmitted infections were received in 2023.

3.4 Reports regarding SD plasma (Omniplasma®)

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® was rolled out as a standard plasma product for transfusion. Omniplasma® is an SD plasma produced from Dutch plasma donations. The plasma is collected by Sanquin and then processed by another party. Instructed by the pharmacist, it is distributed via Sanquin. Fresh Frozen Plasma (FFP) is still supplied by Sanquin for pediatric use and other special indications. Figure 1 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 (classified as definite, probable or possible) have been reported by TRIP to Lareb, except in cases of new antibody formation where cellular products have also been administered, and for incidents unrelated to product quality (reporting 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. TRIP hemovigilance reporting helps maintain a complete picture of the transfusion chain at the same time.

A total of 17 reactions related to SD plasma and one incident were reported to TRIP in 2023, compared to 24 reports in 2022. One reaction with unlikely imputability is not considered further in this report. Four reactions were classified as serious, all with severity grade 2 and possible imputability (Table 21). Eight reports also involved the administration of short-lived blood products prior to the reaction or incident. The largest numbers of reactions, as before with FFP, are the allergic reactions.

Table 21 Reports relating to SD Plasma in 2023 (N = 17)

Type of reaction	Non-serious reactions		Serious reactions[a]	
	Only SD	SD in combination	Only SD	SD in combination
Allergic reaction	7	1		1
Mild non-hemolytic febrile reaction		2		
Non-hemolytic transfusion reaction		1		
Other reaction	1		1	1
Circulatory overload				1
Incorrect blood component transfusedb		1		

[a] *Severity grade ≥ 2 and definite, probable or possible imputability*
[b] *Identification error with AB0 risk, incidentally compatible, see § 3.1*

4 GENERAL

4.1 TRIP working methods 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 to improve transfusion safety. The incidence of known adverse effects of blood transfusions is tracked and previously unknown reactions to transfusion of current or new blood products can be detected in a timely fashion.

The TRIP foundation (Transfusion (and Transplantation) Reactions In Patients) was founded in 2001 by representatives of the various professional associations 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 contacts at 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/trip-reports. TRIP is advised by the Hemovigilance and Biovigilance Advisory Boards, which consist of representatives of the professional associations.

In principle, reporting to TRIP is anonymous and voluntary. Nevertheless, it is regarded as the professional standard by the Healthcare Inspectorate (IGJ) and the national Blood Transfusion Policy Guidelines 2020. Reporting to TRIP is separate from the hospital's responsibility to provide quality of care.

Reporters of transfusion reactions and incidents are asked to provide the results of relevant tests and 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 the quality and/or safety of blood components. In the Netherlands, these requirements have been implemented in 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 submit serious reports (severity grade 2 or higher) to the Healthcare Inspectorate and to 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 the figures for the distributed blood components. Each year, TRIP and Sanquin match up relevant serious reports which have been submitted via 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 submitted 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 a national level depends on the participation of all the reporting institutions. In 2023, there were 80 contact addresses for hospitals. In total, TRIP received reports from 74 hospitals (before the cut-off date). Five hospitals indicated that there had been no reports in the TRIP reporting categories in 2023. One hospital had not provided any information about reports when this annual report was drawn up. The participation rate among hospitals for reporting and submitting data on administered blood products is 79/80 (99%).

In addition to the hospitals, there are eight 'designated institutions' which have been licensed by the Ministry of Health, Welfare and Sport to receive blood components from Sanquin and and provide transfusions to their patients. Four of the eight licensed institutions submitted data in 2023, of which three reported that they had not administered any blood components in that year. Four institutions informed TRIP that the blood component figures and reports of any reactions would be provided by the transfusion labs with which they have contracts for the provision of blood components.

