EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Directorate B - Health systems, medical products and innovation
B4 – Medical products: quality, safety, innovation

SUMMARY OF THE 2022 ANNUAL REPORTING OF SERIOUS ADVERSE REACTIONS AND EVENTS FOR BLOOD AND BLOOD COMPONENTS

(DATA COLLECTED FROM 01/01/2021 to 31/12/2021 AND SUBMITTED TO THE EUROPEAN COMMISSION IN 2022)

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1. INTRODUCTION

Every year millions of European citizens benefit from blood transfusion as a result of different medical procedures supported by many healthcare specialties. However, the use of any substance of human origin carries some risk, particularly the possible transmission of diseases from the donor, incompatibilities or other potential adverse effects to the recipient.

These risks can be controlled and minimised by the application of a comprehensive set of safety and quality measures as laid down in the EU Blood legislation. Despite these measures, rare adverse events can occur and, in line with the legislation[1], these must be identified and reported at national and EU level (when appropriate) through national haemovigilance and surveillance systems. For the purpose of promoting an internationally harmonised approach to reporting such unintended events, the legislation defines Serious Adverse Reactions (SAR) as incidents observed during or after transfusion, which may be attributable to the quality and safety of blood components and where actual harm to a donor or recipient has occurred. Serious Adverse Events (SAE) are incidents which may affect the quality or safety of blood and blood components with a risk of harm, but where no harm has ultimately occurred.

In line with obligations defined in the EU legislation,[2] EU member states submit an annual report to the European Commission (hereinafter referred to as "the Commission") on the SAR which occurred in recipients of blood and blood components, and SAE which occurred at any stage in the chain from donation to clinical application. Since 2012, this report has also included information on SAR in donors of blood and blood components, submitted on a voluntary basis.

In 2021, the Serious Adverse Reactions and Events (SARE) exercise was conducted via an online form for the first time; the Vigilance Expert Subgroup (VES), made up of representatives nominated by National Competent Authorities (NCAs), helped the Commission to test this new online reporting form, and the *VES subgroup for SARE reporting improvement* contributed to updating the *Common Approach* document with user instructions on how to submit data via the form.

This report summarises SARE data for the year 2021 submitted to the Commission by 30 European countries and includes major findings, general conclusions and trends in European transfusion services in terms of SARE occurrence and distribution (by category and type).

[1] Directive 2005/61/EC of 30 September 2005 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards traceability requirements and notification of serious adverse reactions and events.

[2] Article 8 of Directive 2005/61/EC provides that member states shall submit to the Commission an annual report, by 30 June of the following year, on the notification of serious adverse reactions and events (SARE) received by the competent authority using the formats in Part D of Annex II and C of Annex III.

2. EXECUTIVE SUMMARY

The main findings for 2021 are listed below:

- Similar to the previous year, **30 countries** comprising **26 EU member states** plus Iceland, Liechtenstein, Norway and the United Kingdom (Northern Ireland) contributed to the SARE exercise[3].

- Of these, 23 countries indicated completeness of data, six indicated 75-99% completeness and one country indicated unspecified data completeness.

- Across the 30 countries, over **20.6 million units** of blood or blood components were **issued** for transfusion (compared to 22.1 million in 2020). The data on recipients (reported by only 19 countries) indicates that more than **2.9 million patients** received at least one transfusion.

- In total, **2 814 SAR** in **recipients** (imputability levels 1-3) were reported by 27 countries. However, only **1 379 SAR** were likely, probably or certainly caused by the transfusion (imputability level 2 or 3). This number is slightly lower than in the previous reporting year (2 967), which can be explained by the fact that the United Kingdom (UK), previously a major contributor, ceased reporting as a whole in 2021 following its withdrawal from the EU.

- **Febrile non-haemolytic transfusion reaction (FNHTR)** (24.2%) was the most commonly reported type of SAR, followed by **anaphylaxis/hypersensitivity** (15.7%) and **transfusion-associated circulatory overload (TACO)** (13.4%).

- There were **25 deaths** classified as probably or certainly caused by transfusion (imputability level 2 or 3). According to the data provided, some of these transfusion-related deaths could not be directly attributed to the quality and safety of blood components, but rather to lapses in clinical practice or unpredictable reactions. However, only three countries provided final investigation results on reported deaths (Belgium, France and Poland), while most investigation results were missing, incomplete or unclear, making it impossible to know if these deaths were preventable and what lessons, if any, could have been learned.

- In total, **2 734 SAE** were reported by 24 countries, indicating a slight decrease compared to the previous year (3 018). Similar to SAR, the decrease was due to the UK no longer reporting as a whole. Three quarters of all SAE were reported by only four countries (Romania, Belgium, France and Germany), so it is important to note that SAE reporting rates vary considerably between countries. The majority of SAE were attributed to **component defect** (38%), followed by **human error** (35%) and **system failure** (12%). This represented a change compared to the previous year, when human error (44%) and system failure (29%) were the leading types of SAE. Of the SAE classified as component defects, 73% were attributed to post-donation (information not known at the time of donation), donor selection and testing-related events.

- Data on **SAR in donors (2 946)** were voluntarily reported by 23 countries (5 less than the previous year) indicating a 26% decrease in reported SAR among blood donors compared with the previous year, which reflects the lower number of reporting countries.

[3] Greece provided the DG SANTE report after the deadline; data was not included in the analysis.

3. DATA COLLECTION AND ANALISYS

This report provides a summary of the national data submitted to the Commission by **26 EU member states** plus Iceland, Liechtenstein, Norway and Northern Ireland pertaining to the reporting period from 1 January to 31 December 2021. It also includes a comparison with the data from previous years and general conclusions.

In 2021, the Commission provided NCAs with improved tools to facilitate a standardised online data reporting approach:

1) ***An electronic reporting template*** for national data collection and submission to a DG SANTE-hosted database.
2) ***The Common Approach, version 2022*** complementing the electronic reporting template with a definition of reportable SAR and SAE, an updated recommendation on reporting methodology and other clarifications.

The reporting countries and VES verified the accuracy of EDQM's analysis and interpretation of SARE data for 2021.

4. MAJOR FINDINGS

4.1 Data completeness

The annual data on SARE for blood and blood components were reported by 26 EU member states and four non-EU countries (Iceland, Liechtenstein, Norway and Northern Ireland) comprising aggregated data from 3 307 reporting blood establishments. The UK ceased reporting as a whole in 2021 (the first year post Brexit), which explains the reduction in the number of establishments compared to 2020.

Regarding data completeness, 23 out of 30 reporting countries confirmed 100% completeness of national data, while six countries provided 75-99% of the expected data. One country was not able to provide information on completeness of national data. Similar to previous years, not all countries were able to provide complete data on all denominators (i.e. blood units issued, blood units transfused and number of recipients), which affected the analysis and reliability of results. Therefore, this report provides a partial insight into SARE related to blood/blood components, rather than a comprehensive view of the safety and quality of European transfusion services.

Iceland, Liechtenstein, Norway and Northern Ireland submitted their national data on a voluntary basis, thus contributing to a broader picture of the quality and safety of European transfusion services.

4.2 Denominators

4.2.1 Number of blood collections

Twenty-eight countries (AT, BE, BG, HR, CY, CZ, DK, EE, FI, FR, DE, IS, IE, IT, LV, LT, LU, MT, NL, NO, PL, PT, RO, SK, SI, ES, SE, and NI) reported a total of 16 242 768 **whole blood collections** in 2021. This was similar to the previous year when 16 510 040 collections were reported by 26 countries.

In terms of **apheresis collection**, 27 countries (all of the above except SE) reported a total of **6 035 995** collections.

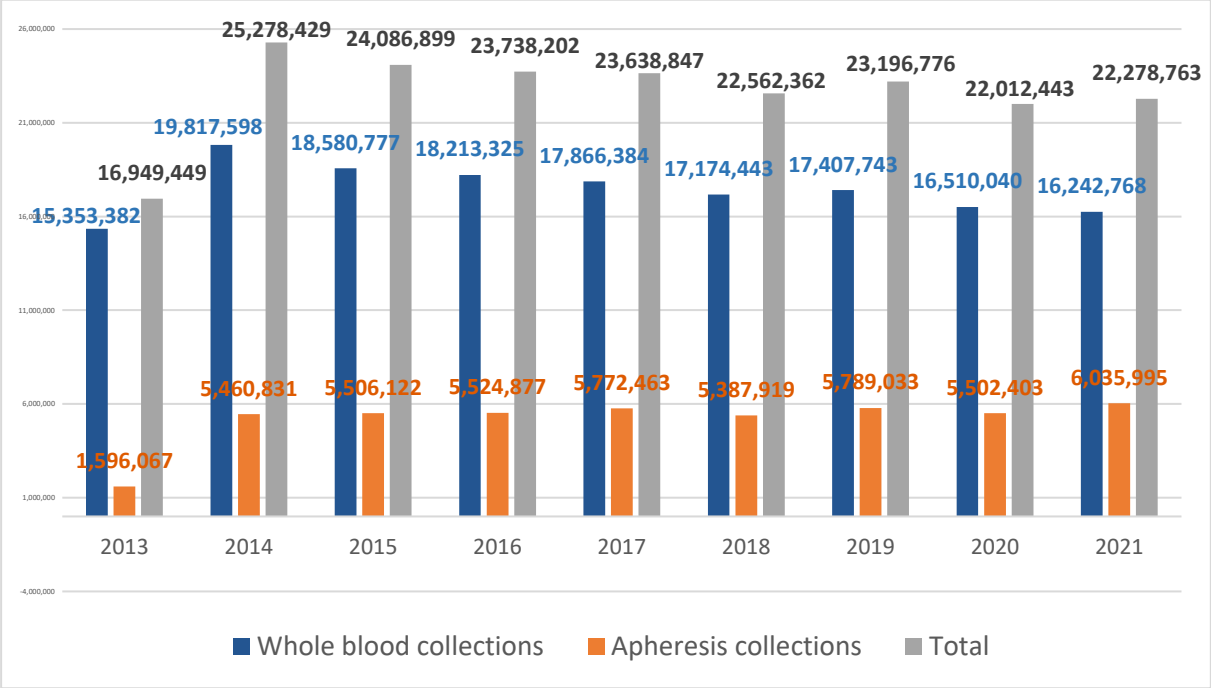

Figure 1. Whole blood, apheresis and total number of collections: 2013-2021 comparative data

4.2.2 Number of blood component units issued

Regarding the units of blood components issued**,** 25 countries (AT, BE, BG, HR, CY, CZ, DK, EE, FI, FR, DE, IS, IT, LV, LT, LU, MT, NL, PL, PT, RO, SK, SI, SE and NI) provided data. Four of the remaining countries (DE, ES, LI and NO) did not report the number of units issued but did provide the number of units transfused. As in previous exercises, it is considered that all units transfused must have previously been issued, hence the numbers for units transfused have been included in the total number of units reported as issued.

A total of **20 633 199 issued units** of blood and blood components were reported in 2021. *Figure 2* shows a breakdown of units issued by type of blood component (including data on transfused units from DE, ES, LI and NO). Where possible, the number of units of COVID-19 Convalescent Plasma (CCP) (5 906 units) were excluded from the total number of units of plasma issued.

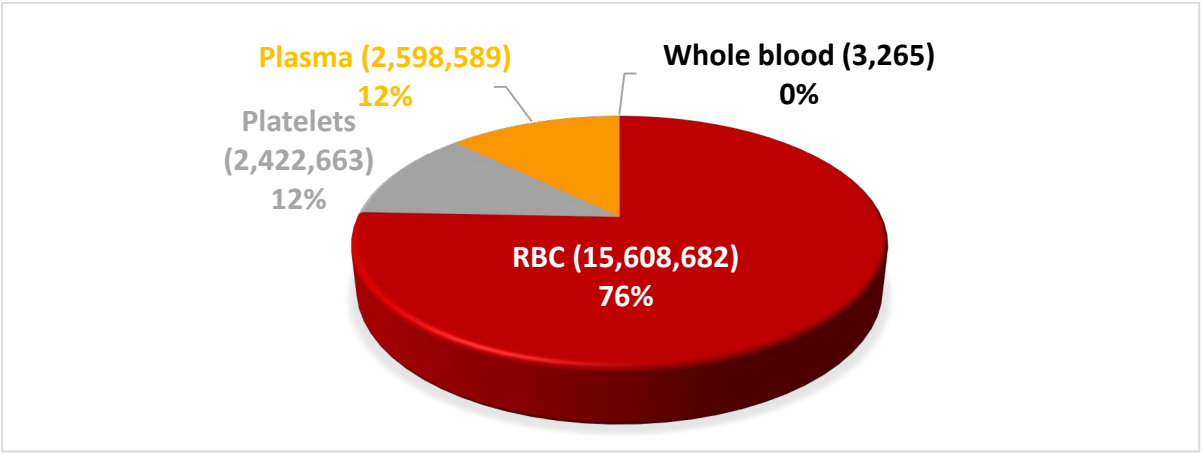

Figure 2. Units issued per blood component type (absolute values and percentage); data 2021

4.2.3 Number of blood component units transfused

Concerning the units of **blood components transfused**, a total of **17 808 869** units were reported as transfused by 26 countries (AT, BE, BG, HR, CY, CZ, DK, EE, FR, DE, HU, IS, IE, IT, LV, LI, LU, MT, NL, NO, PT, RO, SK, ES, SE, and NI). Where data on CCP were provided, those units were subtracted from the total number of plasma units transfused (4 909 CCP units).

