

TRIP REPORT 2022

HEMOVIGILANCE

EXTENDED VERSION



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TRIP REPORT 2022

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EXTENDED VERSION



The TRIP report 2022 hemovigilance, extended version, is published under the responsibility of the TRIP
(Transfusion and Transplantation Reactions in Patients) Foundation.

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FOREWORD

In this Hemovigilance 2022 report, we endeavour to inform you once more about the yearly reports and findings of this important subject matter. This annual report has been published since 2003 and it remains vital to continue monitoring the reports and use its figures to assess the extent to which (patient) safety of labile blood components is indeed guaranteed. The high participation rate of Dutch hospitals is and remains striking, as well as the willingness to report incidents and any questions arising from them. It is a sign that the Dutch hemovigilance community is certainly not suffering from 'reporting fatigue'.

We have attempted to present the data in this annual report as clearly as possible to make the interpretation of the data a bit easier. To this end, we tried to limit the amount of text and display tables and figures in such a way that the information can be viewed efficiently.

In terms of the substance of the incidents and reactions reported, there seems to be a stable picture compared to 2021. The percentage of respiratory complications reported remains consistently high. Last year, my predecessor, Jaap Jan Zwaginga, suggested that the COVID pandemic could possibly have an exacerbating effect. Given the stable number of reports, this does not seem to be the case. If we take into account that not all reactions will be reported, and therefore there will be underreporting, this observation does provide food for thought. After all, shortness of breath, for example caused by circulatory (over)load, is a complication that could be addressed before starting the transfusion. Despite the measures taken by TRIP, such as the development of the TACO tool, raising awareness within the clinics about this complication must remain a continuous point of attention.

In conclusion, many individuals have once again undertaken a considerable amount of work, leading to the creation of this report with recommendations. It is impossible to thank everyone for their input. Still, there is one person who deserved a special mention: From the start, Jo Wiersum-Osselton has been our tower of strength for Hemovigilance Netherlands! Her tireless efforts as national coordinator have led TRIP to achieve its current outstanding level! We are very grateful for her hard work. Jo herself always emphasises that hemovigilance is a joint, constantly innovating activity. Let's keep going together and, together with the TRIP team ensure that hemovigilance provides us with ever better resources to improve the safety of blood transfusions.

Dr Peter A.W. te Boekhorst
President TRIP Foundation

1 MAIN FINDINGS 2022

1.1 Hemovigilance in 2022

In 2022, a total of 1,281 reports were submitted to TRIP before the cut-off date (28 February 2023) for this report. These included 1,167 reports of reactions and 133 reports of adverse events (incidents), with 19 reports describing a combination of an incident and reaction. The numbers are stable compared to 2021.

The number of reports should be seen in relation to the number of units distributed and transfused (Figures 1 and 2). A similar number of red blood cell and platelet concentrates were distributed in 2022 as in 2021. 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 2.32 per 1,000 blood components compared to an average of 2.49 in 2017-2021, and the number of severe reactions is 0.22 per 1,000 blood components (2017-2021: 0.24).

In 2022, one serious report of post-transfusion bacteremia, which showed *Actinomyces* 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). The relevance of a positive culture result is not always easy to judge in reports of transfusion reactions, which has led to Recommendation 1. There were no reports of viral transmissions. The reports indicate a very low incidence of infections transmitted by blood transfusion: 1 in about 487,000 units transfused.

In line with previous years, respiratory transfusion reactions are the leading cause of transfusion-associated morbidity and mortality. TACO is the transfusion reaction with the highest number of serious reports and transfusion-associated deaths. In 2022, six reports with at least possible imputability were assessed as TRALI, the highest number of cases received in the past five years. In one report in which TRALI occurred during the transfusion of an RBC unit, the donor was found to have HLA class I and II antibodies directed against the patient's HLA antigens.

In 2022, the number of incidents was comparable to 2021. In the reporting category Incorrect Blood Component Transfused (IBCT), in 13 reports it was not taken into account that the recipient should receive matched units to prevent irregular antibody formation as described in the hospital protocol. This poses a risk of allo-immunisation due to non-compliance with preventive selection criteria. Three times the transfusion of the wrong product led to a reaction and once a reaction led to the discovery of an IBCT. Three times, an IBCT led to new antibody formation. Most near misses arose from identification errors at sampling at the time of the transfusion request (29/34) which were most often discovered because a blood group discrepancy was found (16/34). In the other incidents category, in 57% of the cases units were partially or completely lost.

As in other years, the participation of hospitals in hemovigilance is high, 81 out of 82 transfusing hospitals (99%) provided information. Besides hospitals, there are eight designated institutions in the Netherlands that can independently request and transfuse blood components; information was received from all eight institutions.

The 2022 annual report is the twentieth TRIP hemovigilance report to be published. The first annual report, from 2003, described the start of the national hemovigilance system, with a hospital participation of 80% and 1,092 reports submitted. The system quickly grew into a mature system with national support, thanks to the collaboration with hospitals and other partners in the blood transfusion chain. This has enabled TRIP to contribute to national and international scientific research, such as on TRALI, with the aim of increasing the safety of blood transfusion.

In conclusion, this twentieth annual hemovigilance report shows a safe and stable picture of the blood transfusion chain in the Netherlands in 2022. This robust hemovigilance system offers the opportunity to monitor changes in the transfusion chain, for instance by as intensive monitoring after the introduction of new products, and in addition to analysing reactions and incidents, also to learn from each other's best practices.

1.2 Recommendations

Recommendation	Who?
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 good working methods with regard to the sending in material for (blood) culture (see Blood Transfusion Policy Guidelines).	Medical microbiologists, clinicians, hemovigilance professionals and TRIP
2 Identifying best practices within hemovigilance and promoting them, by looking for differences in practice that are not clearly adressed in the Blood Transfusion Policy Guidelines.	Hemovigilance professionals, Hemovigilance Platform Netherlands and TRIP

1.3 Follow-up to previous years

- 1 Strengthening the post-authorisation monitoring of new blood components by facilitating routes for reporting and supporting hemovigilance professionals in additional tasks, including conducting clinical research. This also applies to products not administrated by transfusion, such as serum eye drops.

Development:

In 2022, Sanquin's non-DEHP pilot study used the TRIP reporting system and the possibility of allowing Sanquin to view reaction reports through this system. TRIP carried out additional checks on the required information in the reports and generated overviews of the relevant reference numbers of the reports from the participating hospitals. This method will be continued for the follow-up study in 2023. The reporting system also offers the opportunity to report reactions to new products that are not administered via transfusion, such as serum eye drops; no reports were received regarding these products in 2022.

2 OVERVIEW OF 2022 HEMOVIGILANCE DATA

2.1 Overview of 2022 hemovigilance data in comparison with previous years

Of the 1,281 reports received by TRIP before the cut-off date for this report, 28 February 2023, 1,148 reports concerned reactions. A total of 114 incidents were reported, with 19 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.

TRIP records reports of transfusion reactions and incidents for all types of labile blood components, as well as for SD plasma (Omniplasma[®], see Chapter 3.4). Definitions of incident types, transfusion reactions, severity and imputability can be found on the TRIP website under Hemovigilance and Hemovigilance definitions, as well as in the relevant chapters of this report. Since 2021, TRIP has only registered the formation of a new allo-antibody in cases where there was an incident, the national recommendations for optimal matching to prevent antibody formation could not be met, or a transfusion reaction occurred. As expected, this report contains a number of reports of new antibody formation; in most cases, this concerns an additional category in combination with a reaction.

One report describes a mild non-hemolytic febrile reaction after administration of granulocytes. Such reports also find their way within the biovigilance system, as TRIP sporadically receives reports regarding granulocyte products from (stem)cell laboratories.

In 2022, TRIP received three reports of a reaction after transfusion of COVID-19 convalescent plasma (CCP) (2021: 19 reports). Due to the small number, this annual report does not include a separate analysis of these reports as in the two previous annual reports. The reports are described in Chapter 2.4.

Two labile blood products (prepared from small pools of donor units) have been supplied by Sanquin for several years now and are not considered 'classic' blood components for transfusion.

- 1 Fitrix[®] is a fibrin glue made of two components (cryo-precipitate and thrombin, frozen) from donor blood for local administration on wounds.
- 2 Serum eye drops are prepared as a 50% preparation from small pools of male AB donor blood. In 2022, the distribution of eye drops increased by more than half compared to 2021.

Reports on these products are registered by TRIP in principle and are important because of the need for intensive monitoring of these newly authorised products. No reports on these products have been received to date.

Reported data are presented in the following tables and figures:

Table 1	Reported incidents, 2018-2022
Table 2	Reported transfusion reactions, 2018-2022
Table 3	Number of reports per type of blood component in 2022
Table 3a	Types of blood components for each type of reaction or incident in 2022*
Table 3b	Types of reactions and incidents for each type of blood component in 2022*
Table 4	Severity grade 4 reports in 2022
Table 5	Severity grade 4 reports (with definite, probable or possible imputability) 2013-2022
Table 6	Late reports from 2021 (received after 28 February 2022)
Figure 1	Distributed units of blood components per year, 2013-2022
Figure 2	Transfusion reactions per type of blood component, 2018-2022
Figure 3	Imputability of transfusion reactions, 2018-2022

Figure 4 Severity of transfusion reactions, 2018-2022

Figure 5 Serious transfusion reactions per year, 2018-2022

* Additional online tables can be accessed through hyperlink

Table 1 Reported incidents, 2018-2022

Incident	2018	2019	2020	2021	2022	Number of hospitals with reports in 2022
Incorrect Blood Component Transfused	41	42	44	26	28	18
Near miss	35	70	41	29	34	14
Other incident	94	87	100	74	68	24
Calculated risk situation	11	17	8	8	1	1
Other categories of incidents ^a	15	20	10	8	2	2
Total	196	236	203	145	133	40

^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 (2 in 2022; see Chapter 3.3).