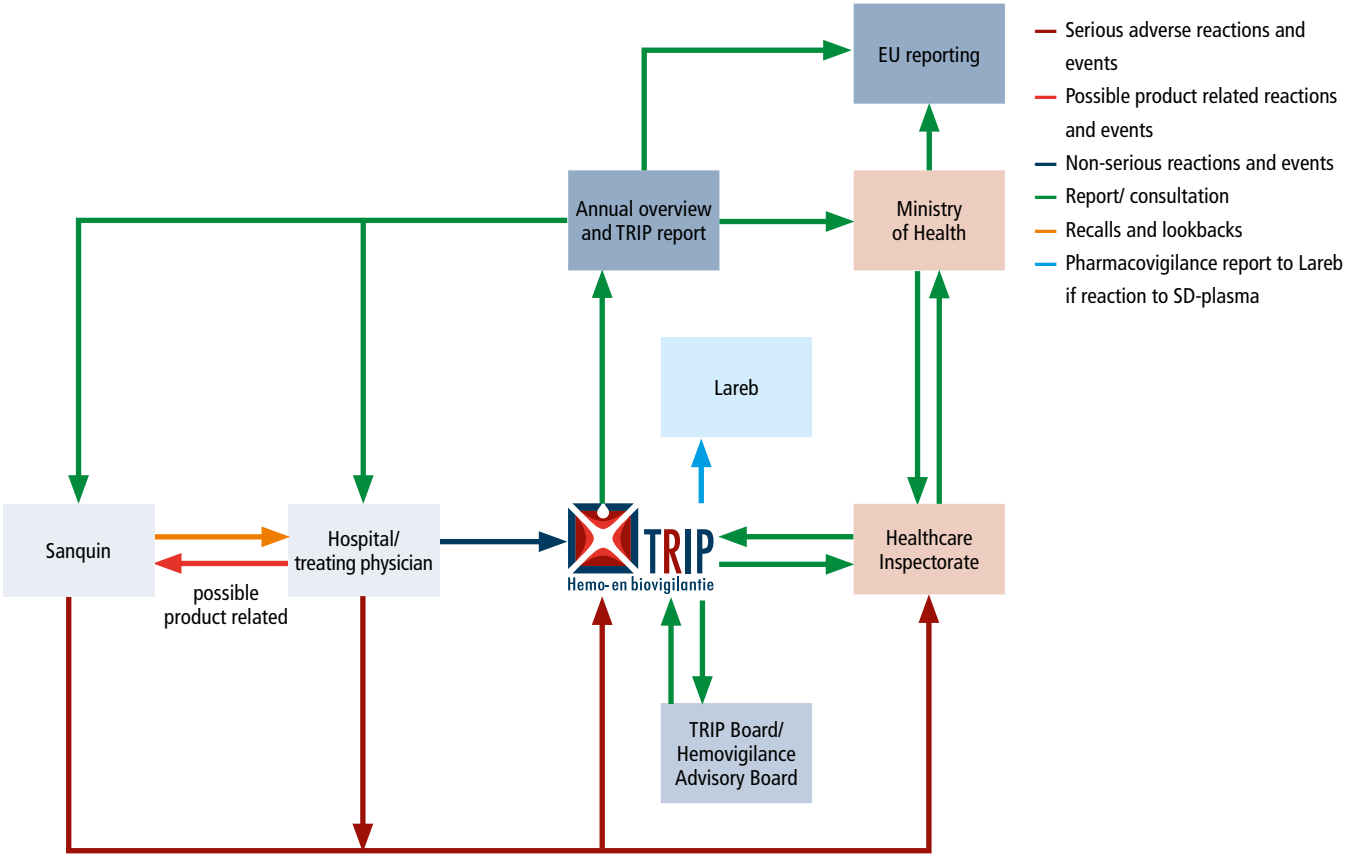

Figure 15 Flow of hemovigilance information and outputs in the Netherlands

LIST OF TERMS AND ABBREVIATIONS

AHTR	Acute hemolytic transfusion reaction
AIHA	Auto-immune hemolytic anemia
AML	Acute myeloid leukemia
APTT	Activated partial thromboplastin time
BC	Blood component(s)
BNP	Brain-type natriuretic peptide
CCP	COVID-19 convalescent plasma
COVID-19	Coronavirus disease 2019
CT	Computed tomography (imaging)
DEHP	Di(2-ethylhexyl)phtalate, plasticiser used in the production of PVC
DHTR	Delayed hemolytic transfusion reaction
ED	Emergency Department
EU	European Union
FFP	Fresh frozen plasma
Hb	Hemoglobin
HLA	Human leukocyte antigen
IBCT	Incorrect blood component transfused
ICU	Intensive Care Unit
IGJ	Inspectorate for Healthcare and Youth
IQR	Interquartile range
Irrab	Irregular antibodies
Mild NHFR	Mild non-hemolytic febrile reaction
NaCl	Sodium chloride 0.9%, solution for infusion
NHTR	Non-hemolytic transfusion reaction
NM	Near miss
NVB	Netherlands Blood Transfusion Association
OI	Other incident
PAS-E	Platelet additive solution-E with acetate, potassium, magnesium and phosphate
PLT	Platelet concentrate
POCT	Point of care testing,a method of performing a laboratory test next to or near the bed
PTP	Post-transfusion purpura
RBC	Red blood cell concentrate
Rh	Rhesus factor
Sanquin	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®
T&S	Type and Screen, compatibility test
TACO	Transfusion-associated circulatory overload, volume overload associated with blood transfusion
TAD	Transfusion-associated dyspnoea
TA-GvHD	Transfusion-associated graft versus host disease
Tf	Transfusion
TR	Transfusion reaction
TRALI	Transfusion-related acute lung injury
TRIP	TRIP Foundation (Transfusion and Transplant 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	Quality, Complaints and Disputes in Healthcare Act