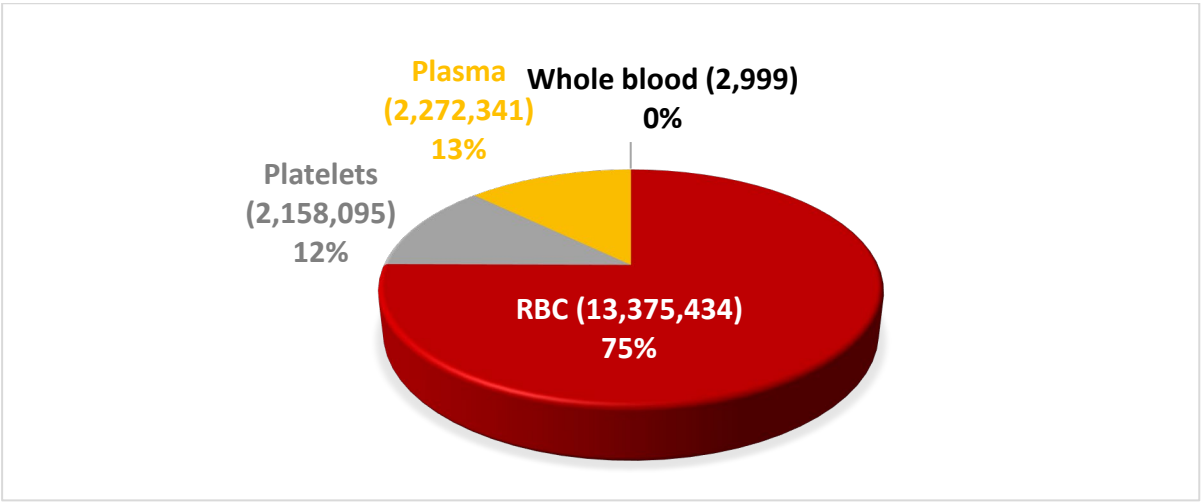

Figure 3. Units transfused per blood component (absolute values and percentage); data 2021

4.2.4 Number of blood component units issued and transfused by country

The number of units issued and transfused as reported by each country is presented in *Table 1*. Where only the number of units transfused was reported (DE, ES, LI and NO), the units transfused were considered as units issued on the principle that the number of blood components issued was greater than or equal to the number of units transfused (only issued products are suitable for transfusion). The same data (in millions) is represented graphically in *Figure 4*.

Country	Number of units issued	Number of units transfused
Austria (AT)	323 548	313 628
Belgium (BE)	518 514	512 521
Bulgaria (BG)	238 582	197 206
Croatia (HR)	256 870	245 223
Cyprus (CY)	87 467	84 050
Czechia (CZ)	569 628	567 467
Denmark (DK)	254 611	255 219
Estonia (EE)	63 869	62 349
Finland (FI)	211 621	N/A
France (FR)	3 005 234	2 817 261
Germany (DE)	4 983 716	4 983 716
Hungary (HU)	535 512	214 322
Iceland (IS)	14 552	13 389
Ireland (IE)	145 501	144 185
Italy (IT)	2 964 204	2 885 769
Latvia (LV)	92 038	91 115
Liechtenstein (LI)	221	221
Lithuania (LT)	127 126	N/A
Luxembourg (LU)	24 237	23 785
Malta (MT)	23 059	17 892
Netherlands (NL)	457 317	440 791
Norway (NO)	212 938	212 938
Poland (PL)	1 556 981	N/A
Portugal (PT)	372 143	352 078
Romania (RO)	674 654	655 704
Slovakia (SK)	341 234	341 234
Slovenia (SI)	101 897	N/A
Spain (ES)	1 883 734	1 883 734
Sweden (SE)	543 175	447 945
Northern Ireland (NI)	49 016	45 127
Total	**20 633 199**	**17 808 869**

Table 1. Number of units issued and transfused by country (in millions); data 2021

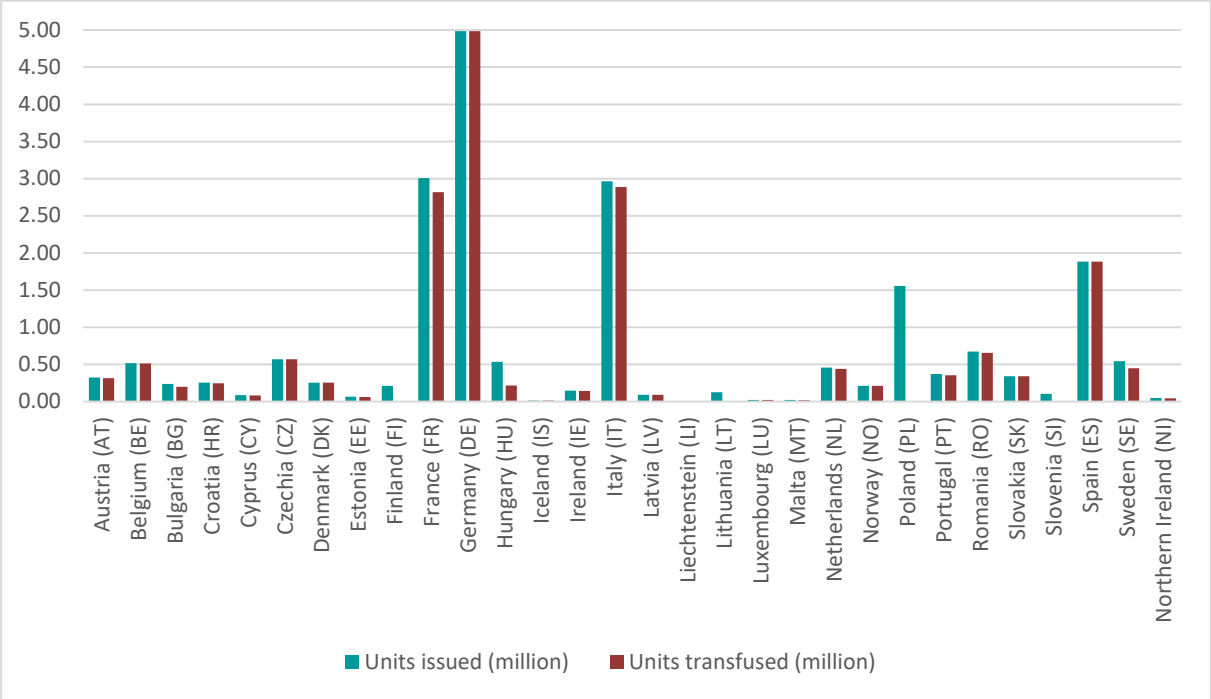

Figure 4. Number of units issued and transfused by country (million); data 2021

4.2.5 Number of recipients transfused

According to data reported by 19 countries (AT, BE, BG, HR, CY, CZ, DK, ES, FR, IS, IE, IT, LI, LU, MT, NI, NL, PT, and SE), **2 752 465** patients were transfused in 2021 (*Figure 5*). In addition, Romania reported 159 842 recipients for whom for the type of blood component transfused was not specified.

When interpreting these results, be advised that they do not reflect the fact that a given patient might have received more than one blood component; these patients were counted more than once.

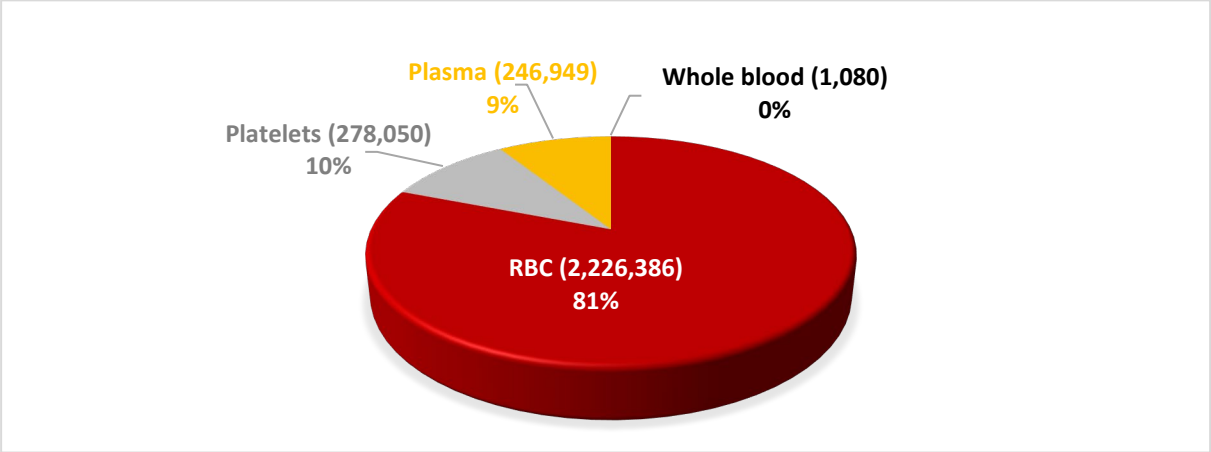

Figure 5. Recipients transfused per blood component; data 2021

Considering the demographic data of the reporting countries as of 1 January 2021[44], the incidence of issued and transfused blood components per 1 000 population is presented in *Figures 6 and 7.*

[4] https://ec.europa.eu/eurostat/web/population-demography/demography-population-stock-balance/database; https://www.nisra.gov.uk/publications/census-2021-table-lookups (Following Brexit, UK = Northern Ireland only)