Table 2 Reported transfusion reactions, 2018-2022

Reaction	2018	2019	2020	2021	2022	Severity grade $\geq 2^a$	Number of hospitals with reports in 2022
Circulatory overload	134	91	112	102	100	33	46
TRALI	4	6	2	1	7	5	6
Transfusion-associated dyspnoea	5	4	8	5	13	1	10
Acute hemolytic transfusion reaction	16	16	15	9	9	7	9
Delayed hemolytic transfusion reaction	4	3	6	5	6	2	6
New antibody formation	654	724	627	5	3	0	2
Anaphylactic reaction	58	25	48	20	30	10	19
Other allergic reaction	134	104	86	93	84	1	31
Non-hemolytic transfusion reaction	360	317	304	303	296	17	61
Mild non-hemolytic febrile reaction	327	284	298	327	306	4	56
Post-transfusion bacteremia/sepsis	72	84	74	58	60	7	34
Post-transfusion viral infection	0	0	0	0	0	0	0
Other reaction	288	257	330	245	252	25	60
Other categories of transfusion reactions ^b	0	3	0	0	1	0	1
Total TR	2,056	1,918	1,910	1,173	1,167	112	73
Total severity grade $\geq 2^a$	121	104	140	122	112		
Total reports	2,198	2,112	2,081	1,300	1,281		

^a Imputability definite, probable or possible.

^b Concerns reports of other post-transfusion infections (2019;3, 2022;1), no reports received in the other categories (such as post-transfusion purpura or TA-GvHD).

Table 3 Number of reports per type of blood component in 2022

Type of blood component	Units distributed in 2022	Units administrated in 2022 ^a	No. of reports		Reports per 1000 Blood components	
			All	Serious ^b	All	Serious ^b
Red blood cell concentrate	393,860	380,836	1,033	90	2.62	0.23
Platelet concentrate	51,466	50,102	145	13	2.82	0.25
Fresh frozen plasma	1,862	901	0		0.00	
SD plasma ^c		53,109	12	0	0.23	0.00
Fitrix [®] fibrine glue	13	14	0		0.00	
Serum eye drops	1,673	1,350	0		0.00	
Anti-COVID-19 plasma	445	433	3	2		
Other blood components			1	0		
Combinations ^d			50	7		
No blood components involved (incidents)			37			
Total	449,319	486,745	1,281	112	2.56^e	0.22^e

^a Data received from 81/82 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.

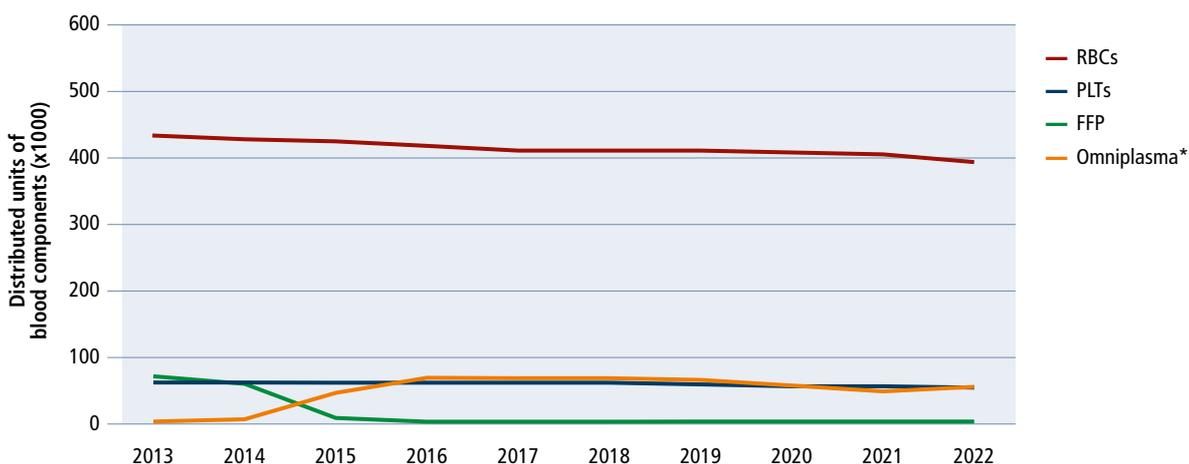


Figure 1 Distributed units of blood components, 2013-2022

* For SD plasma (Omniplasma[®]), the units transfused are reported for 2013-2015 because of the roll-out phase; the units transfused in 2021 and 2022 are reported because distribution data was not available.

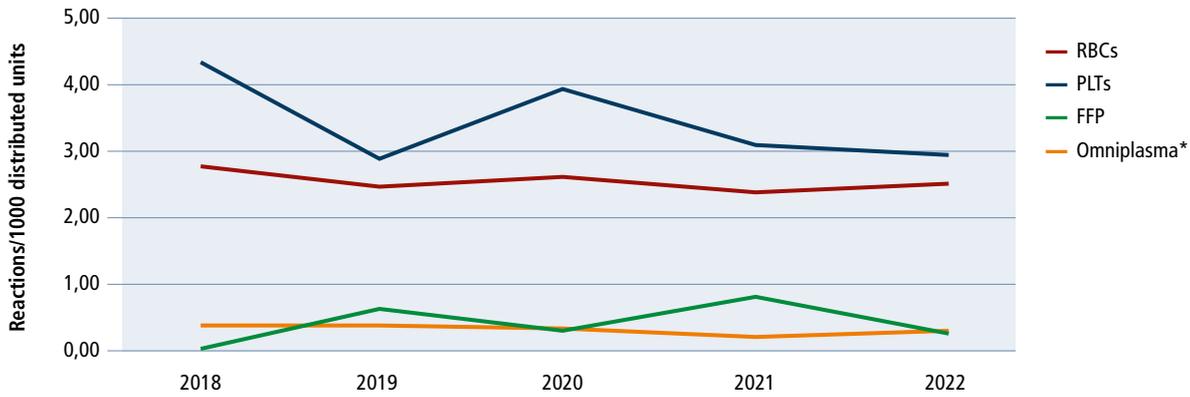


Figure 2 Transfusion reactions per type of blood component, 2018-2022

* For SD plasma (Omniplasma®), only units transfused are reported in 2021 and 2022.

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.).

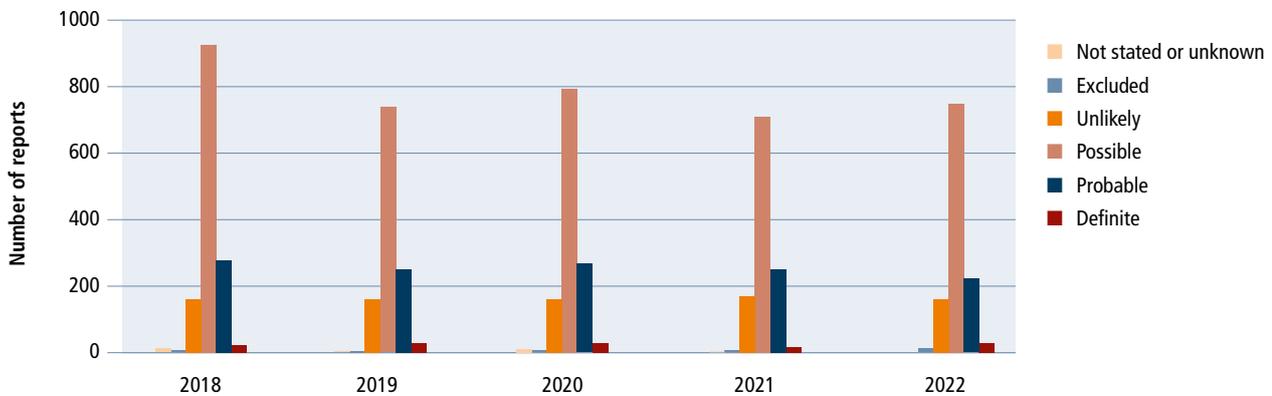


Figure 3 Imputability of transfusion reactions, 2018-2022

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

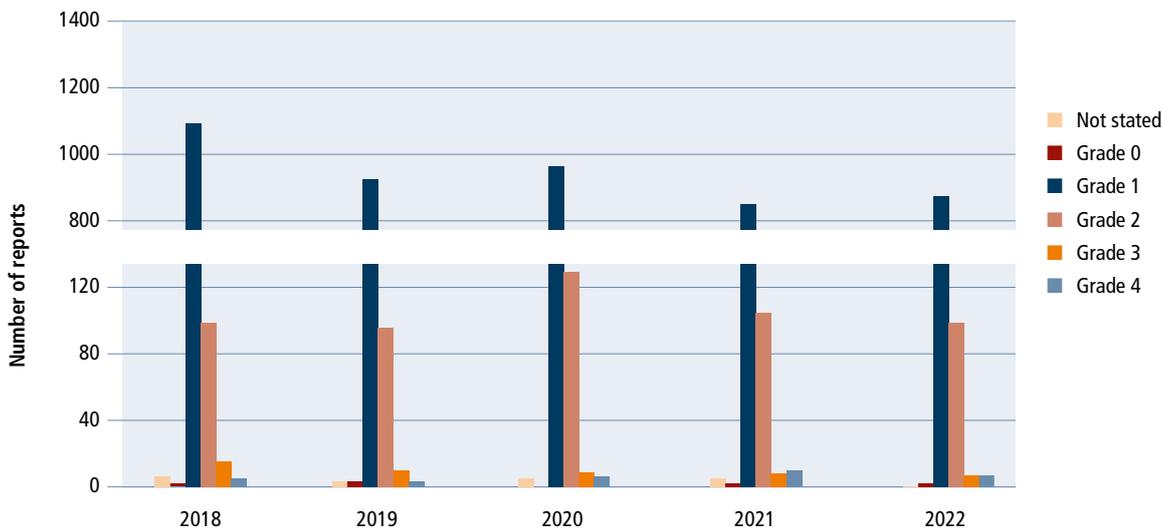


Figure 4 Severity of transfusion reactions (definite, probable, possible imputability), 2018-2022

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

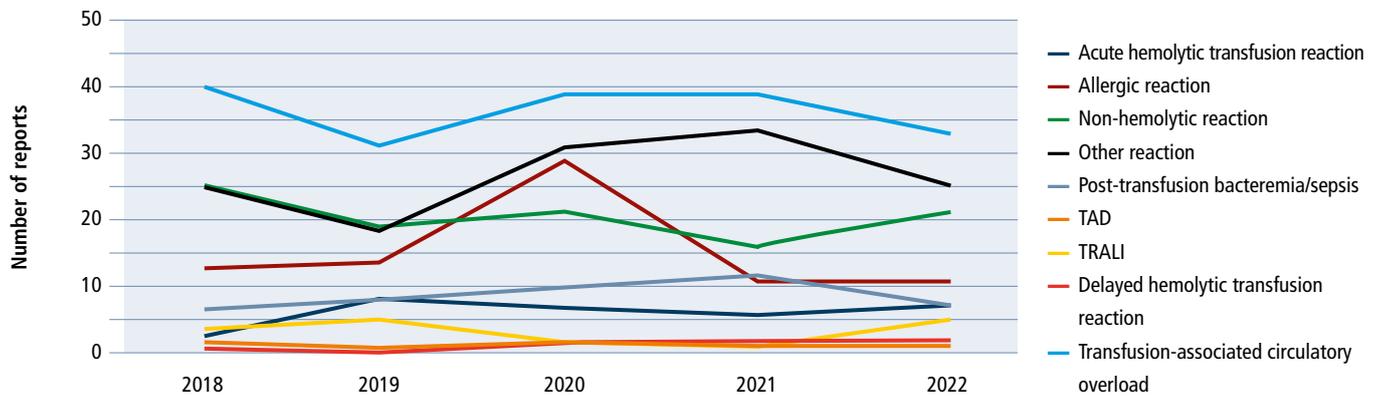


Figure 5 Serious transfusion reactions (definite, probable, possible imputability), 2018-2022

Table 4 Severity grade 4 reports in 2022

Reaction	Blood component	Sex, age group	Imputability	Symptomatology
TRALI	RBC	M, 70-80	Probable	Patient with MDS develops fever, chills and saturation drop during transfusion (Tf). Chest x-ray shows clouding of lungs; HLA class 1 and 2 antibodies are found in donors directed against patient's antigens. Also <i>E. coli</i> bacteremia in patient. Ventilation administered, nevertheless died that same day.
Other reaction	COVID-19 convalescent plasma	F, 60-70	Possible	See Chapter 2.4, Table 8
Circulatory overload	RBC	F, 40-50	Possible	Lymphoma, recent autologous stem cell transplant. Two hours after Tf; dyspnoea, saturation drop and tachycardia. Little response to furosemide. Initially stabilised, but acute deterioration one day later, despite resuscitation patient died.
Circulatory overload	RBC	F, 70-80	Possible	Patient with metastatic lung carcinoma and clinical decline, Tf in preparation for chemotherapy. After 20 ml, increase in temp, blood pressure and pulse, O ₂ saturation drop, rapid deterioration. Chest x-ray showed progression of pulmonary vascular definition and the diagnosed tumor; NT-proBNP elevated 1.5 times. Palliative care policy in place because of seriously ill condition, death within 24 hours.
Circulatory overload	RBC	M, 80-90	Possible	Extensive cardiac history and signs of fluid overload; hemorrhage and collapse after traumatic decatheterisation. At 2nd EC, a saturation drop, followed by blood pressure drop and accelerated pulse with pre-existing atrial fibrillation. Also <i>Klebsiella oxytoca</i> bacteremia. Patient died two days later.
Circulatory overload	RBC, PLT	M, 60-70	Possible	After high-dose melphalan and stem cell transplant for multiple myeloma; dyspnoea, stridor and increase in blood pressure are observed after Tf. Chest X-ray showed some pulmonary vascular overload, NT-proBNP elevated. Patient died five days later.
Circulatory overload	RBC	M, 80-90	Possible	After Tf to a patient with myelofibrosis and increased bleeding tendency; a saturation drop of up to 79% Chest X-ray showed a vascular overload. Patient died of respiratory failure.
Circulatory overload	RBC	F, 80-90	Unlikely	After Tf of 20 ml in a patient with triple vessel disease and aortic valve stenosis; dyspnoea, saturation drop to 74% and reduced responsiveness. Patient died as a result of cardiac asthma.
Circulatory overload	RBC	M, 70-80	Unlikely	After 20 ml of red blood cells in a patient with COVID-19, pneumonia and refractory AML, dyspnoea, drop in saturation, drop in blood pressure and tachycardia. Palliative care policy started in the event of a pre-existing poor clinical condition. Patient died three days later.
Post-transfusion bacteremia/sepsis	RBC	F, 70-80	Unlikely	After 20 ml of red blood cells in a patient with cardiovascular risk, osteomyelitis and sepsis; chills, dyspnoea, decreased consciousness and stridor. The blood culture showed <i>Escherichia coli</i> and <i>Pseudomonas aeruginosa</i> , but a link with the transfusion seems unlikely.

Table 5 Severity grade 4 reports (with definite, probable or possible imputability), 2013-2022

Reaction	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	Total
Acute hemolytic transfusion reaction			2						1		3
Other reaction	2		1	1	1	2			2	1	10
Post-transfusion bacteremia/sepsis		2							1		3
Post-transfusion purpura		1									1
TRALI			2	1	1	1	1			1	7
Delayed hemolytic transfusion reaction									1		1
Circulatory overload		3	2	3	6	2	2	6	5	5	34
Total	2	6	7	5	8	5	3	6	10	7	59

2.2 Late reports from 2021

After the deadline for submitting reports for reporting year 2021, 21 reports were still received from that year (Table 6). This number is lower than a year earlier, when TRIP strictly adhered to the cut-off date (28 February) for the first time and 98 reports were received after the deadline. The late reports for 2021 came from eight 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 three serious reactions with a severity grade 2 or higher; one other reaction with new antibody formation in the additional category (severity grade 2, imputability probable), one other reaction with dyspnoea (severity grade 3, imputability possible) and one circulatory overload (severity grade 3, imputability probable). In accordance with the mandatory procedure, these three reports have been added to the overview for the European Commission for 2022, see Section 2.3.

Table 6 Late reports from 2021 in the 2022 report (N = 21)

Reporting category	Severity grade		
	1	2	3
Other allergic reaction	2		
Mild non-hemolytic febrile reaction	4		
Non-hemolytic transfusion reaction	4		
Other reaction	6	1	1
Post-transfusion bacteremia/sepsis	2		
Circulatory overload			1

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 2022 or late reports from 2021, in accordance with EU overview

Severity grade Imputability	2 or 3			4		Total
	Definite	Probable	Possible	Probable	Possible	
Hemolytic transfusion reaction (ABO)	2					2
Hemolytic transfusion reaction (immunological, non-ABO)		2				2
Hemolytic transfusion reaction (non-immunological)	2	2	1			5
Allergic reaction	2	5	4			11
Febrile reaction	1	4	16			21
Other reaction		3	23		1	27
TAD			1			1
TRALI		3	1	1		5
Circulatory overload	2	13	14		5	34
Total	9	32	60	1	6	108

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 2022, CCP was applied in two different studies, but mainly based on 'compassionate use' for immuno-compromised patients. The number of units distributed is higher (445 v. 322) and the number of units reported as applied is lower than in 2021 (433 v. 525). This could be explained by the larger percentage of units that were used in a study context (blind) in 2021, as a result of which control units were added to the total in 2021 and the figures are not comparable.

Table 8 presents the three reactions reported to TRIP from three hospitals in 2022 after the application of CCP. Due to the small number of reports, no sub-analysis of these reactions was done, as was done for the reactions after transfusion of CCP (N = 21) in the 2021 annual report.

Table 8 Reports regarding CCP in this report (N = 3)

Reaction	Sex, age group	Severity	Imputability	Symptomatology
Anaphylactic reaction	F, 60-70	1	Definite	Dyspnoea, drop in saturation, coughing and swelling of the tongue at the end of transfusion, treated with clemastine, hydrocortisone IV, and oxygen supplementation via nasal cannula, with full recovery.
Other reaction	M, 70-80	2	Probable	Patient with lymphoma. During Tf, temperature increased $\geq 2^{\circ}\text{C}$, chills, dyspnoea and drop in saturation. Chest X-ray showed bronchopathy/bronchitis and suspicion of infiltrate. Ultimately full clinical recovery.
Other reaction	F, 60-70	4	Possible	Very weak patient with pneumonia due to COVID and Aspergillus infection in non-Hodgkin's lymphoma. Respiratory deterioration prior to Tf, further deterioration several hours after Tf, patient died within 24 hours.

3 DISCUSSION OF REPORTS PER CATEGORY

3.1 Incidents in the transfusion chain

Incorrect Blood Component Transfused (IBCT)

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

28 reports, in line with last year (26 reports)

Number of reporting hospitals: 18 (22%), range 1-4 reports per hospital.

- Preventive policy to prevent the formation of irregular antibodies (including in recipients who are already known to have an antibody) was not followed 13 times, which led to the formation of a new antibody (2x anti-K, anti-c) in three cases.
- In one of the 13 cases, in which the preventive policy to prevent the formation of irregular antibodies was not followed, TRIX information was present, which could have prevented the error, but the information was missed when processing the request.
- Of the eight cases in which there was a chance that ABO-incompatible blood was transfused (ABO risk), five cases involved a mix-up of blood bags, patients or patient data. This resulted in an acute hemolytic transfusion reaction (see case description below) twice.
- One mild non-hemolytic febrile reaction after reconnection of an already disconnected unit.
- One other reaction. IBCT discovered during investigation into the transfusion reaction.
- One other incident followed by a IBCT (described under other incident).

TRIP risk classification

As in previous years, TRIP has assessed all the reports of Incorrect Blood Component Transfused to establish 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 described on the website.

In 2022, the Irrab prevention policy constituted the largest risk group (13). In this risk group, no action was taken in accordance with the applicable hospital regulations regarding the prevention of irregular antibody formation in a specific target group. In this group, rhesus phenotyping was omitted five times, despite the fact that the recipient was known to have an antibody or was a woman under 45 years of age. In three cases, it was not known or communicated that it concerned a patient with an indication for preventive matched units. In two cases, matching was done for a part of cDEK, but one rhesus type was omitted, resulting in an anti-c and anti-K. In three cases, the information on the unit was misinterpreted, resulting in K-positive units being issued.

One TA-GVHD risk case involved a patient who had an indication for irradiated RBC units in connection with the treatment of an underlying medical condition (to prevent transfusion-associated graft versus host disease). The requesting provider was not aware that the treatment in question was an indication for irradiated units. The laboratory was also not informed of the indication for irradiated products for this patient by any other means, as is usual. As a result, the patient received a non-irradiated product twice, without a reaction. The second TA-GVHD risk case concerned a digital problem and was discussed in the Report of the month 2023-2.

A reaction in addition to the incident was reported twice, namely a mild non-hemolytic febrile reaction and another reaction with a drop in blood pressure. In the second report, the investigation into the transfusion reaction showed that the preventive matching protocol had not been followed during a previous transfusion.