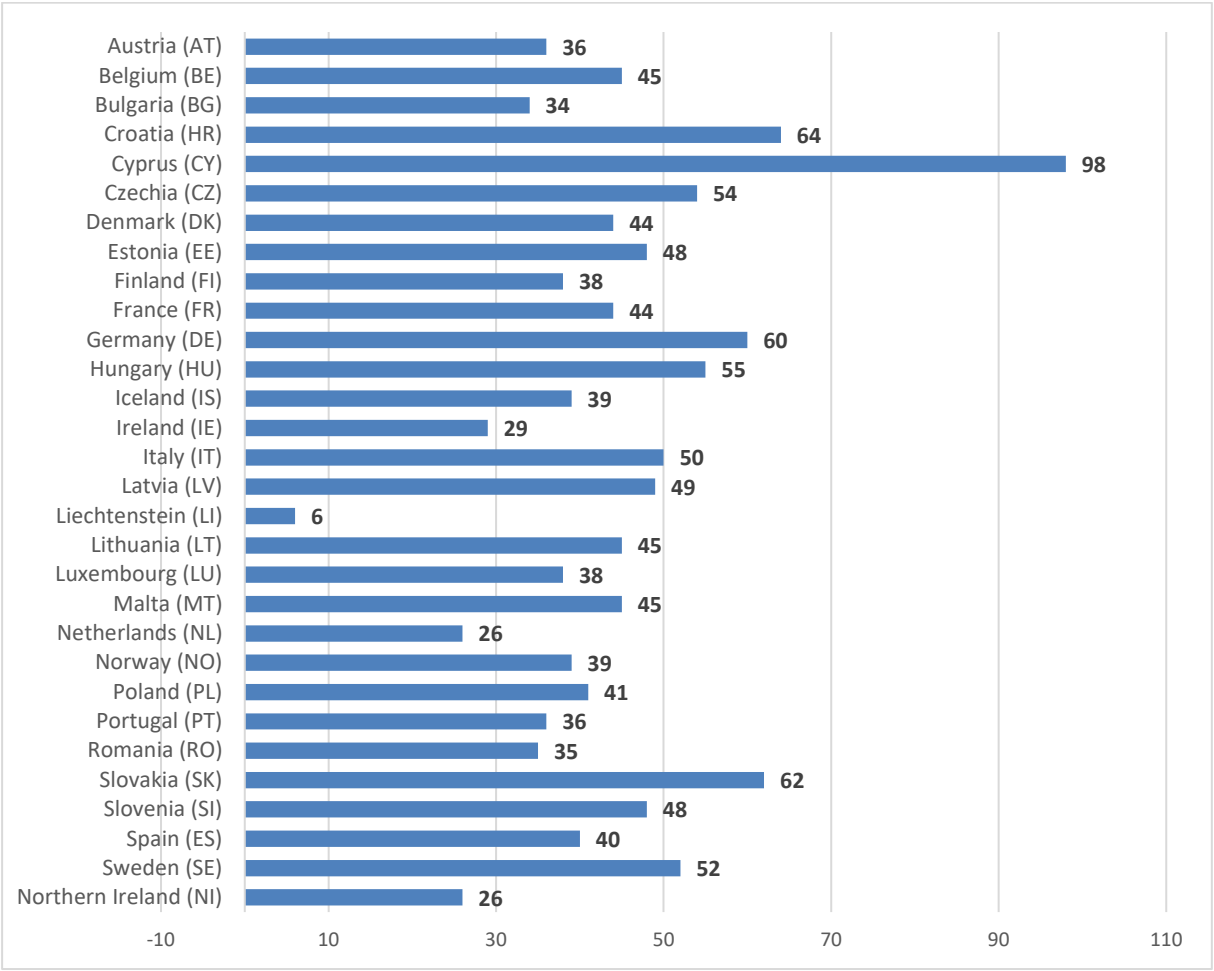

Figure 6. Number of blood units issued per 1 000 population; data 2021

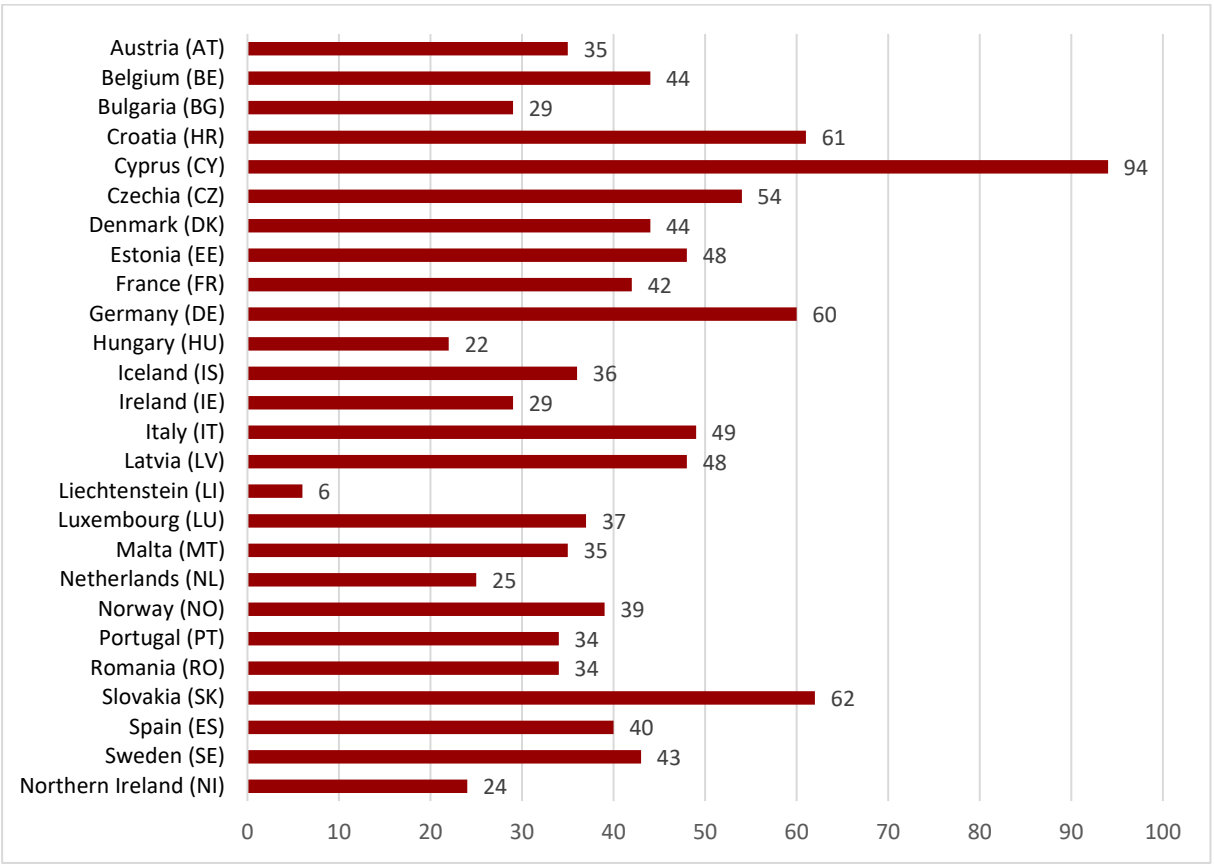

Figure 7. Number of blood units transfused per 1 000 population; data 2021

The incidence of blood component units transfused (per million population), calculated for each reporting country, is presented in *Table 2* below. Countries that did not provide data for at least one type of component were not included.

Country	Red blood cells	Platelets	Plasma	Whole blood
	Number of units transfused (pmp)	Number of units transfused (pmp)	Number of units transfused (pmp)	Number of units transfused (pmp)
Austria (AT)	30 923	3 841	346	
Belgium (BE)	34 949	5 668	3 739	
Bulgaria (BG)	14 886	3 576	10 047	2.9
Croatia (HR)	43 451	7 020	10 283	
Cyprus (CY)	72 168	6 615	15 022	
Czechia (CZ)	40 109	4 474	9 355	133.0
Denmark (DK)	31 226	6 067	6 409	
Estonia (EE)	33 495	5 282	8 094	4.5
France (FR)	33 422	4 945	3 272	2.0
Germany (DE)	42 279	7 165	10 489	
Iceland (IS)	27 091	5 564	3 650	
Ireland (IE)	24 328	4 472		0.2
Italy (IT)	40 747	3 999	3 970	0.3
Latvia (LV)	28 310	4 500	15 317	
Liechtenstein (LI)	5 505	77	77	
Luxembourg (LU)	28 789	4 881	3 803	
Malta (MT)	26 985	3 893	3 790	
Netherlands (NL)	22 225	2 957	42	
Norway (NO)	27 450	4 406	7 538	102.6
Portugal (PT)	28 139	4 939	1 109	1.0
Romania (RO)	18 258	5 579	10 270	41.4
Slovakia (SK)	37 606	4 425	20 469	
Spain (ES)	31 962	4 853	2 927	0.2
Sweden (SE)	35 013	4 509	3 631	4.3
Northern Ireland (NI)	18 747	3 197	1 767	

Table 2. Incidence (number of units transfused per million population by blood component and by country); data 2021

4.3 Serious adverse reactions in recipients

4.3.1 General information

The incidence of SAR in 2021 was **7.3 per 100 000 units transfused** (see section 4.3.2). Although the result suggests a decrease in SAR incidence compared to the previous year (8.99), it is important to keep in mind when interpreting these data that they are incomplete and inconsistent across the reporting countries in terms of denominators and SAR reporting.

Twenty-five SAR (imputability 2-3) resulted in death. In terms of the type of blood component involved, 19 fatalities were associated with red blood cell (RBC) transfusion (76%), four with platelet transfusion (16%) and two with transfusion of more than one blood component (8%).

A summary of this is presented in *Figure 8*. SAR from countries that did not report the number of units transfused were excluded.

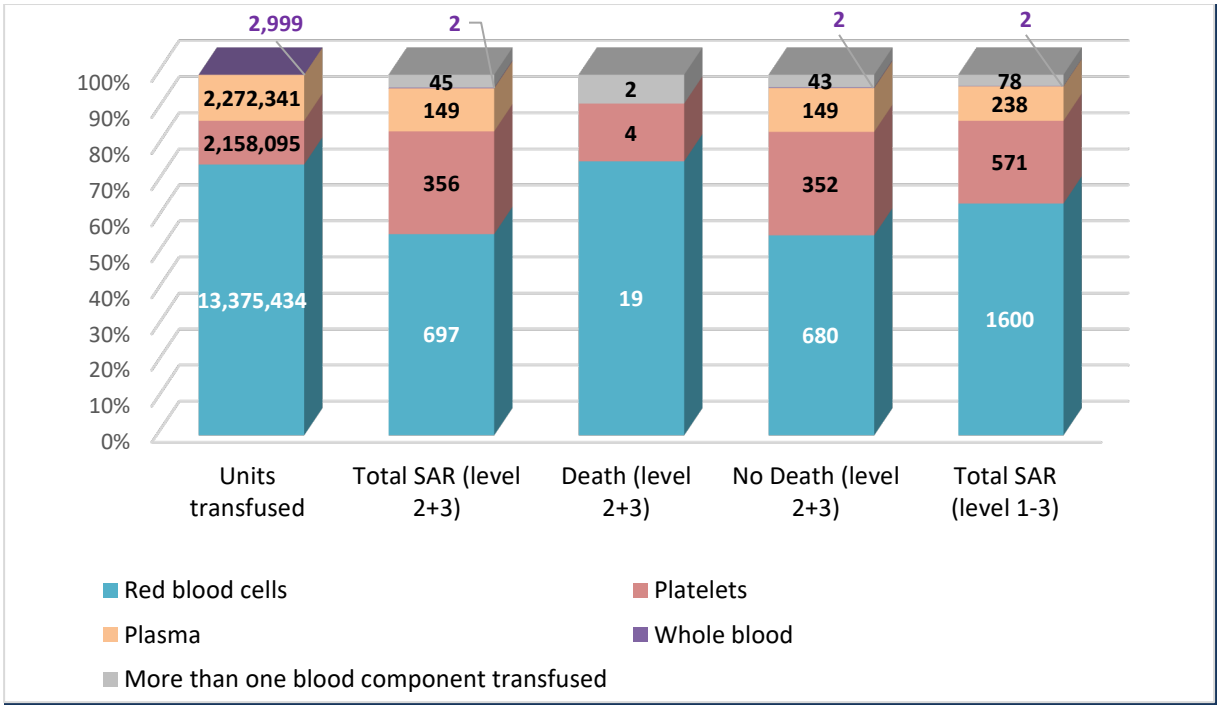

Figure 8. Number of SAR and fatalities by imputability level and by type of blood component; data 2021

The majority of the reported SAR (level 2 or 3) were associated with transfusions of RBC, followed by platelets and plasma. The percentage of SAR by type of blood component is presented in *Figure 9*.

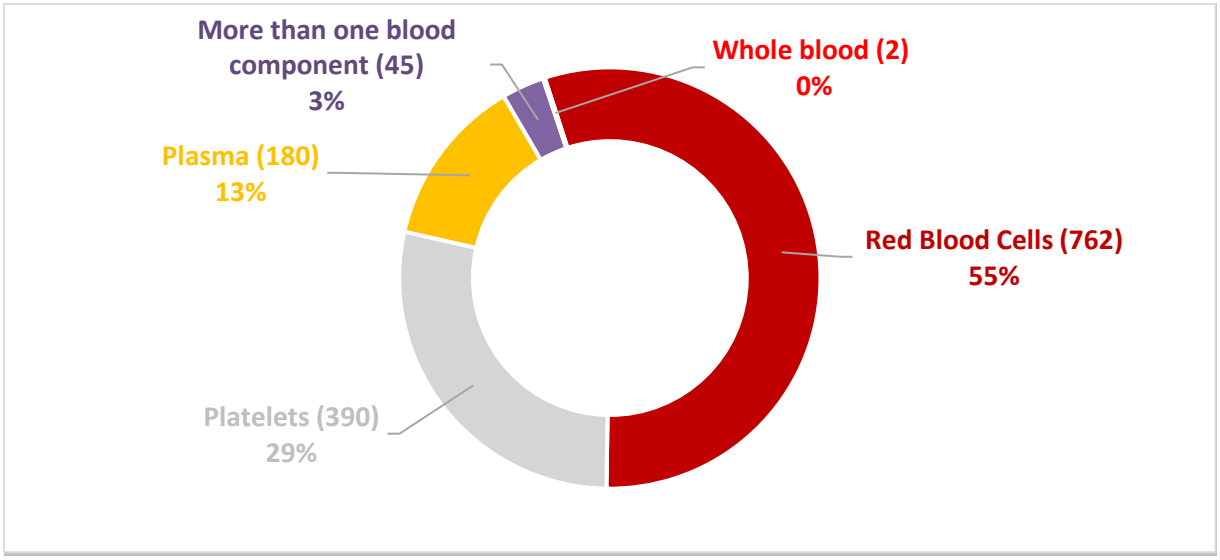

Figure 9. Data on SAR by blood component type; data 2021

The distribution of SAR imputability 1-3 and 2-3 by country and by blood component is represented in *Figures 10 & 11*.