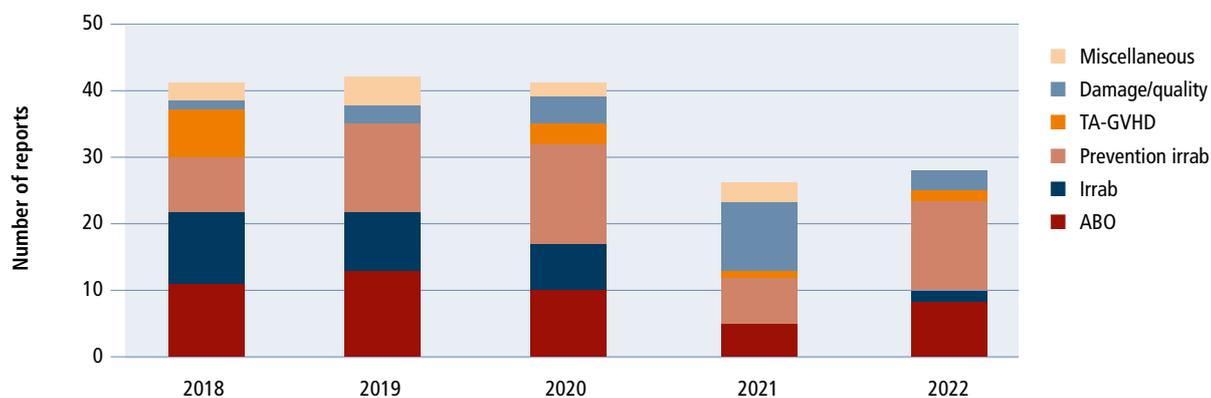


Figure 6 Incorrect Blood Component Transfused 2018-2022: subdivided according to risk group

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 a non-irradiated blood component)

Damage/quality = Risk of (potentially) reduced quality of a blood product due to damage

Incorrect Blood Component Transfused (ABO risk) with acute hemolytic reaction

- Nurse A goes to the laboratory to collect a RBC unit for patient X (O pos). However, by mistake, the nurse also has a sticker for patient Y (B pos) in her pocket. The sticker that is handed over to the laboratory is for patient Y. The lab technician tells the nurse that the order has not (yet) gone through, but gives the unit (patient Y had also received a unit the day before) with the comment to officially place the order in the system. Ten minutes after Tf, the patient develops symptoms; temperature increase of $\geq 2^{\circ}\text{C}$, shivering, drop in saturation (92% to 82%), tachycardia, tachypnoea, crepitations and later bloody sputum. Unit is stopped and a diuretic is given, as circulatory overload is suspected. When checking the transfusion form, nurse B discovers that patient Y's details are on the form and that the unit is blood group B pos. The transfusion protocol is initiated, concluding that an acute hemolytic transfusion reaction occurred. Within two days, the patient has recovered fully from the transfusion reaction.
- Two reserved RBC units arrive on the ward via the pneumatic tube for two patients (X: O pos and Y: A pos). Patient X is non-responsive and in an acute condition. Initially, their condition improves. However, an acute pulmonary deterioration occurs after CT. Patient is vasovagal, has chills, is tachycardic and hypertensive (from 114/45 mm Hg to 149/127 mm Hg), with suspected aspiration. Patient is given oxygen. On the ward, the nurse finds out that patient X received a unit of RBC intended for patient Y.

Case studies (in Dutch) in the category Incorrect Blood Component Transfused can be found at www.tripnet.nl in the Report of the Month section (Melding van de maand)

Report of the Month 2022 – 3: Pneumatic tube transport

Report of the Month 2022 – 4: IV fails during transfusion

Report of the Month 2023 – 2: Digitisation in the blood transfusion chain – 2

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.

34 reports, number of reporting hospitals 14 (17%), range 1-9 reports per hospital

- 16 near misses were detected in time because of blood group discrepancy.
- In 19 reports, the incidents were prevented by planned checks on the ward and in the laboratory.
- One case concerned the finding on internal checks that there were 9 instances of blood group discrepancies, the cause of which was not clear. These were all reported back to the relevant departments.
- In 29 reports, there was a potential ABO risk.

Table 9 Near miss reporting

Occurrence*	N	Where detected	N	How detected	N
Investigation prior to transfusion (request)	29	Planned check	16	Blood group discrepancy	15
				Discrepancy with previous results	1
		Alertness of ward staff	4	Check of results and form	1
				Not mentioned	1
				Wait for results	1
				Discrepancy with previous results	1
		Alertness of lab technician	5	Discrepancy with previous results	2
				Wait for second sample	1
Form/tube discrepancy	2				
Not mentioned	4	Not mentioned	4		
		Transfusion	2	Alertness of ward staff	1
Processing of request	2	Planned check on ward	1	Identity check at bedside	1
		Alertness of ward staff	1	Self check	1
Transfusion chain outside of hospital	1	Planned check in lab	1	Blood group discrepancy	1

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

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 2022 – 1: two tasks

Report of the Month 2022 – 3: Pneumatic tube transport

Other incident (OI)

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

68 reports, number of reporting hospitals: 24 (29%), range 1-10 reports per hospital.

- 10 reports in which a reaction was also observed (5x other reaction: 2x NHTR, 2x mild NHFR, 1x TACO).
- One report in which an incorrect blood product was registered in the additional category. This report involved an infusion pump that pumped blood from the patient. After discovery, the flow direction was reversed and some of the contents of the bag were returned to the patient.
- 39 units were (partially) lost, of which 25 were not 'errors' (see below).

Classification by type of error

Following on from last year, categorisation of 'other incidents' is again based on the type of error and whether the product was (partially) lost. As reported above, more than half of the incidents led to loss or partial loss of the blood component. These 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 largest group of other incidents are classified as 'other' (27). In 'other', 20 times the unit was running subcutaneously despite the protocol checks (including after 10 minutes) or the unit was accidentally punctured. This was also the most common reason for unit losses (22/39).

Table 10 Reports of other incidents in 2022, subdivided according to type of error

Type of error	N	Loss (or partially loss)	N	Description	N
Administration error	1	No	1	— Request was incorrectly copied, resulting in PLT being booked out and administered	1
Assessment error	10	Yes	4	— Units were collected/spiked/requested too soon or returned to the laboratory without notification	4
		No	6	— High Hb after 2 units, questioning whether the second unit would have been necessary	2
			— Two units issued and administered, while 1 unit was ordered	1	
			— Reaction reported too late, causing delay in implementation of transfusion protocol	1	
			— Transfusion form not completed	1	
— Indication (prothrombin time) initially incorrectly interpreted (APTT mistaken for PT), resulting in 2 units of SD plasma being given unnecessarily without reaction	1				
Storage error	3	Yes	3	— Unit was stored for too long/wrongly	3
Blood sampling error	10	No	10	— Transfusion based on Hb determination from infusion arm, blood gas, diluted sample	7
			— Transfusion based on erroneous Hb determination (cause unclear)	3	
Communication error	5	Yes	2	— More units received due to lack of clarity	2
		No	3	— Unit administered while it should have been reserved	1
			— Transfusion outside office hours not reported	1	
— Transfusion form not completed	1				
Laboratory	1	No	1	— Units not prepared, which meant T&S had to be performed again and transfusion was delayed	1
Procedural error					
Technical error	2	No	2	— Infusion system did not work as required	1
				— The manufacturer indicated that a laboratory test can give unexplained reactions	1
Transfusion error	9	Yes	5	— Infusion/infusion pump possibly not (properly) checked (infusion not connected properly, transfusion not started, runs subcutaneously)	5
		No	4	— Infusion/infusion pump possibly not (properly) checked (incorrect infusion rate; infusion does not run or runs subcutaneously)	1
			— Infusion of unit was not turned on, but the NaCl was turned on or was running together with another infusion	2	
			— Unit running too long (>6 hours)	1	
Other	27	Yes	25	— Infusion (system) became clogged due to the patient's underlying condition, which stopped the plasmapheresis using SD plasma and several units of SD plasma were lost	1
— Infusion (system) checked, but was (later) subcutaneous or failed			15		
— Unit accidentally punctured when spiking (leak)			5		
— Infusion line came loose from the bag			2		
— Measurement error causing the transfusion to be stopped or given unnecessarily			2		
— Transfusion reaction not reported to the laboratory, but to the blood bank			1		
	No	2	— No tube available for emergencies	1	

Case studies (in Dutch) in the category other incident can be found at www.tripnet.nl in the Report of the Month (Melding van de maand):

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

1 report

- The report concerns an emergency situation.
- The situation did not lead to a reaction.

In an emergency situation with acute severe blood loss and low blood pressure, three units of RBC were issued and administered. Patient was already familiar with anti-E. Because of this anti-E, the patient should have received matched units as a preventive measure. Due to the emergency situation, rhesus typing could not take place. This did not lead to a transfusion reaction. The units were RhE-neg.

Conclusion Incidents in the transfusion chain

In 2022, 28 reports were classified as incorrect blood component administered (2021: 26 reports). In this category, 13 reports did not take into account that the recipient should have received matched units to prevent irregular antibody formation as described in the hospital protocol. The reason for matching may be certain therapies, an underlying condition or, for example, status after stem cell transplant. Three times, the administration of the wrong product led to a reaction and once a reaction led to the discovery of an IBCT. Three times, an IBCT led to new antibody formation.

In the case of near misses, the number of reports was in line with last year, 34 reports. Most near misses occurred during examination prior to the transfusion (request) (29/34) and they were most often discovered because of a blood group discrepancy (16/34). In previous years too, a near miss was most often detected due to blood group discrepancy.

This year, the 'other' incidents were grouped by type of error. In 57% of the reports, a unit was partially or completely lost. In 40% of the cases, this was not a 'real' error, but usually involved running the unit subcutaneously despite planned checks or accidentally puncturing a bag.

The reported calculated risk situation concerned an emergency situation, in which the preventive policy for irregular antibodies (Rh_c) was not taken into account.

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, manifested by at least one pulmonary feature (criterion A or B). In all, at least 3 of the criteria below must be met. See also notes 1 to 6 on www.tripnet.nl.

- A New or worsening respiratory problems
- B Features of new or worsening pulmonary edema 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 the fluid balance
- E Biomarker result(s) consistent with TACO

(link <https://www.tripnet.nl/volume-overbelasting-transfusion-associated-circulatory-overload-taco/>)

- In 2022, 100 reports of TACO were reported by 46 hospitals (56%), with a range of 1 to 7 reports per hospital.
- TACO was reported four times as a additional category of another type of transfusion reaction.
- 96 (96%) 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 29% of the total number of serious reactions. TACO is the transfusion reaction with the highest number of serious reports.
- In five cases, the patient died after transfusion.
- Twelve times, TACO was reported as an additional category of another type of transfusion reaction, due to additional findings that were inconsistent with TACO. TACO was reported once in combination with an incident in which, after the occurrence of dyspnoea complaints during the transfusion of two RBC units, two additional units were given due to a communication error.
- TACO is most often seen after transfusion of red blood cells (Figure 7).

Table 11 Overview of TACO reports in 2022 with definite, probable or possible imputability

	TACO N = 96
Sex (%)	
Female	56 (58%)
Male	40 (42%)
Age (years)	78 (69-85)
Time interval between start of transfusion and occurrence of transfusion reaction (hrs:min)	2:57 (1:10-6:47)
Severity grade of transfusion reaction (%)	
Severity grade 1	62 (65%)
Severity grade 2	27 (28%)
Severity grade 3	1 (1%)
Severity grade 4	5 (5%)
Unknown/not assessable	1 (1%)
Imputability (%)	
Definite	5 (5%)
Probable	35 (36%)
Possible	56 (58%)

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

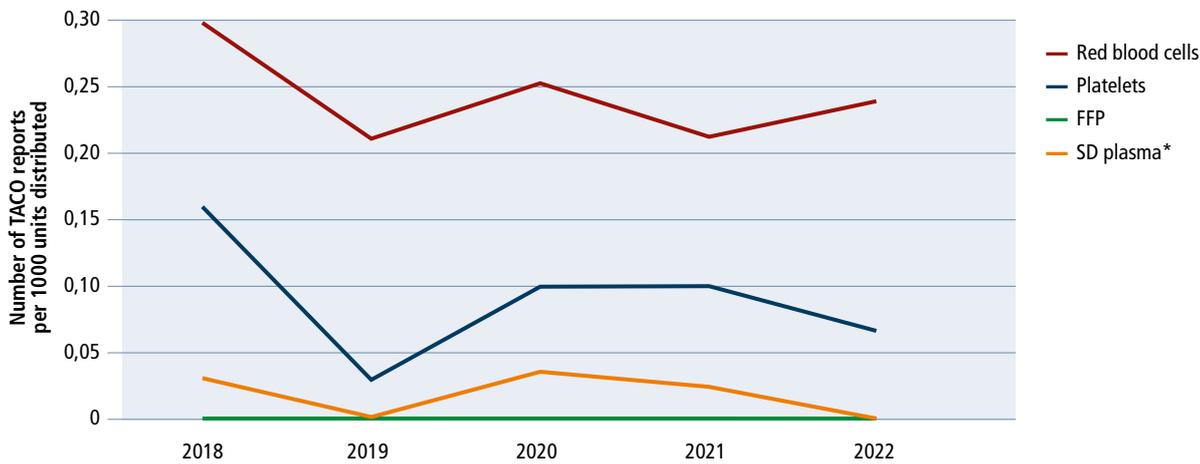


Figure 7 Number of TACO reports with definite, probable, possible imputability per 1,000 blood components distributed, 2018-2022

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 in 2021 and 2022, reactions for these years are shown per 1,000 units transfused.

Transfusion-related acute lung injury (TRALI)

Features of acute lung injury such as dyspnoea and hypoxia during or within 6 hours after a transfusion; chest X-ray shows bilateral pulmonary infiltrates.

- In 2022, seven TRALI reports were registered, reported by six different hospitals.
- TRALI was once registered as an additional category together with a TACO report.
- Six reports were assessed as at least possibly related to the transfusion. This is the highest number of reports received in the past five years, as well as the highest number of cases after administration of red blood cell units (Figure 8). Based on the registration of TRALI reports in the coming years, it will be assessed whether this is a trend.

Definite, probable, possible TRALI (Table 12)

- TRALI was once registered as an additional category in combination with the transfusion reaction TACO. The proposed redefinition of the TRALI consensus definition by Vlaar and colleagues describes the occurrence of a combination of these two reactions¹. 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 significant left atrial hypertrophy is present.
- TRALI occurred five times after administration of RBC units, whether or not in combination with platelets, and once after administration of the combination of one unit of PLT and SD plasma (Figure 8).
- Two reactions were reported to Sanquin as a suspected TRALI, but are not known as such to TRIP. After the initial suspicion, Sanquin concluded in both cases that the diagnosis of TRALI was unlikely.
- In four of the six TRALI cases known to TRIP, Sanquin investigated the presence of leukocyte antibodies in the serum of the patient and the donors:
 - In one case, both HLA class I and HLA class II antibodies directed against the patient's HLA antigens were detectable in the donor involved. In addition, non-specific granulocyte reactive antibodies were detected in the patient's serum.
 - In another case, HNA-2-specific autoantibodies were found in one of the donors. Sanquin describes that these findings need to be confirmed again due to their rarity.
 - In the other two cases, the serological tests did not provide an explanation for the clinical picture.

Table 12 Overview of TRALI reports in 2022 with definite, probable or possible imputability

	TRALI N = 6
Sex (%)	
Female	2 (33%)
Male	4 (67%)
Age (years)	57 (27-74)
Time interval between start of transfusion and occurrence of transfusion reaction (hrs:min)	1:00 (0:29 – 3:14)
Severity grade of transfusion reaction (%)	
Severity grade 1	1 (17%)
Severity grade 2	2 (33%)
Severity grade 3	2 (33%)
Severity grade 4	1 (17%)
Imputability (%)	
Probable	4 (67%)
Possible	2 (33%)

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

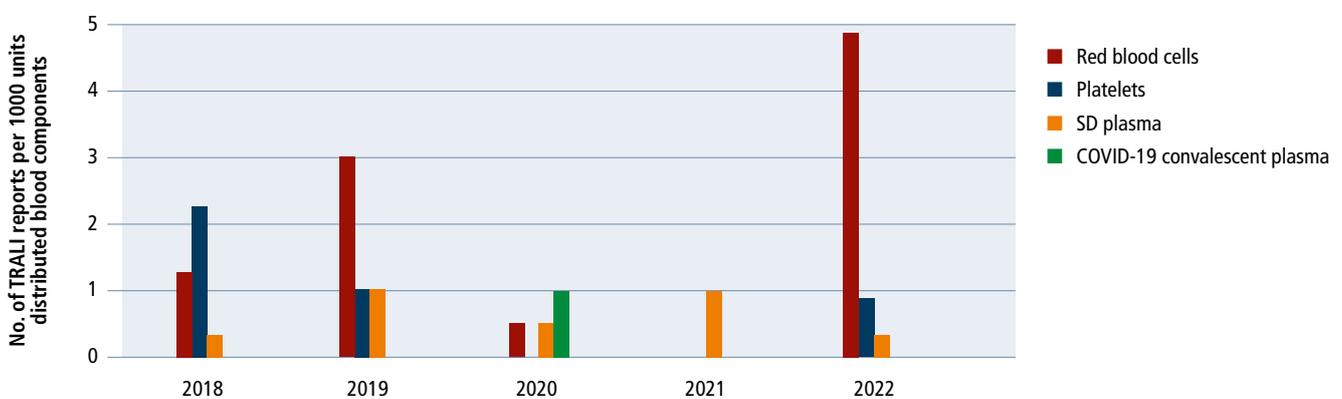


Figure 8 Number of TRALI case per type of blood component (definite, probable or possible imputability), 2018-2022

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

Transfusion-associated dyspnoea (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 feature and they cannot be explained by the patient's underlying medical condition or another known medical cause.

- TRIP registered 13 reports of TAD, all with definite, probable or possible imputability.
- TAD was reported twice as the additional category with another type of transfusion reaction, due to additional findings that were not consistent with TAD.
- In eight of the 12 TAD cases, in addition to dyspnoea or a drop in saturation, a temperature increase or chills were also observed.

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 with definite, probable or possible imputability

TAD N = 12	
Sex (%)	
Female	2 (17%)
Male	10 (83%)
Age (years)	75 (37-90)
Time interval between start of transfusion and occurrence of transfusion reaction (hrs:min)	1:07 (0:00- 12:15)
Severity grade of transfusion reaction (%)	
Severity grade 1	11 (92%)
Severity grade 2	1 (8%)
Imputability (%)	
Probable	2 (17%)
Possible	10 (83%)

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

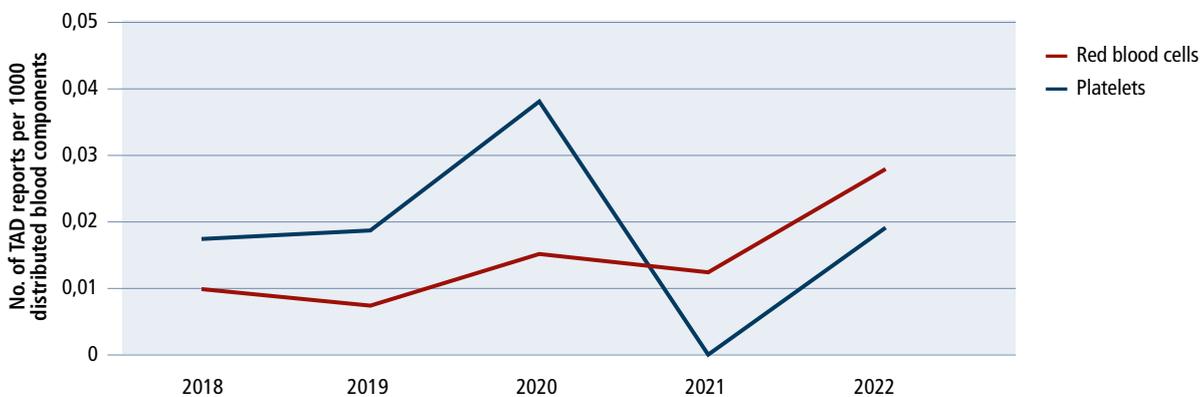


Figure 9 Number of TAD reports with definite, probable, possible imputability per 1,000 blood components distributed, 2018-2022

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

Conclusion on respiratory transfusion reactions

Also in 2022, respiratory transfusion reactions are the group of transfusion reactions with the highest mortality rate. Six out of the seven (86%) deaths 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 TACO or TRALI. In addition, respiratory transfusion reactions were responsible for a significant degree of transfusion-related morbidity. International coordination of the classification of respiratory transfusion reactions is necessary to standardise data collection and contributes to a better understanding of this complex group of transfusion reactions. An international partnership, of which TRIP is a part, is working on a standardised reporting form for respiratory transfusion complications. A publication has recently been published, describing the development of a model for this reporting form and drawing up a flowchart, which can contribute to a standardised way of assessing respiratory transfusion reactions².