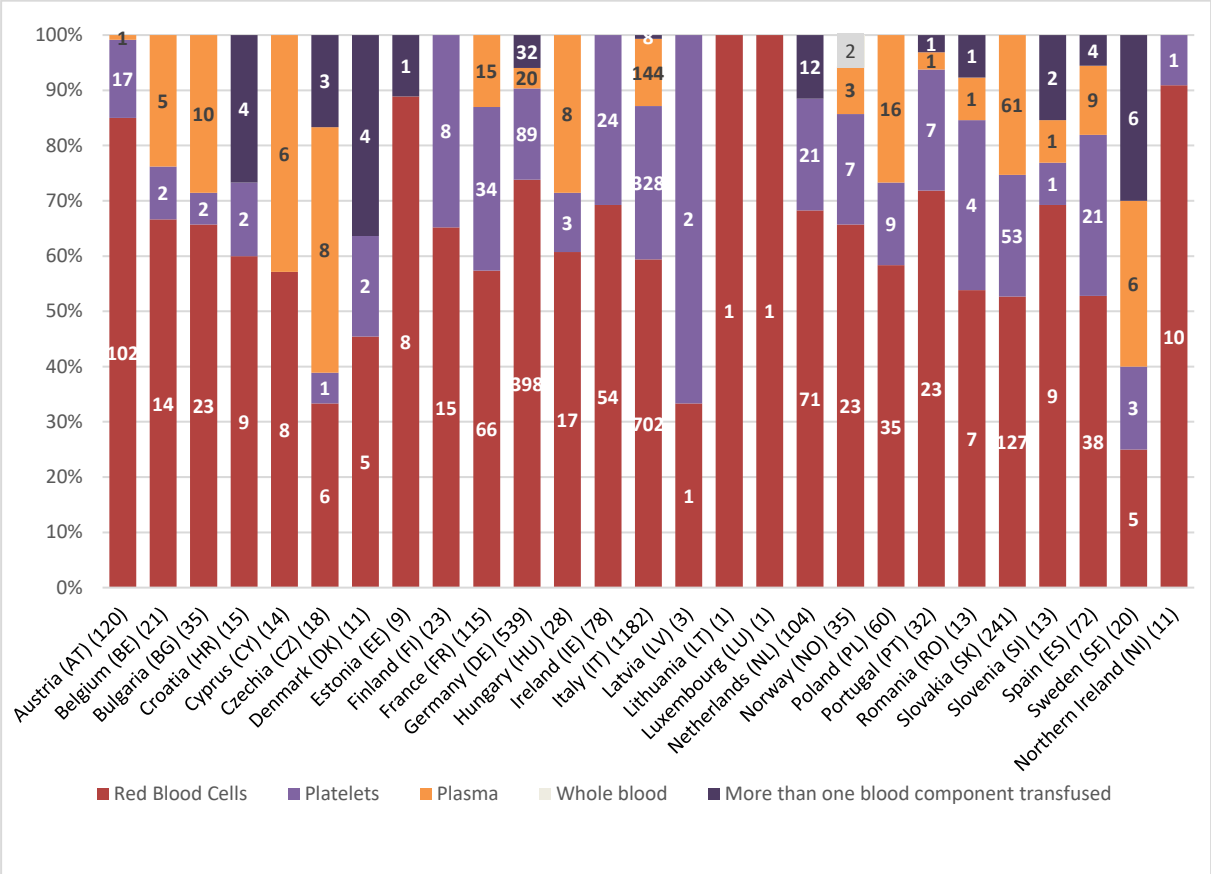

Figure 10. Number of SAR of imputability level 1-3 by country and type of blood component; data 2021

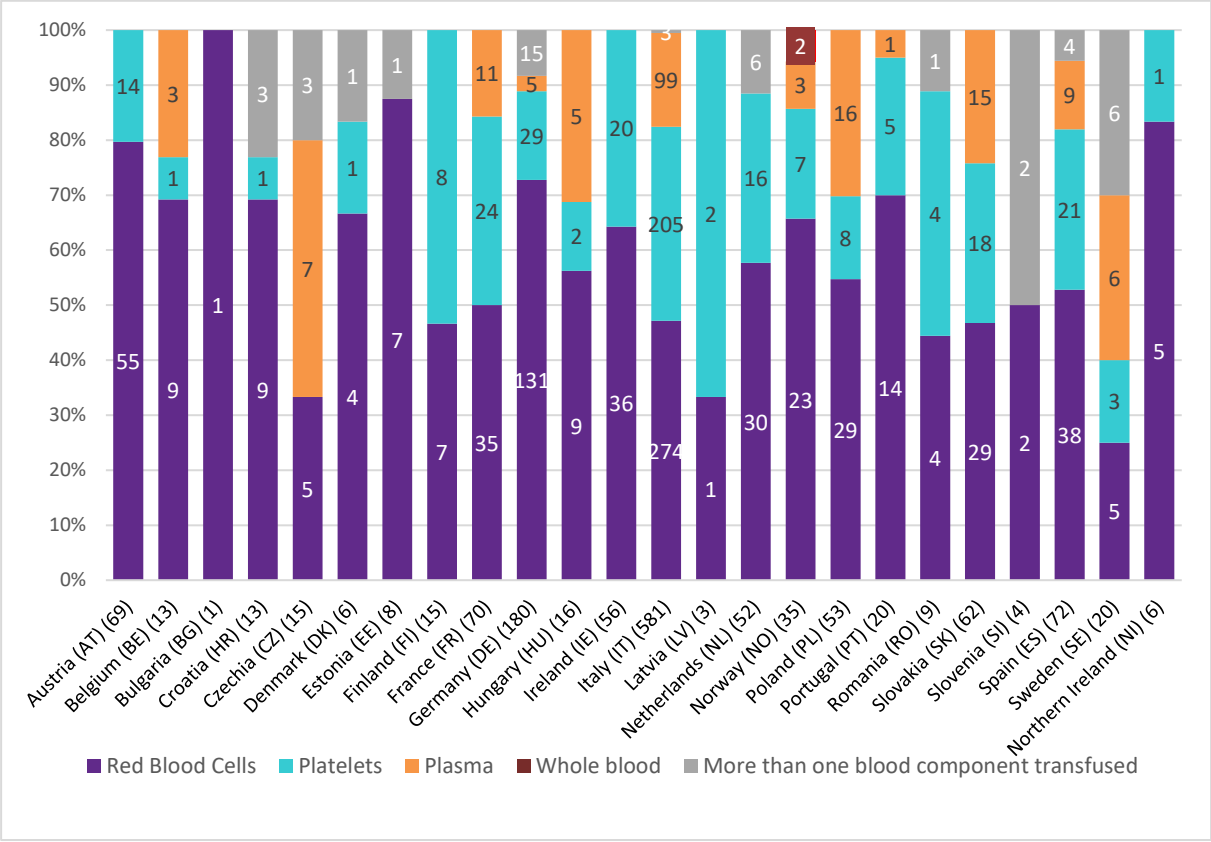

Figure 11. Number of SAR of imputability level 2-3 by country and type of blood component; data 2021

4.3.2 Incidence of SAR by type of blood component

As shown in *Table 3*, the risk associated with the transfusion of **platelets** is significantly higher compared to other blood components (based on data from those countries who provided the number of SAR and units transfused, per type of blood component). SAR from countries that did not report the number of units transfused have not been included (FI, LT, PL and SI).

The incidence of SAR associated with transfusion of platelets (number of SAR associated with the transfusion of platelets per 100 000 units of platelets transfused) was **17.3**, **7.2** for plasma and **5.4** for RBC.

Component type	Units transfused	Total SAR (level 1-3)	Total SAR (level 2+3)	SAR (2+3) incidence (per 100 000 units transfused)	Deaths (level 2+3)	Percentage of deaths among SAR 2-3	Deaths incidence (per 100 000 units transfused)
Red blood cells	13 375 434	1 718	724	5.4	19	2.6%	0.14
Platelets	2 158 095	623	374	17.3	4	1.1%	0.18
Plasma	2 272 341	298	164	7.2	0	0%	0
Whole blood	2 999	2	2	66.7	0	0%	0
More than one blood component transfused	-	76	43	NA	2	4.6%	NA
Total	**17 808 869**	**2 717**	**1 307**	**7.3**	**25**	**1.7%**	**0.13**

Table 3. Incidence of SAR by type of blood component; data 2021

As some participating countries reported partial data, the interpretation of these results should take into consideration this limitation.

4.3.3 SAR by type of reaction

According to the classification in *Figure 12*, the most common type of SAR was **FHTR** (24.2%), followed by **anaphylaxis/hypersensitivity** (15.7%) and **TACO** (13.4%).

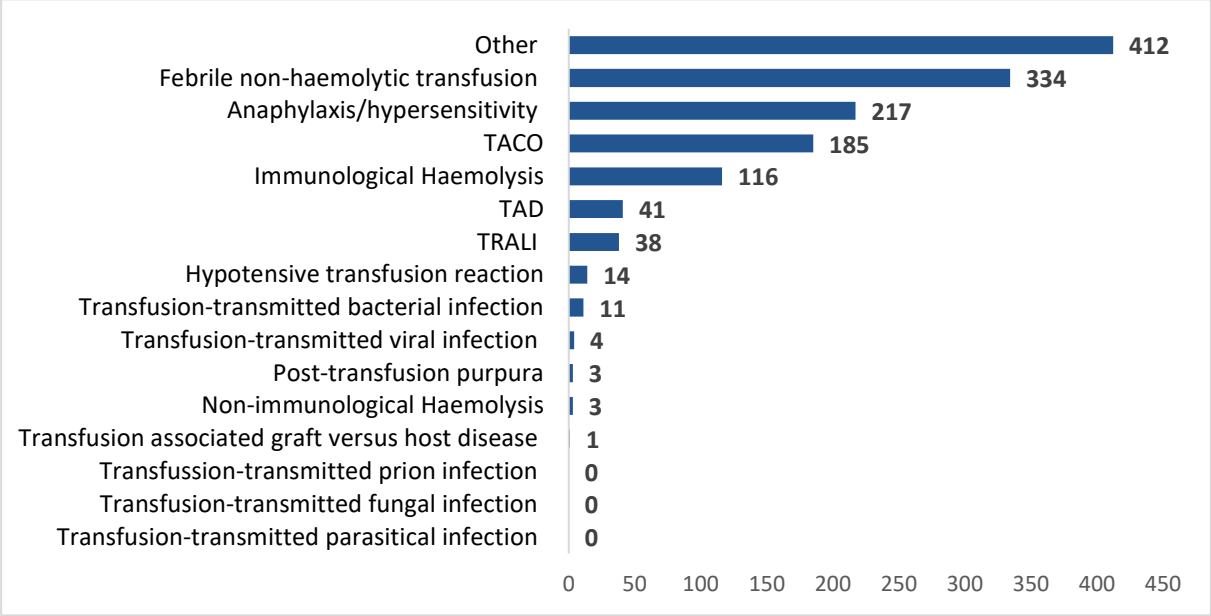

Figure 12. Distribution of SAR by type of reaction; data 2021

As was the case in previous years, unclassified SAR remains the most prevalent group (30%). A detailed account of the types of reactions in recipients classified as "others" is available in *Figure 13*. Greater clarification is required here in order to address the potential issue of classification accuracy.

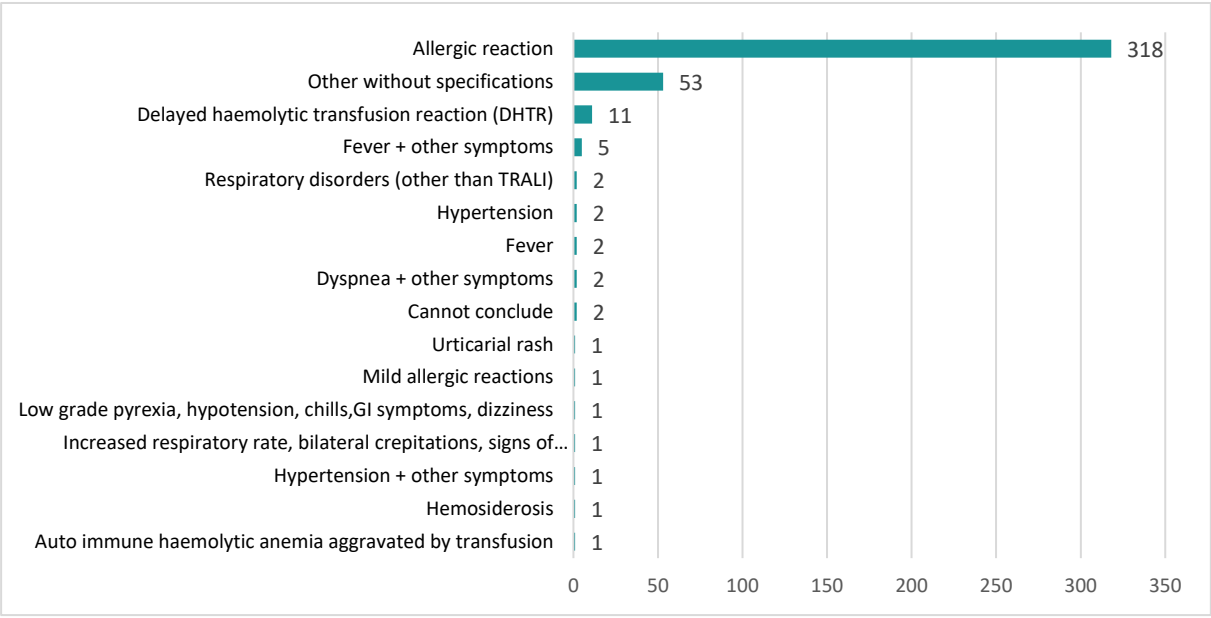

Figure 13. Distribution of SAR classified as "Others", by subtype of other reaction; data 2021

A detailed presentation of SAR (imputability level 2-3) by type of reaction and type of blood component is available in *Table 4* below.