References

- 1 Vlaar APJ, Toy P, Fung M, et al. A consensus redefinition of transfusion-related acute lung injury. *Transfusion* 2019;59:2465-76.
- 2 van Wonderen, SF, Peters, AL, Grey, S, Rajbhandary, S, de Jonge, LL, Andrzejewski, C, et al. Standardized reporting of pulmonary transfusion complications: Development of a model reporting form and flowchart. *Transfusion*. 2023; 63(6): 1161– 1171.

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.

Nine reports (all involving red blood cell transfusion, see Table 14)

- One reaction with severity grade 2 due to ABO-incompatible transfusion, discontinued on occurrence of symptoms of transfusion (IBCT is the registered reporting category and the case is described in the relevant chapter).
- One reaction with severity grade 3 due to ABO-incompatible transfusion. Incorrect blood component transfused (IBCT) is the registered reporting category and the case is described in the relevant chapter (see Chapter 3.1)
- Two reports concern patients with previously undetected irregular antibodies; in one case, the blood components were antigen-positive for the antibody elicited in the patient. In the second report, the irregular antibodies were not investigated. Both reports gave new antibody formation as an additional category.
- Seven reports were assessed as serious. Two reports were not serious (severity grade 1), involving an increase in autoimmune hemolysis without indications of serological incompatibility.

Table 14 Acute hemolytic transfusion reactions (AHTRs) in 2022

	AHTR N = 9
Sex (%)	
Female	4 (44%)
Male	5 (56%)
Age (years)	79 (38-93)
Time interval between start of transfusion and occurrence of transfusion reaction (hrs:min) ^a	3:00 (0:10- 4: 11)
Severity grade of transfusion reaction (%)	
Severity grade 1	2 (22%)
Severity grade 2	6 (67%)
Severity grade 3	1 (11%)
Imputability (%)	
Definite	4 (45%)
Probable	2 (22%)
Possible	3 (33%)
Cause	
Irregular antibodies that were not previously demonstrated (anti-Kpa; anti-Fya)	2
(chronic) autoimmune hemolytic anemia	3
ABO incompatibility (reporting category IBCT)	2
No clear cause was demonstrated	2

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

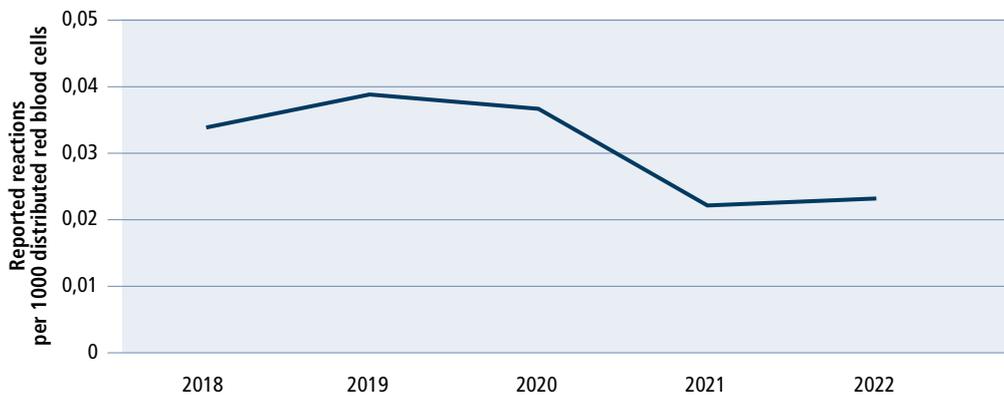


Figure 10 Reports of acute and delayed hemolytic transfusion reactions relative to the number of red blood cell concentrates distributed, 2018-2022

The figure shows reports with definite, probable or possible imputability, including hemolytic reactions associated with Incorrect Blood Component Transfused (ICBT) or demonstration of new antibody formation.

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.

- Six reports (all involving red blood cells).
- All reports were registered as AHTR, four of which have an additional category of new antibody formation (1x anti-Jk(a), 1x anti-E, 1x anti-Fyb and in the last report: anti-Jk(a) with anti-E).
- In two reports, hemolysis was discovered by chance, with one report demonstrating an AHTR after the formation of a new antibody.

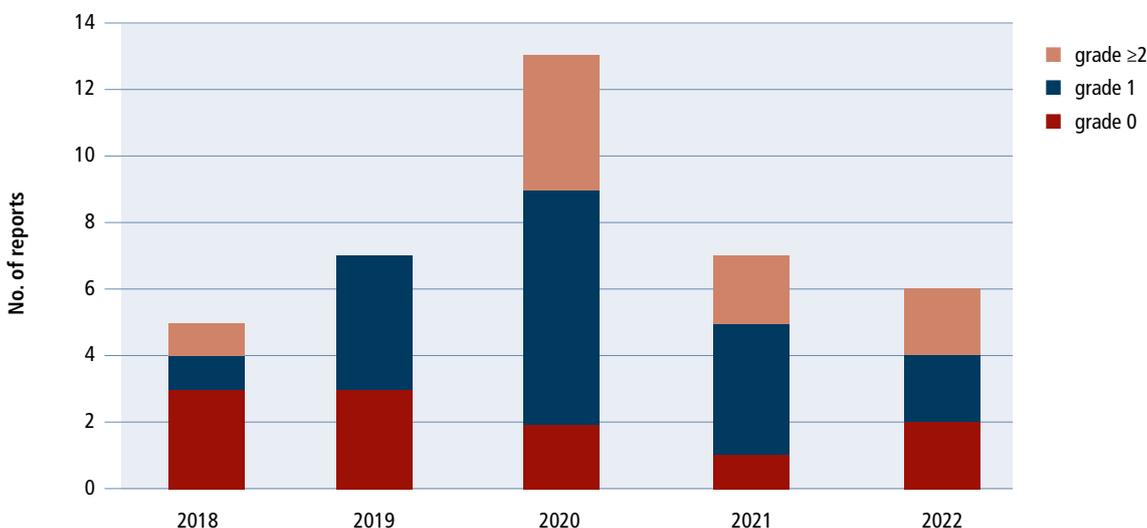


Figure 11 Severity of reports of delayed transfusion reactions (definite, probable, possible imputability), 2018-2022

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.

- Three reports of new antibody formation during an incident. In addition, new antibody formation was reported seven times with a reaction (1x other reaction; 1x NHTR, 1x AHTR; 4x VHTR). See the relevant chapters.
- One case concerned antibody formation during transfusion of platelets; female patient > 45 yrs, who formed HLA antibodies. This also involved an NHTR.

Anaphylactic reaction and other allergic reactions

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 114 reports of anaphylactic and other allergic reactions (30 and 84, respectively), compared to the same number (20 and 93, respectively), including late reports, from 2021.
- Number of reporting hospitals: 37 (45%), range 1-27 reports per hospital.
- Number of reports with definite, probable, possible imputability is 110 (97%), anaphylactic reaction 28 (97%) and other allergic reactions 82 (98%).
- The number of reports (N = 11) of severe allergic reactions (grade 2 and higher) with definite, probable or possible imputability has been stable since 2018 (Figure 12) with the exception of a higher number in 2020 (N = 28).
- Eight times, another allergic reaction was reported as an additional category, 3x for mild NHFR, 3x for non-hemolytic transfusion reaction, 2x for circulatory overload.
- The number of reports of allergic reactions when administering platelets have remained lower after the transition to PAS-E storage solution. See the NVB-TRIP 2022 poster.
- Information on the reports is summarised in Table 15.

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

	Anaphylactic reaction (N = 28)	Other allergic reactions (N = 82)
Sex (%)		
Female	14 (50%)	35 (43%)
Male	14 (50%)	47 (57%)
Age (years)	45 (IQR 23.5-67.5)	35 (IQR 19-68)
Severity grade (%)		
Severity grade 1	18 (64%)	81 (95%)
Severity grade 2	8 (29%)	1 (5%)
Severity grade 3	2 (7%)	
Imputability (%)		
Definite	4 (14%)	4 (5%)
Probable	16 (57%)	45 (55%)
Possible	8 (29%)	33 (40%)
Component (%)		
RBC	8 (29%)	34 (41%)
PLT	17 (61%)	39 (48%)
SD plasma	1 (4%)	5 (6%)
COVID-19 convalescent plasma	1 (4%)	-
Combination of blood components	1 (4%)	4 (5%)
Symptoms (number of reports)		
Itching, urticaria, redness	18	82
Glottal edema	9	-
Increase in temperature 1-2°C	3	6
Increase in temperature ≥ 2°C	2	-
Chills	5	2
Unresponsive / less responsive	1	-
Dyspnoea / saturation drop	12	-
Hypotension	11 (≥ 20 mm Hg syst and/or diast)	3 (partly explained by clinical situation, no additional therapy)
Nausea/vomiting/diarrhoea	2	-

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

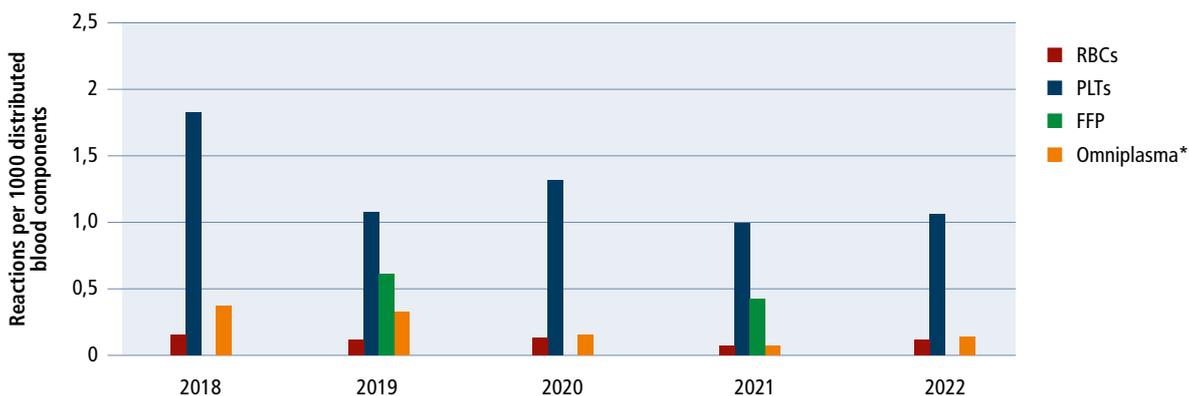


Figure 12 Number of allergic reactions with definite, probable or possible imputability per 1000 blood components distributed

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

* For SD plasma (Omniplasma®), only units transfused were reported in 2021 and 2022.

Conclusion on allergic reactions

The number of allergic reactions involving platelets have been lower since 2018, when the switch to PAS-E storage fluid (platelet additive solution-E with acetate, potassium, magnesium and phosphate) was made, while the number of reports involving red blood cells do not show such a decrease.

In the diagnosis and treatment of allergic reactions, the clinical picture and severity are important, and there is little added value in dividing them into the subgroups of other allergic reactions versus anaphylactic reactions. With effect from reporting year 2023, TRIP will merge the subgroups in their report.

Non-hemolytic reactions

Non-hemolytic transfusion reaction (NHTR)

Rise in temperature of $\geq 2^{\circ}\text{C}$ (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)

Rise in temperature $\geq 1^{\circ}\text{C}$ ($< 2^{\circ}\text{C}$) 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 602 reports of non-hemolytic reactions, non-hemolytic transfusion reactions and mild non-hemolytic febrile reactions (296 and 306, respectively), compared to 630 reports (303 and 327, respectively) including late reports from 2021.
- Number of reporting hospitals: 66 (80%), range 1-85 reports per hospital.
- Number of reports with definite, probable, possible imputability is 530 (88%), NHTR 256 (86%) and mild NHFR 274 (89%).
- The number of reports (N = 17) of severe non-hemolytic transfusion reactions (grade 2 or higher) with definite, probable or possible imputability is similar to that in 2021 (N = 16).
- Thirteen times, a mild NHFR or an NHTR were reported as the additional category in combination with an other type of transfusion reaction: 5x with an allergic reaction, 4x circulatory overload, 3x other reaction and 1x dyspnoea associated with transfusion.
- Information on the reports is summarised in Table 16.
- The picture is similar to last year.

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

	NHTR (N = 256)	Mild NHFR (N = 274)
Sex (%)		
Female	112 (44%)	144 (53%)
Male	144 (56%)	130 (47%)
Age (years)	65 (IQR 53-75)	70 (IQR 53-78)
Severity grade (%)		
Severity grade 1	239 (93%)	270 (99%)
Severity grade 2	17 (7%)	4 (1%)
Imputability (%)		
Definite	3 (1%)	
Probable	41 (14%)	41 (15%)
Possible	212 (77%)	233 (85%)
Component (%)		
RBC	209 (82%)	256 (93%)
PLT	34 (9%)	11 (4%)
SD plasma	1 (0%)	0
Other - granulocytes	0	1 (0%)
Combination of blood components	12 (5%)	6 (2%)
Symptoms (number of reports)		
Rise in temperature of < 1°C	10 (4%)	20 (7%)
Rise in temperature of 1-2°C	92 (34%)	250 (91%)
Rise in temperature ≥ 2°C	136 (50%)	0
Chills	166 (61%)	0
Tachycardia	31 (12%)	54 (20%)
Hypertension	28 (19× ≥ 20 mm Hg syst and/or diast)	16 (13× ≥ 20 mm Hg syst and/or diast)
Hypotension	15 (3× ≥ 20 mm Hg syst and/or diast)	7 (3× ≥ 20 mm Hg syst and/or diast)
Dyspnoea/tachypnoea	10 (4%)	4 (1%)
Nausea/vomiting/diarrhoea	16 (6%)	2 (1%)

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

Other reactions

Transfusion reaction which does not fit into the categories above.

- 252 reports in 2022.
- Comparable to 2021 (245 including late reports).
- The number of other reactions characterised by dyspnoea, which was lower in 2021 than the year before, returned to the level of previous years in 2022 (49 with definite, probable or possible imputability) and was comparable to 2020.
- The number of other reactions with hypotension was 59 in 2022, compared to 52 in 2021.
- In 2022, the category of other reactions with (possibly) prominent cardiac symptoms was reported 20×, compared to 12× in 2021.
- Over the past five years, the reaction category 'other' has been one of the second largest categories of reports with severity grade 2 or higher and definite, probable or possible imputability.
- The additional category 'other' reaction was registered for three reports of reactions: 1× with NHTR to indicate a short-term irregular pulse during the reaction and 2× with TACO, 1× to indicate a drop in blood pressure and 1× due to new swelling of the eyes during the reaction, where it was unclear whether this was related to the transfusion.

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 Types of reactions registered as 'other' reactions (broken down as in previous TRIP reports)

Type of reaction	2021	2022	2022 Imputability definite, probable	2022 Imputability possible	2022 ≥ gr 2 ^a
Reactions with hypotension	52	59	6	38	4 (1)
Subgroup hypotensive reaction (ISBT) ^b	5	7	1	3	0 (0)
Reactions met dyspnoea	46	60	8	41	13 (13)
Hypertension	12	13	2	9	1 (1)
(Possibly) cardiac	12	20	3	12	3 (1)
Did not fully meet TRIP definitions of standard categories	64	43	11	18	0 (7)
Other symptoms/signs	59	57	2	38	4 (11)
Total	245	252	32	156	25 (34)

^a Definite, probable or possible imputability; number in 2022 (number in 2021)

^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 (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 60 reports of post-transfusion bacteremia/sepsis, up from 58 in 2021, including late reports (Table 18). Number of reporting hospitals: 34 (41%), range 1-9 reports per hospital.
- 36 number of reports with definite, probable or possible imputability (60%) (Table 19).
- 7 serious reports of post-transfusion bacteremia/sepsis (grade 2 or higher) with definite, probable or possible imputability, in comparison to 12 in 2021.
- One of the reports of post-transfusion bacteremia/sepsis with a RBC transfusion with the criteria for TTBI in 2022 (Table 20 and Figure 16).
- Two reports of bacterial contamination of blood component were made: In one case, there was a positive culture result on the unit for another reaction including a temperature increase, and in one case, for post-transfusion bacteremia/sepsis (possible TTBI).

Table 18 Overview of reports from hospitals relating to bacterial problems, 2018-2022

	2018	2019	2020	2021	2022
Post-transfusion bacteremia/sepsis (assessed as TTBI)	72 (1)	84 (1)	74 (0)	58 (1)	60 (1)
Post-transfusion bacteremia/sepsis as additional category (not TTBI)	1	0	5	0	8
Bacterial contamination of blood component (including reports of positive bacteriological screening*)	0	1	0	1	0
Bacterial contamination of blood component (including reports of positive bacteriological screening) as additional category	11	12	9	7	2

* 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 = 36	
Sex (%)	
Female	18 (50%)
Male	18 (50%)
Age (years)	74 (IQR 47-78)
Severity grade (%)	
Severity grade 1	29 (81%)
Severity grade 2	7 (19%)
Imputability (%)	
Probable	1 (3%)
Possible	35 (97%)
Component (%)	
Red blood cell concentrate	29 (80%)
Platelet concentrate	5 (14%)
Combination of blood components	2 (6%)
Symptoms (number of reports)	
Increase in temperature 1-2 °C	18
Increase in temperature ≥ 2 °C	17
Chills	18
Dyspnoea/saturation drop/tachypnoea	3
Hypotension (≥ 20 mm Hg syst and/or diast)	2
Hypertension (≥ 20 mm Hg syst and/or diast)	5
Tachycardia	10

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

Post-transfusion other infection

Demonstration of an potentially blood-transmitted infection with an agent other than a virus or bacterial species in a patient during or some time after administration of a blood transfusion; a causal link may or may not be confirmed.

In 2022, one report was registered in the reporting category other post-transfusion infection, with unlikely imputability. There was a finding of *Candida albicans* in the blood culture of one patient with fever, following endoscopy and transfusion for gastrointestinal bleeding. The patient was treated with antifungal medication and completely recovered from the reaction.