SAR Type (Level 2+3)	Red blood cells		Plasma		Platelets		Whole blood		More than one blood component transfused		All		
	No Death	Death	No death	Death	No Death	Death	No Death	Death	No Death	Death	No Death	Death	Total
Anaphylaxis/hypersensitivity	57	1	47	0	98	0	0	0	15	0	217	0	217
Immunological haemolysis due to ABO incompatibility	44	8	6	0	3	0	1	0	1	0	55	8	63
Immunological haemolysis due to other allo-antibody	49	2	0	0	1	0	0	0	0	1	50	3	53
Non-immunological haemolysis	3	0	0	0	0	0	0	0	0	0	3	0	3
Post-transfusion purpura	1	0	1	0	0	0	0	0	1	0	3	0	3
Transfusion-related acute lung injury (TRALI)	19	0	7	0	5	1	0	0	5	1	36	2	38
Transfusion-transmitted bacterial infection	1	0	0	0	6	3	0	0	1	0	8	3	11
Transfusion-transmitted parasitical infection	0	0	0	0	0	0	0	0	0	0	0	0	0
Transfusion-transmitted fungal infection	0	0	0	0	0	0	0	0	0	0	0	0	0
Transfusion-transmitted viral infection	2	0	0	0	1	0	0	0	1	0	4	0	4
Transfusion-associated graft-versus-host disease	0	0	0	0	0	0	0	0	1	0	1	0	1
TACO	156	8	4	0	6	0	0	0	11	0	177	8	185
Febrile non-haemolytic transfusion	240	0	8	0	81	0	0	0	5	0	334	0	334
TAD	26	0	3	0	11	0	1	0	0	0	41	0	41
Hypotensive transfusion reaction	10	0	1	0	3	0	0	0	0	0	14	0	14
Other	135	1	103	0	171	0	0	0	2	0	411	1	412
Total	**743**	**20**	**180**	**0**	**386**	**4**	**2**	**0**	**43**	**2**	**1 354**	**25**	**1 379**

Table 4. Number of SAR (Imputability levels 2-3) by type of reaction and blood component; data 2021

4.3.4 Transfusion-related deaths

4.3.4.1 Type of SAR associated with death

Out of 25 transfusion-related deaths, the majority were associated with TACO (8), followed by immunological haemolysis (11), bacterial infection (3) and TRALI (2):

- **TACO** (8) - following RBC transfusion
- **Immunological haemolysis** (11) - following RBC transfusion and due to other alloantibodies
- **Bacterial infection** (3) – *non-specified* bacterial infections transmitted via platelet transfusion
- **TRALI** (2) - following platelet transfusion (1) and more than one component transfusion (1)
- **Other** (1) - uncategorised adverse reaction following RBC transfusion

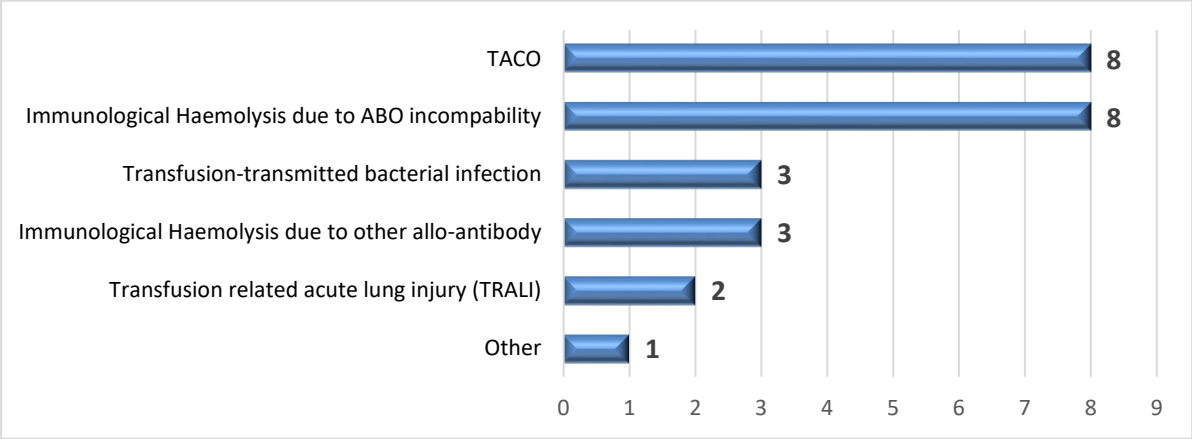

Figure 14. Deaths by SAR type (imputability level 2-3) in absolute values and percentages; data 2021

In addition, **23 deaths** with imputability **level 1** were voluntarily reported by 13 countries (BE, FI, FR, DE, ES, HU, LU, NI, NL, NO, PL, PT, RO and ES), 52% of which were associated with TACO, as shown in *Figure 15*.

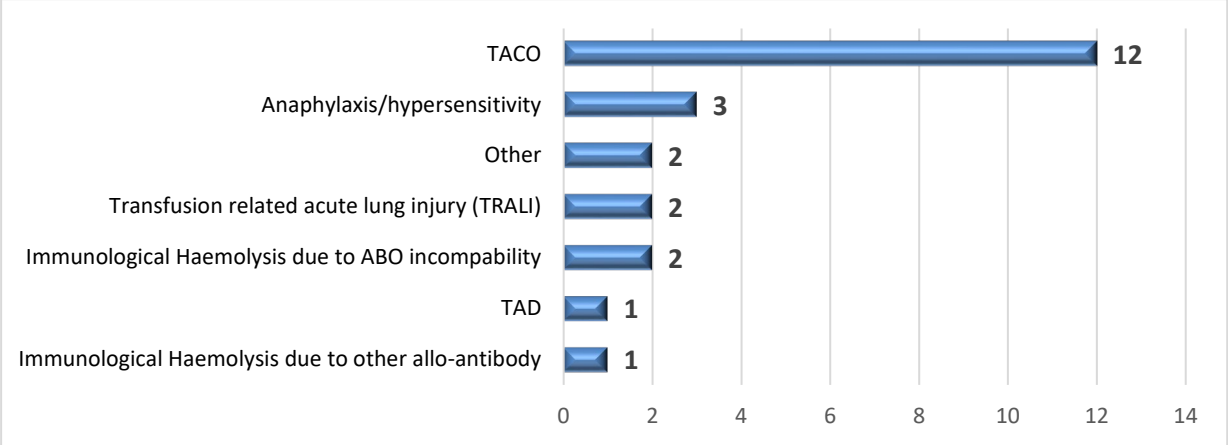

Figure 15. Deaths by type of SAR (imputability level 1) in absolute values and percentages; data 2021

4.3.4.2 Death investigation

Out of the 25 SAR that resulted in death, investigation results were provided for only three deaths by Belgium, France and Poland. The case reports (original text) are available in Annex 1.

4.3.5 International benchmarking

This summary of SARE reports from European countries presents a set of indicators that span the transfusion chain from donor to recipient, and provides an insight, albeit not comprehensive, into haemovigilance practices across Europe and at the level of individual countries.

According to WHO's Global Status Report on Blood Safety and Availability[5], Europe was the WHO region that had the highest percentage of countries with a national haemovigilance system in place (81%).

[5] WHO Global Status Report on Blood Safety and Availability https://www.who.int/publications/i/item/9789240051683

Results on SAR, as well as practical solutions derived from lessons learned by other jurisdictions across the world where well-established systems are in place, were consulted. Relevant data from the Australian, Canadian and Japanese national reports are presented below.

According to the **Australian Haemovigilance Report** 2019-2020 published by the National Blood Authority[6], 61.5% of adverse events were related to red cell transfusions, followed by platelets (24.7%) and fresh frozen plasma (10.2%). Out of 326 transfusion-related SAE reported in the period 2015-2020, TACO and anaphylactic reactions accounted for 52.5% of reported SAE, followed by allergic reactions and FNHTR (17.8% and 14.4%, respectively). A breakdown of SAE by imputability score and outcome severity indicated that four reported deaths were possibly or likely to be related to transfusion, with two anaphylactic reactions, one TRALI and one ABO incompatibility; 40% of reported SAE (131/326) were life-threatening, and 59% (191/326) were reported to be related to severe morbidity, including 53 TACO, 44 FNHTR and 38 allergic reactions.

The Canadian Transfusion Error Surveillance System (TESS) summary for 2020-2021[7] included 1 192 confirmed events. Of these, 13 (1.1%) caused harm in patients. These adverse transfusion reactions caused by transfusion errors comprised TACO (46%) and 7 cases of other reactions: delayed serological transfusion reaction (2), unspecified adverse transfusion reaction (2), FNHTR (1), severe anaphylactic/anaphylactoid allergic reaction (1) and harm associated with transfusion delay (1).

The 2021 Haemovigilance Report by the Japanese Red Cross Society (JRCS)[8] states that SAR accounted for 24.6% of all adverse reactions and mainly comprised severe allergy, dyspnoea, and hypotension. In April 2021, the JRCS started evaluating TRALI and TACO cases based on new criteria (Transfusion. 2019; 59:2465-76, ISBT Working Party on Haemovigilance in collaboration with IHN and AABB.2018.).
As a safety measure against TRALI, the JRCS manufactures fresh frozen plasma (FFP) preferentially derived from 400 mL whole blood donations from male donors. While almost 100% of FFP made from 400 mL whole blood donations are derived from male donors, less than 20% of FFP made from 200 mL whole blood donations and 70% of FFP made from apheresis donations are derived from male donors. Since TACO is a form of cardiac failure due to circulatory overload, it is important to understand the patient's potential risk of cardiac failure by measuring pre-transfusion NT-pro BNP levels or confirming any kidney function insufficiency.
In 2021, 41 haemolytic adverse reactions were reported by medical institutions, of which 16 were serious cases of acute reactions and 25 cases were delayed reactions.
Two cases of HBV infections were confirmed TTIs in 2021. No transfusion-transmitted HCV and HIV cases have been confirmed since the introduction of the nucleic acid amplification test (NAT) on individual samples.
Two cases of transfusion-transmitted bacterial infection (TTBI) involving two divided platelet units prepared from a single apheresis donation were reported. Blood culture tests detected *Morganella morganii* in a platelet component unit that was discontinued during transfusion and two recipients, one of whom died of septic shock. Approximately 1-2 cases of TTBI involving platelet components are confirmed every year. JRCS is planning to implement bacterial screening tests in platelet components.

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[6] Australian Haemovigilance Report 2019 - 2020, National Blood Authority
https://www.blood.gov.au/sites/default/files/Haemovigilance%20Report%202019-20.pdf

[7] TRANSFUSION ERROR SURVEILLANCE SYSTEM (TESS), 2020-2021, Infographic https://www.canada.ca/content/dam/phac-aspc/documents/services/surveillance/blood-safety-contribution-program/transfusion-error-surveillance-system-2020-2021-infographic/PHAC-TESS2021-Info-EN-March1.pdf

[8] Haemovigilance by JRCS 2021, Japanese Red Cross Society, Safety Vigilance Division, Technical Department, Blood Service Headquarters
https://www.jrc.or.jp/mr/english/

Of the nine suspected HBV infections reported in 2021, two were confirmed to be transfusion-transmitted HBV infections, including a spontaneous report on an HBV infection that was identified following hepatitis in the recipient and a case identified through a look-back study that was prompted by the positive conversion of the donor on NAT testing.

4.4 Serious adverse events

4.4.1 General information

The main denominator for SAE is the total number of **blood units processed**. During 2021, a total of **22 961 648** blood units were processed according to data provided by 24 countries (AT, BE, BG, HR, CY, CZ, DK, EE, ES, FI, FR, DE, IS, IE, IT, LV, NI, NL, NO, PL, PT, RO, SI and SE). An overview of data on blood units processed over the reporting years is presented in *Figure 16*.

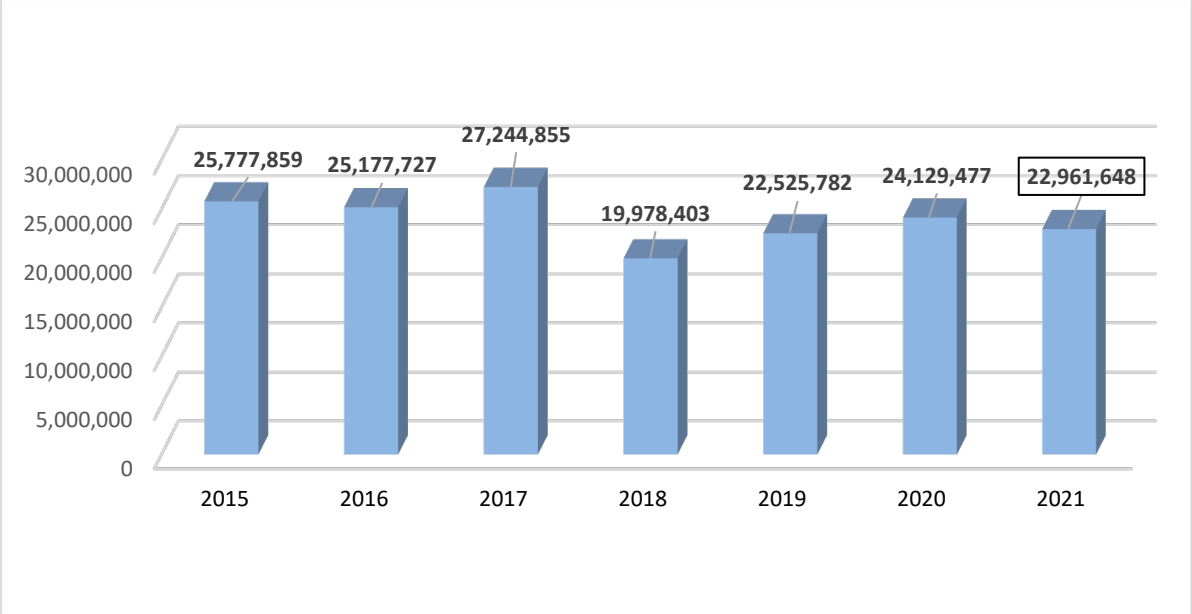


Figure 16. Total number of blood units processed: 2015-2021 comparative data

2 734 SAE were reported in 2021 by 24 countries (AT, BE, BG, HR, CY, CZ, DK, EE, ES, FI, FR, DE, IS, IE, IT, LV, NI, NL, NO, PL, PT, RO, SI and SE). As shown in *Figure 17,* the number of SAE reported varied substantially between reporting countries, similar to previous years. It is recommended to exercise caution when drawing conclusions from these data as 75% of SAE were reported by only four countries (BE, FR, RO and DE).

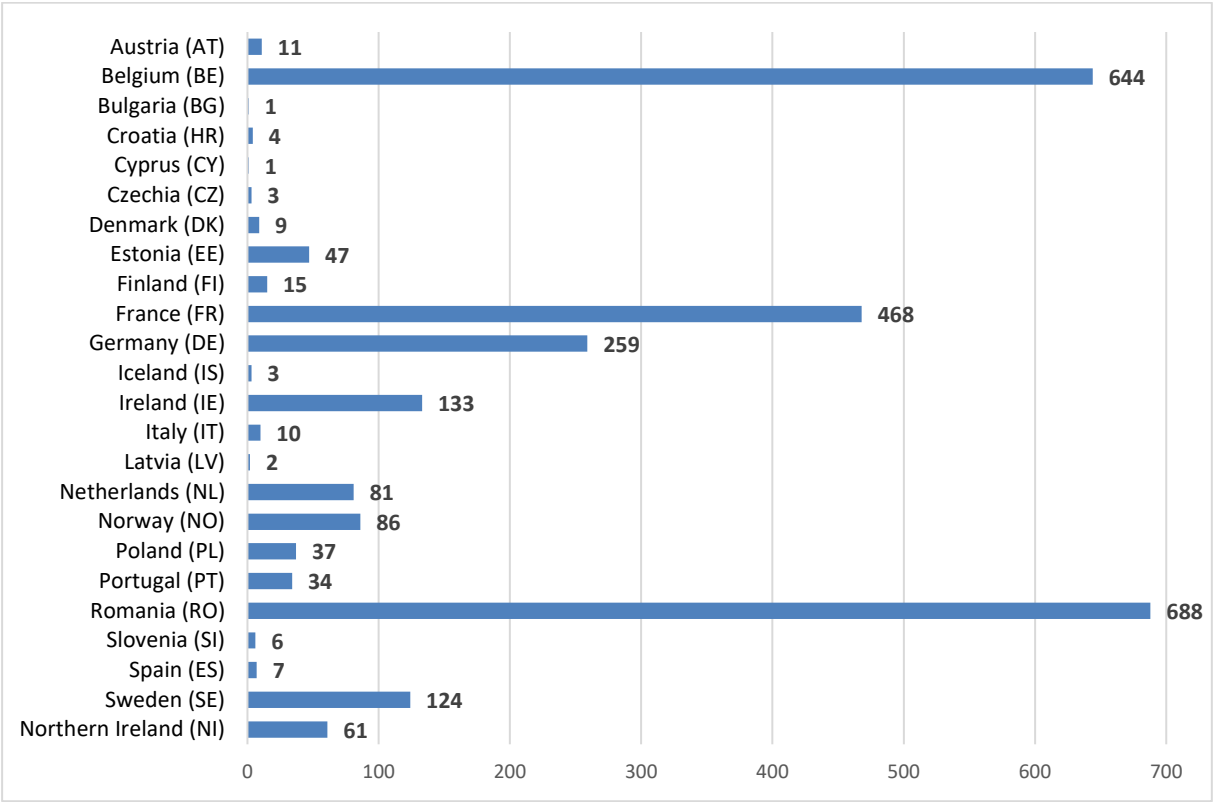


Figure 17. Number of SAE by country; data 2021

The distribution of SAE by type of collection based on data from 16 countries (BE, CZ, DK, FI, FR, DE, IE, IT, NI, NL, NO, PL, PT, RO, SI and SE) is represented on *Figure 18*. Out of 205 SAE, 76% were related to whole blood collection and 24% to apheresis.

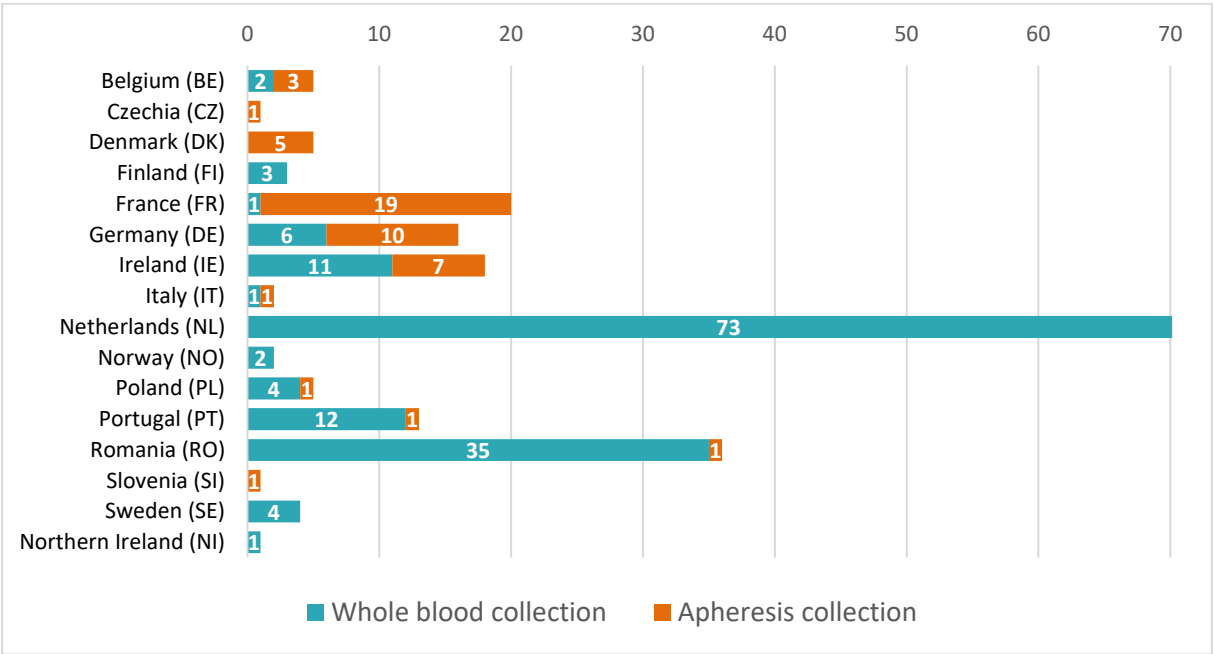


Figure 18. Number of SAE by collection type; data 2021

4.4.2 Incidence of SAE

SAE occur at all stages of the transfusion cycle, from donor selection to clinical services, but the only available denominator is *number of units processed*, which is not optimal. Regardless, it has been used to calculate the incidence of SAE (per 100 000 units of blood/blood components processed).

The incidence of SAE per each reporting country is presented in *Table 5* and *Figure 19* below.

Country	Total number of units processed	# SAE	SAE/100 000 units processed
Austria (AT)	408 702	11	2.7
Belgium (BE)	638 796	644	100.8
Bulgaria (BG)	280 675	1	0.4
Croatia (HR)	189 020	4	2.1
Cyprus (CY)	66 208	1	1.5
Czechia (CZ)	1 506 077	3	0.2
Denmark (DK)	661 814	9	1.4
Estonia (EE)	51 348	47	91.5
Finland (FI)	217 802	15	6.9
France (FR)	3 008 673	468	15.6
Germany (DE)	6 496 821	259	4.0
Iceland (IS)	11 293	3	26.6
Ireland (IE)	138 338	133	96.1
Italy (IT)	3 021 143	10	0.3
Latvia (LV)	58 603	2	3.4
Lithuania (LT)	101 598	0	0.0
Luxembourg (LU)	44 181	0	0.0
Malta (MT)	16 157	0	0.0
Netherlands (NL)	760 000	81	10.7
Norway (NO)	183 592	86	46.8
Poland (PL)	1 397 355	37	2.6
Portugal (PT)	310 757	34	10.9
Romania (RO)	764 037	688	90.0
Slovakia (SK)	195 340	0	0.0
Slovenia (SI)	173 768	6	3.5
Spain (ES)	1 720 402	7	0.4
Sweden (SE)	509 025	124	24.4
Northern Ireland (NI)	43 435	61	140.4
Total	**22 974 960**	**2 734**	**11.39**

Table 5. Incidence of SAE per 100 000 units processed; data 2021

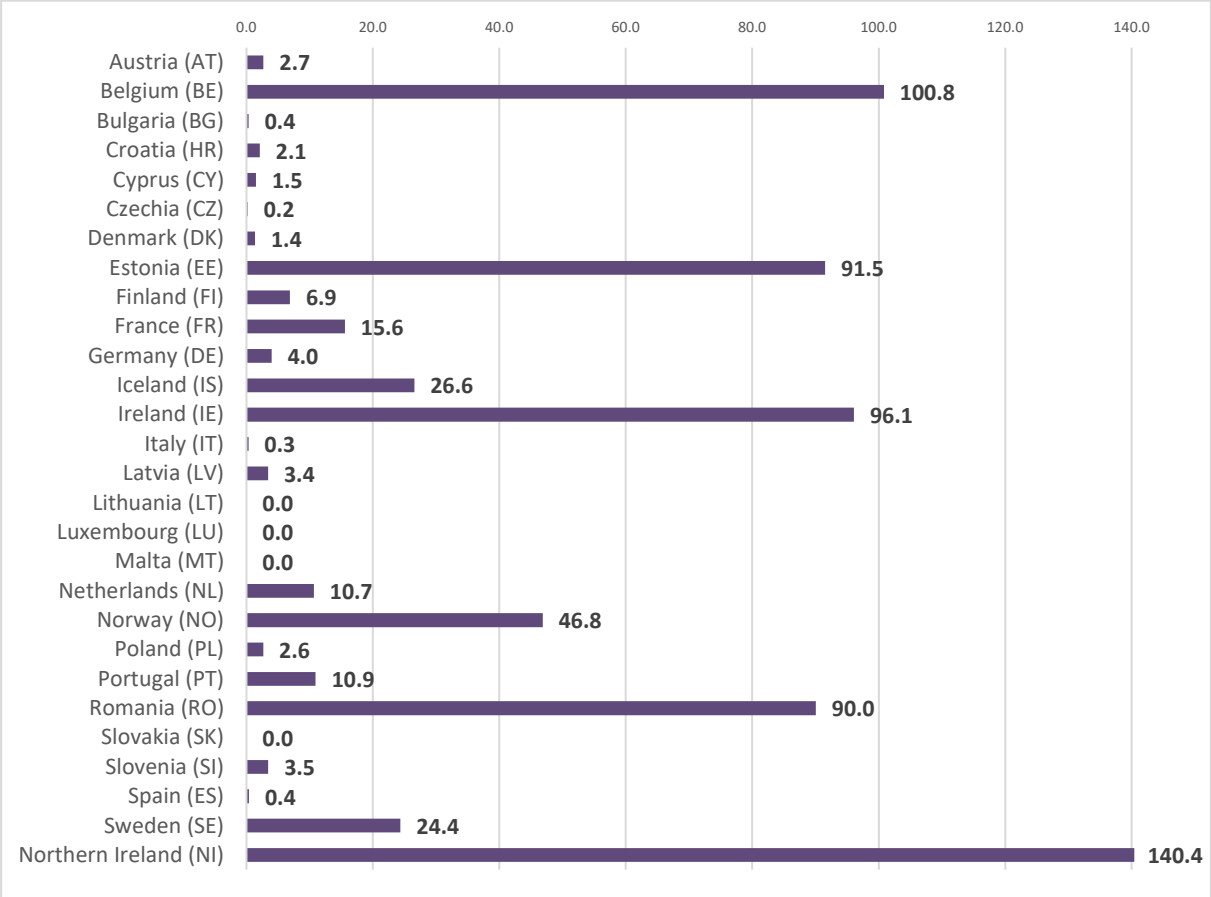


Figure 19. Incidence of SAE per 100 000 units processed; data 2021

4.4.3 SAE by activity step

According to the Common Approach, version 2022, Annex II, SAE are classified by activity step that includes donor selection, whole blood apheresis collection, testing, processing, storage, distribution, component selection, compatibility testing/cross matching, issue and other. Similar to the previous year, SAE classified as **other SAE** were the most represented (31%), followed by those attributed to **testing** (16%), then **donor selection** (12%), **processing (8%)** and **issue** (8%), as shown in *Figure 20*.