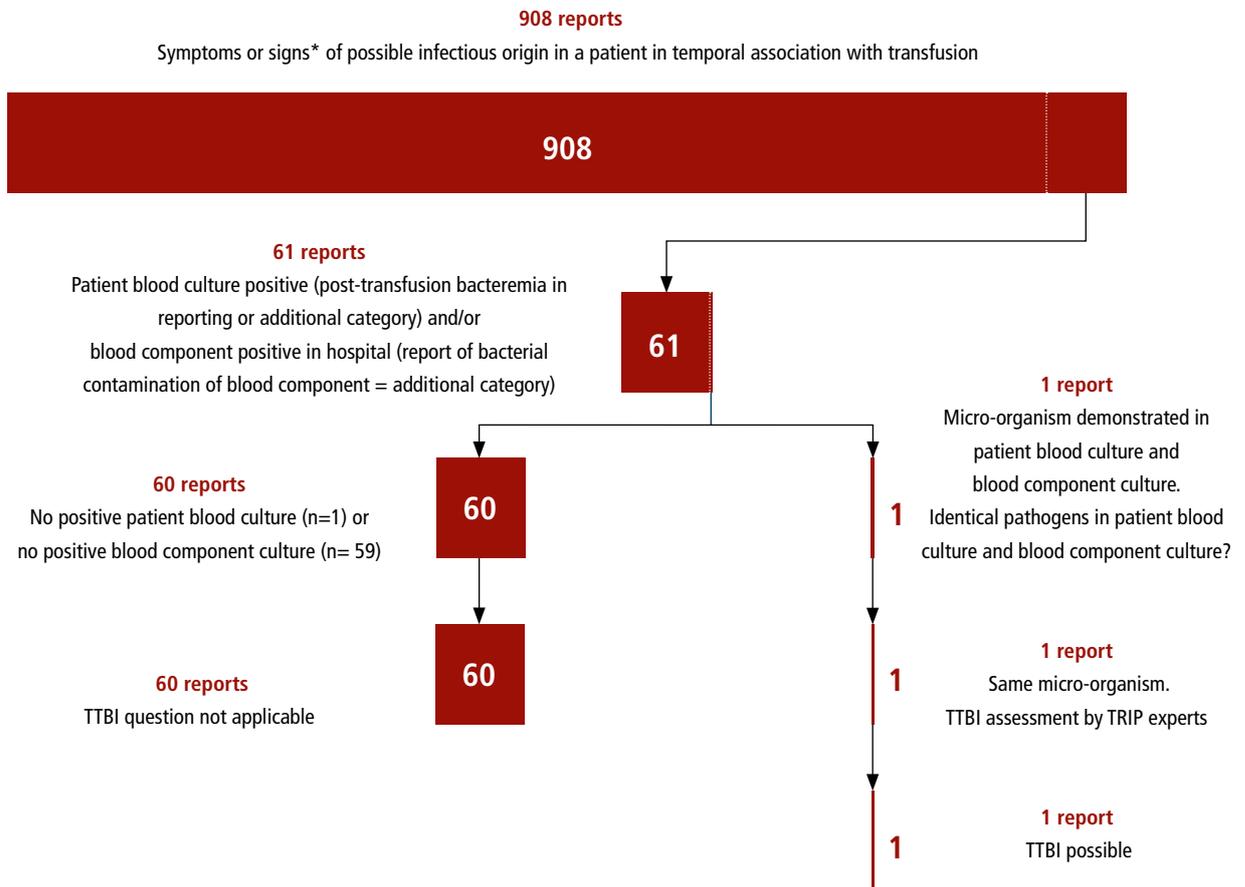


Figure 13 Was it a case of transfusion-transmitted bacterial infection (TTBI)?

* Reactions in 2022 with rise or decrease in temperature > 1°C and/or chills, all imputabilities

Table 20 Assessment of TTBI in 2022 (N = 1, discussed with Expert Committee)

Blood culture pt	Culture BC hosp	Blood component	BactAlert / culture Sanquin	Reporting cat	Severity	Imputability reaction	Imputability TTBI
<i>Actinomyces oris/ viscosus</i>	Actinomyces	RBC concentrate	Remained negative	Post-transfusion bacteriemia/sepsis	1	Possible	Possible

Table 21 Overview of positive bacteriological screening of platelets from units already issued by Sanquin

Total reported by Sanquin	2018	2019	2020	2021	2022
Number already administered (TCs and associated RBC)	100	81	84	73	63*

* In all cases, Sanquin asked the treating physicians whether a transfusion reaction had been observed: no serious reactions were reported.

When submitting reports of transfusion reactions, information is entered about bacterial culture results (blood cultures, culture on the remnant of the blood component) of the patients involved. Nevertheless, TRIP regularly asks additional questions: is a positive bacterial culture result seen as 'real', or as a false positive due to contamination during sampling? In the latter case, a note can be made in the report and the result will have no influence on the reporting category. Also, no (additional) category of bacterial contamination of the blood component is registered. The Blood Transfusion Policy Guidelines recommend that hospitals must have a protocol for supplying material to the microbiology laboratory.

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 2022, 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 2022, no reports of look-backs/recalls were received from hospitals.

Information from Sanquin

In 2022, look-backs were performed according to protocol after 9 seroconversions. 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 2022. In 2022, there was one report of post-transfusion bacteremia/sepsis, which showed Actinomyces in both the patient's blood culture and in the hospital culture of the residual blood component. It may have been a case of transfusion-transmitted bacterial infection (TTBI). The patient recovered well after being given antibiotics. 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 testing remain necessary to properly treat patients with symptoms/signs that may indicate sepsis and to recall any related blood components from circulation.

3.4 Reports regarding SD plasma (Omniplasma®) in 2022

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 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 have been 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. TRIP hemovigilance reporting helps maintain a complete picture of the transfusion chain at the same time.

A total of 22 reactions related to SD plasma and two incidents were received by TRIP in 2022 (Table 22); compared to the 16 reports in 2021. Five reports also involved the transfusion of red blood cell concentrates, two reports involved platelet concentrates and five reports a combination of SD plasma, RBC and PLT. 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 22 Reports associated with SD Plasma in 2022 (N = 24)

Type of reaction	Non-serious reactions		Serious reactions ^a	
	Only SD	SD in combination	Only SD	SD in combination
Anaphylactic reaction	2			
Other allergic reaction	5	3		
Non-hemolytic transfusion reaction	1	1		
Other reaction	2	6		1
TRALI				1
Incidents				
Other incident ^{b,c}	2			

^a Severity grade ≥ 2 and definite, probable or possible imputability.

^b Loss of several units of SD plasma, no reaction, see Chapter 3.1, Table 10

^c One unnecessary transfusion of two units of SD plasma due to an assessment error when interpreting laboratory results, no reaction, see Chapter 3.1, Table 10

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 effects 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 "Publicaties", "Rapporten" (Publications/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 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 2022, there were 82 contact addresses for hospitals. In 2021, TRIP received reports from 73 hospitals (before the cut-off date). Seven hospitals indicated that there had been no reports in the TRIP reporting categories in 2022. One hospital had not provided any information about reports when this annual report was drawn up. One of the hospitals submitted its reports after the cut-off date and was therefore not included in the participation figure for reports. The rate of participation by hospitals in 2022 was 80/82=98% as regards reports and 81/82=99% 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 blood components from Sanquin and provide transfusions to their patients. Three of the eight licensed institutions submitted data in 2022, of which two reported that they had not administered any blood products in 2022 and one institution that they had administered two units to one patient in 2022. Four institutions informed TRIP that the figures for blood components and reports of any reactions would be provided by the transfusion laboratory that supplies the products under contract or by the main location of the institution. One institution was approached regarding a new registration via Farmatec and stated that the same agreement applied to their situation with regard to 2022. For one institution that still had an instruction in 2021/2022, that instruction is no longer current.

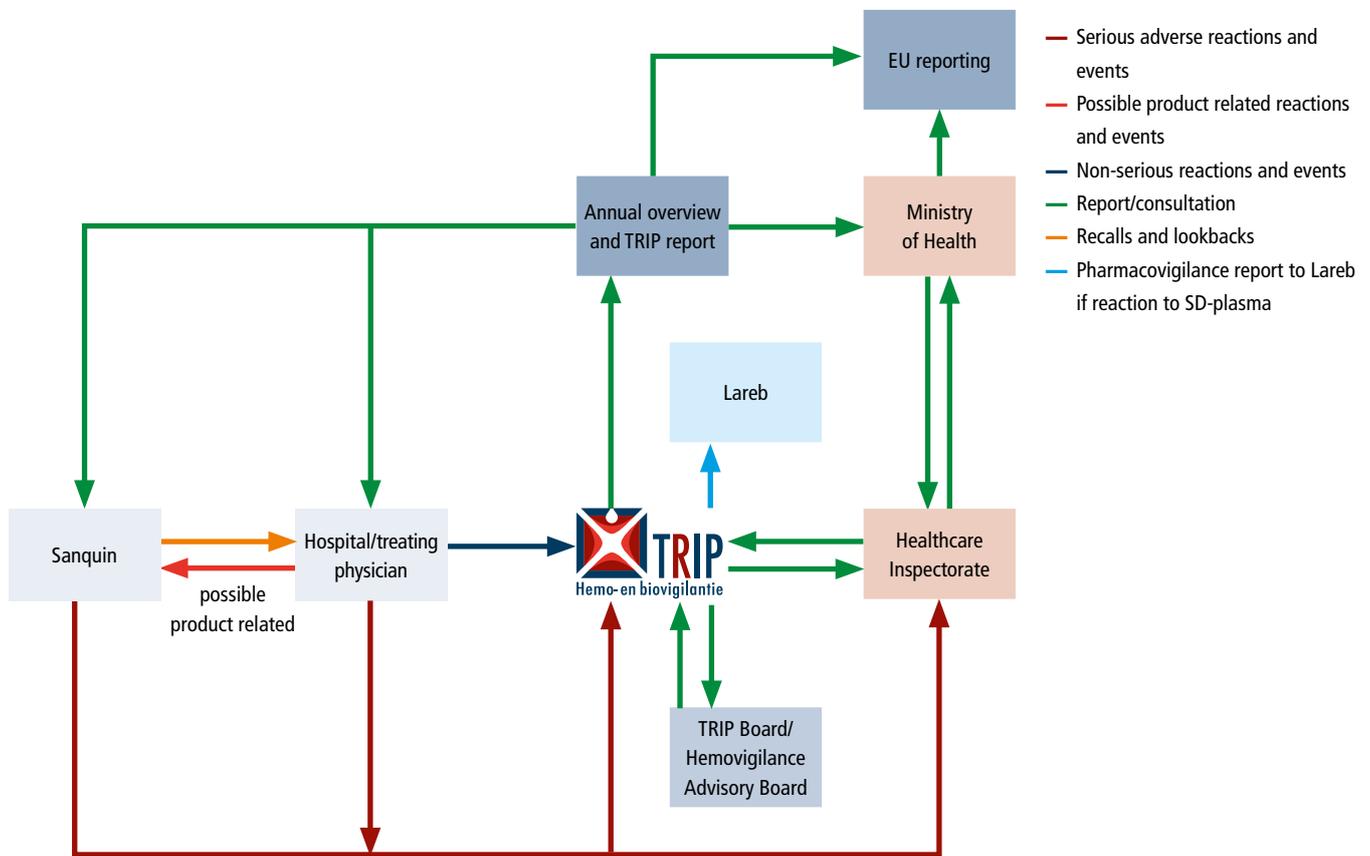


Figure 14 Flow of hemovigilance information and outputs in the Netherlands

LIST OF TERMS AND ABBREVIATIONS

AHTR	Acute Hemolytic Transfusion Reaction
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
EU	European Union
FFP	Fresh frozen plasma
Hb	Hemoglobin
HLA	Human leukocyte antigen
IBCT	Incorrect blood component transfused
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	Dutch blood transfusion society
OI	Other incident
PAS-E	Platelet additive solution-E with acetate, potassium, magnesium and phosphate
PLT	Platelet concentrate
RBC	Red blood cell concentrate
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 Sports
WKKGZ	Quality, Complaints and Disputes in Healthcare Act