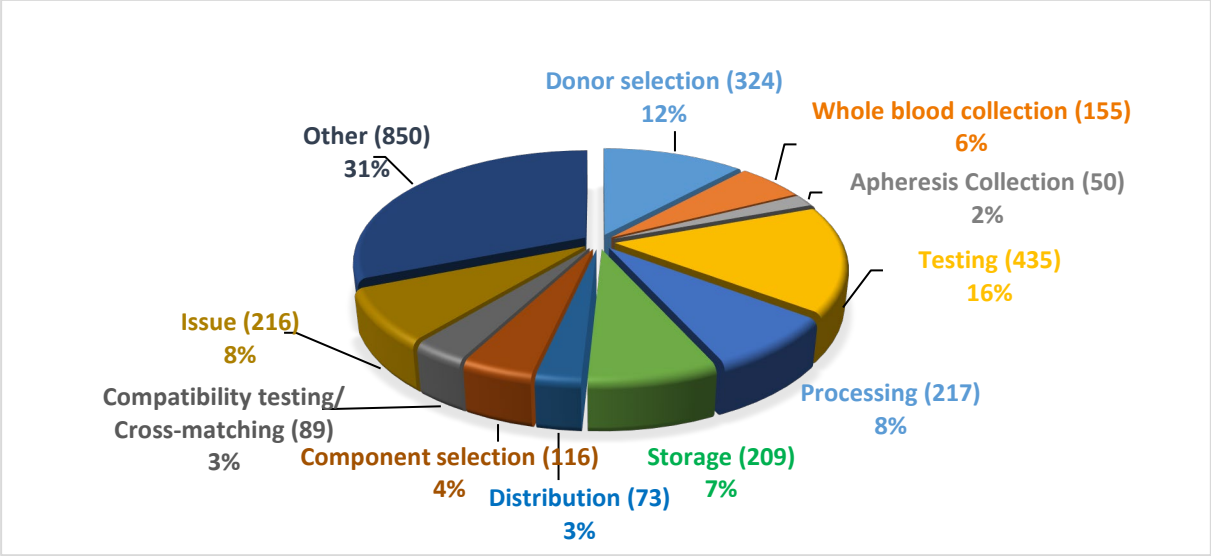


Figure 20. Distribution of SAE by activity step (absolute numbers and percentage); data 2021

As in 2021, there were clear discrepancies between countries in terms of how activity steps were assigned when SAE were identified/occurred: 91% of all SAE classified as attributed to **other** activity steps than the ten listed in the Common Approach, Annex II (850 SAE), were reported by two countries (Belgium and France). This raises the question of accuracy of classifying SAE by activity step, as well as issues of over/under reporting, but it may also be an indication that the activity steps need to be defined in line with current processes specific to blood establishments.

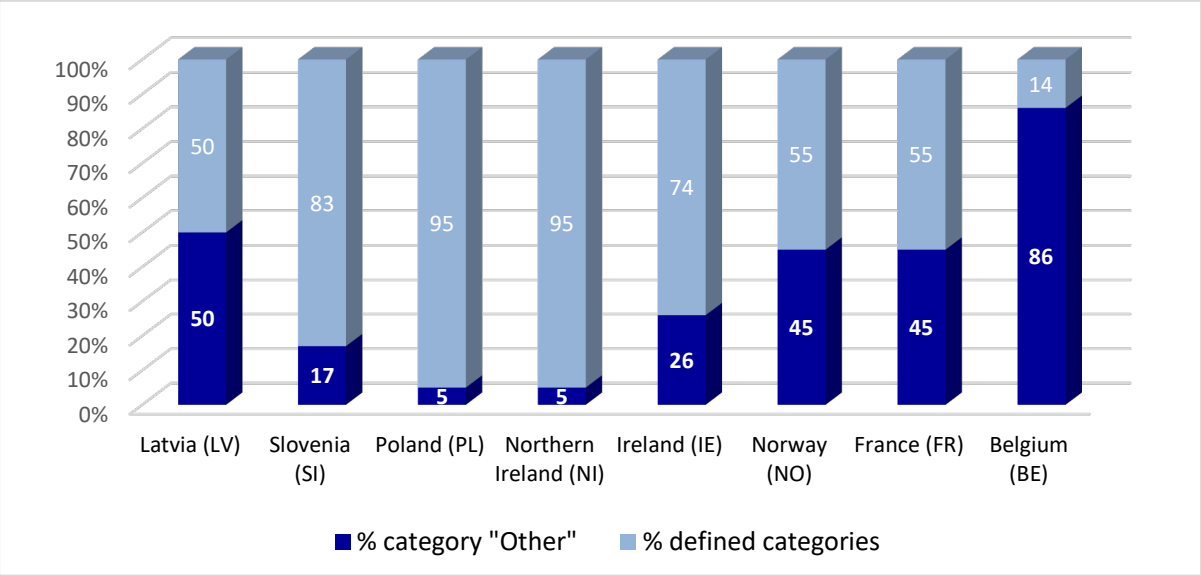


Figure 21. Percentage of SAE reported for activity steps other than the ten steps listed in the Common Approach, Annex II; data 2021

4.4.4 SAE by type of event

The most commonly reported SAE in 2021 were related to **component defect** (38%), followed by **human error** (35%), **system failure** (12%) and **equipment failure** (9%).

The number of SAE classified as human error, although still high, continues to decrease every year. This reflects the efforts made by reporting countries to adapt to the new classification suggested by the VES, which has improved the quality of the data reported.

Over 70% of the 1 037 SAE related to component defect were reported by only two countries: Romania and Belgium (41% and 32%, respectively). In the component defect category, Belgium included possible or confirmed COVID-19 cases, fever and Lyme disease (*Figure 22*).

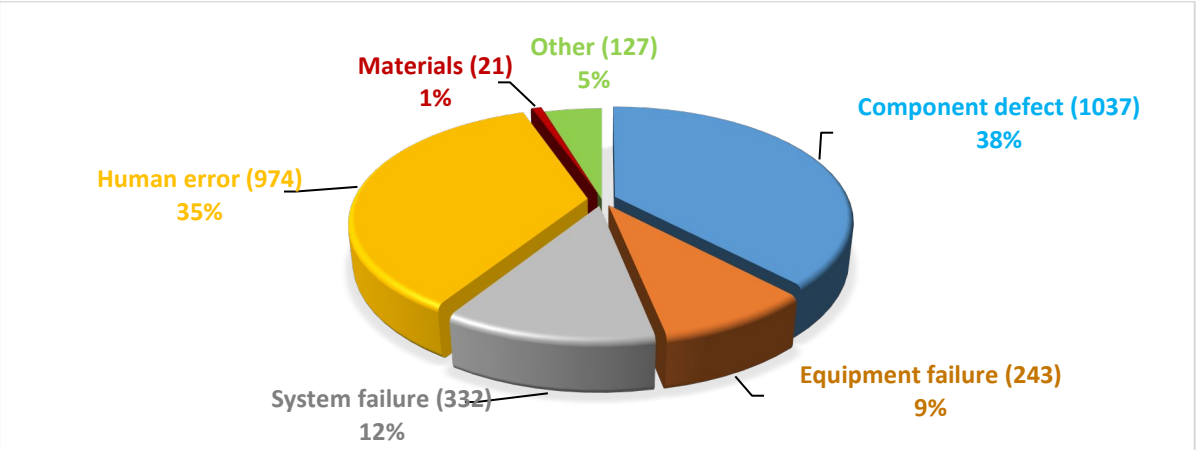


Figure 22. Distribution of SAE by type (absolute numbers and percentages); data 2021

Human error occurs in all activities from donor selection to component issue. The distribution of the 947 SAE classified as human error by activity step is represented in *Figure 23*. The *Other* group included a variety of types of SAR (data entry error, sample processing error, transcription error, incorrect labelling of component, transfusion of invalid sample, special requirement not met, etc.).

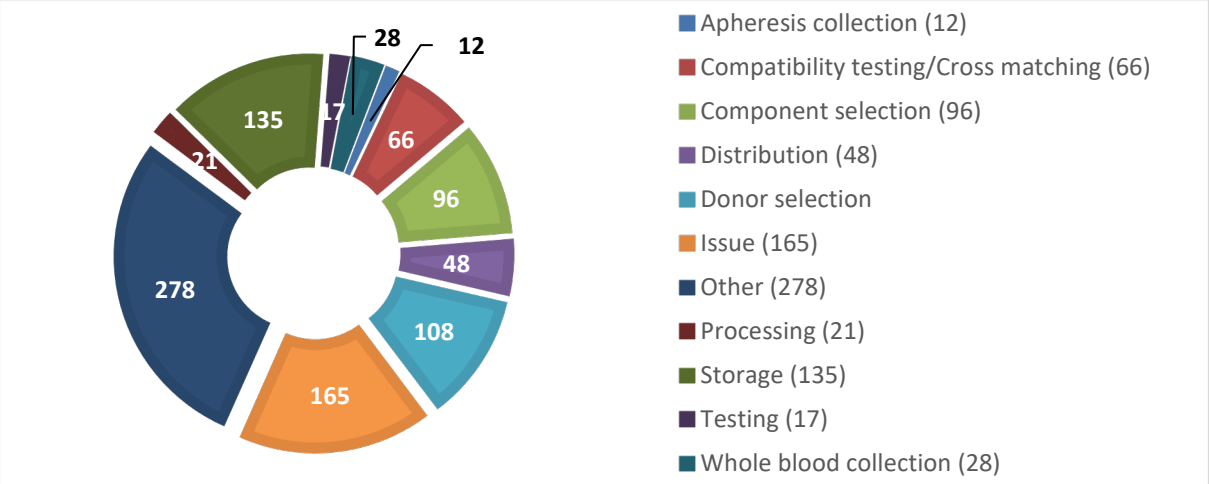


Figure 23. Distribution by activity step of SAE classified as human error; data 2021

A detailed representation of SAE by type for each reporting country is available in *Figure 24* below.

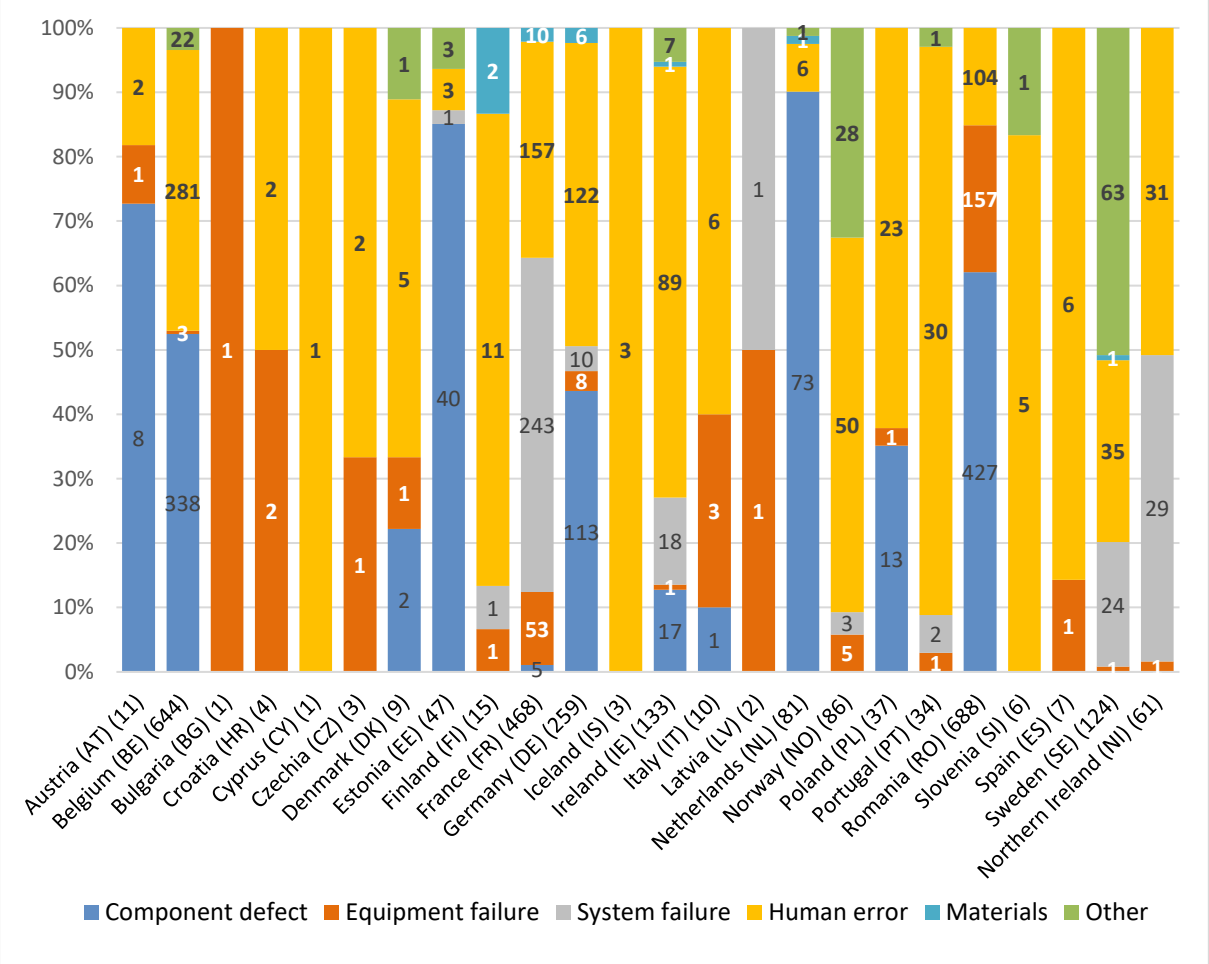


Figure 24. SAE by type and by country; data 2021

4.5 Severe adverse reactions in donors

According to Directive 200/61/EC, SAR in donors are not reportable unless they impact the quality and safety of the blood components[9]. However, as an acknowledgment the value of data on SAR in donors, the Commission encourages member states to submit these reactions on a voluntary basis. Thus, a specific "SAR in donors of blood or blood components" section is included in the reporting template.

In general, SAR in donors should be reported if they were certainly or probably caused by the donation (imputability 2 or 3). However, for donor fatalities, all cases should be reported where a fatality was possibly, probably or certainly related to the donation process (imputability 1, 2 or 3).

Twenty-three countries (AT, BE, BG, HR, CY, CZ, DK, EE, FI, FR, DE, IS, IE, IT, LU, NL, NO, PL, PT, RO, SK, SI and SE) reported, on a voluntary basis, a total of **2 946 SAR in donors**. The comparative data from SARE exercises in the period 2016-2022 (2015-2021 data) is presented in *Figure 25*.

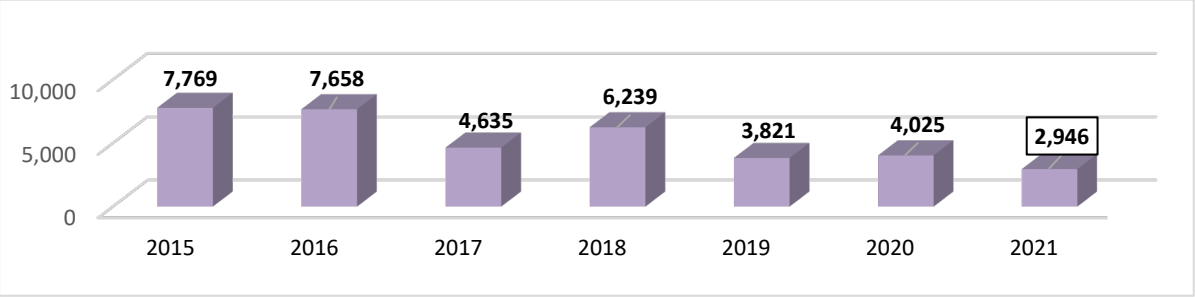


Figure 25. SAR in donors (absolute numbers): 2015-2021 comparative data

Figure 26 shows the number of SAR in donors per 100 000 collections (from those countries who were able to provide total numbers of whole blood collections and apheresis collections).

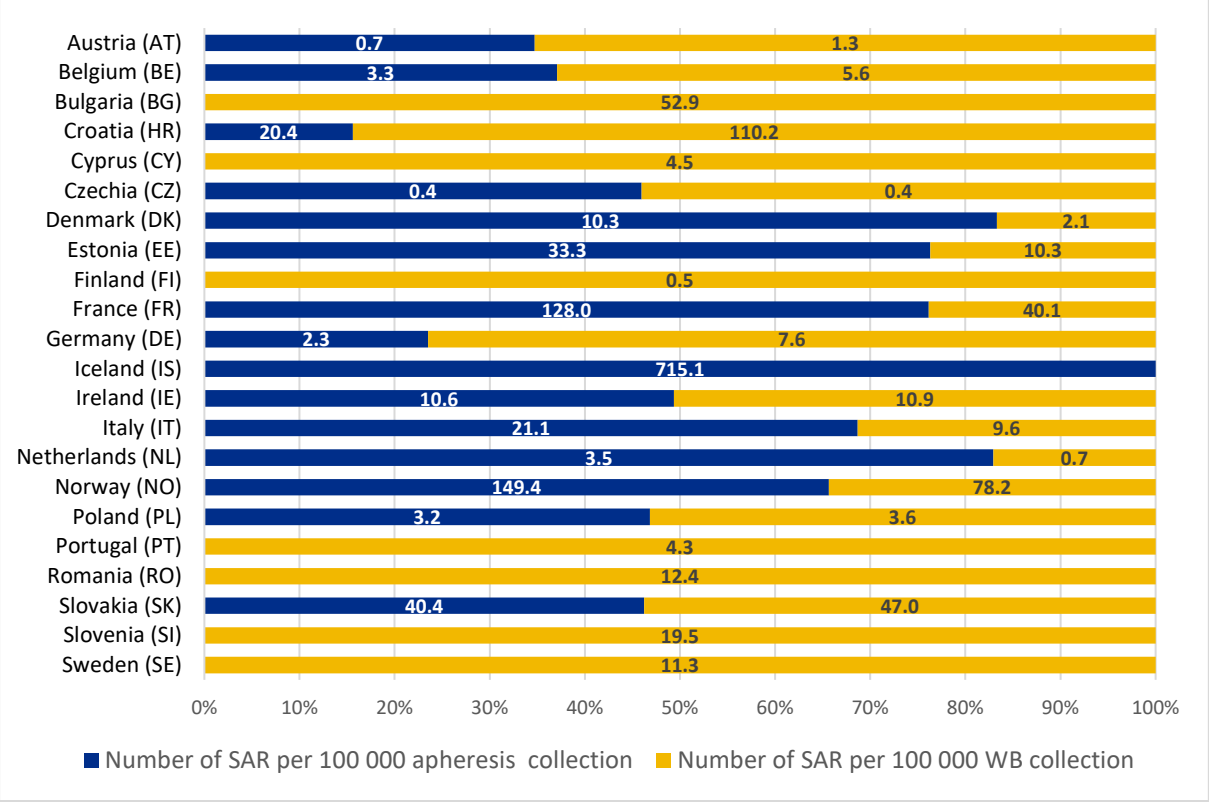


Figure 26. Incidence of SAR in donors per 100 000 collections (absolute numbers); data 2021

[9] Article 5 of Directive 2005/61/EC

Twenty-one countries (AT, BE, BG, HR, CY, CZ, DK, EE, FI, FR, DE, IE, IT, NL, NO, PL, PT, RO, SI, SE and SK) reported a total of **2 262 SAR in donors in relation to whole blood collection**. As shown in *Figure 27*, during *whole blood collection*, **vasovagal reaction** was the most common type of reaction (79%), followed by **other** (14%) and **nerve injury/irritation** (7%).

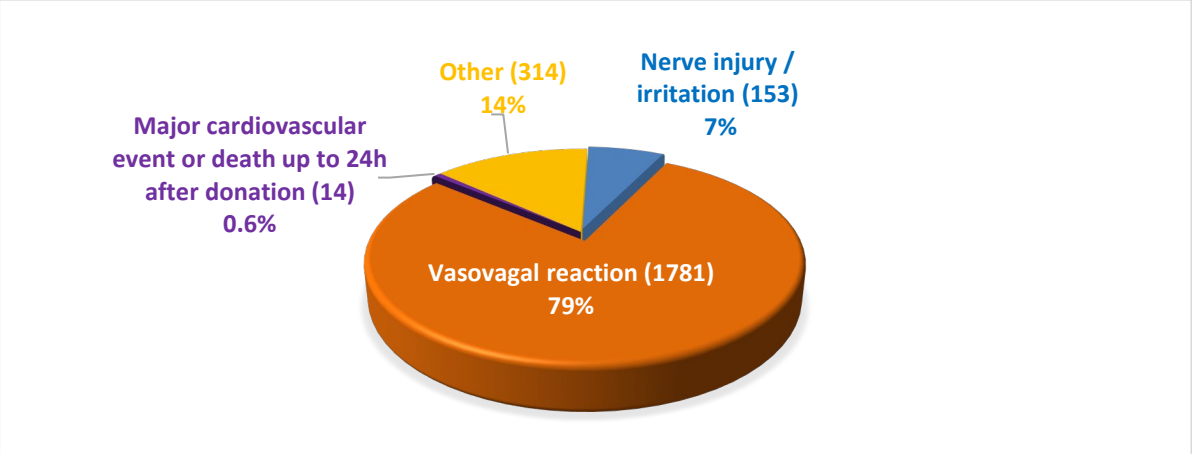


Figure 27. SAR in donors during whole blood collection (absolute numbers and percentages); data 2021

No deaths were encountered among the 12 cases of major cardiovascular events reported by France and Germany. No complications were associated with the two major cardiovascular events reported by Bulgaria and Sweden.

Fifteen countries (AT, BE, HR, CZ, DK, EE, FR, DE, IS, IE, IT, NL, NO, PL and SK) reported a total of **684 SAR in donors following apheresis collection.**

Three countries (CZ, FR and DE) reported four cases of major cardiovascular events with no fatalities.

Distribution of SAR in donors during *apheresis collection* is shown in *Figure 28*.

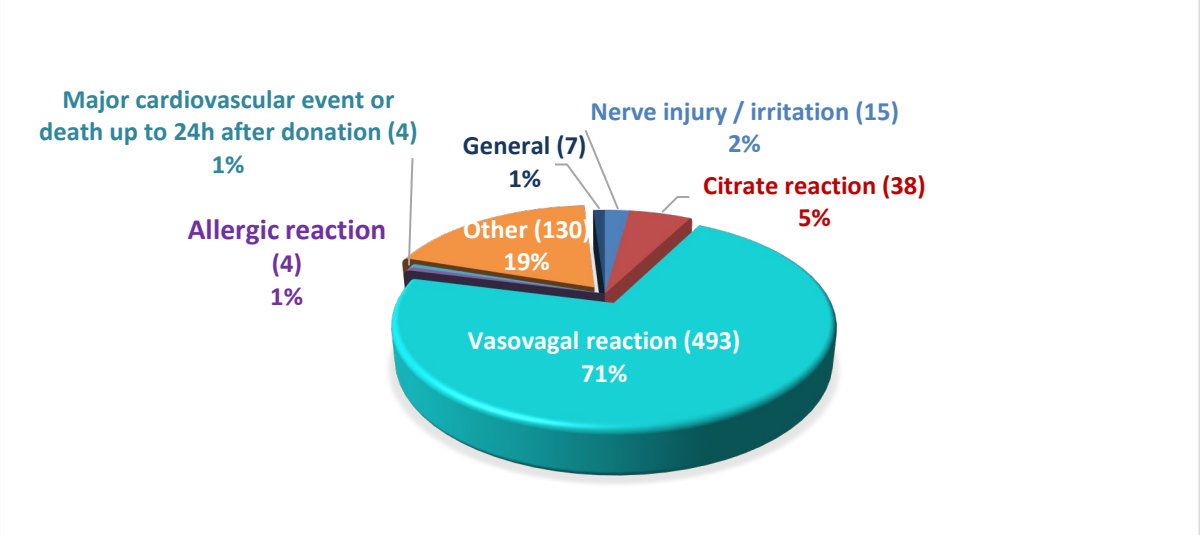


Figure 28. SAR in donors during apheresis collection (absolute numbers and percentages); data 2021

The types of SAR in donors per type of collection and per country is presented in *Figures 29* and *30* below. Only countries that reported SAR in donors by type of collection were included in the analysis.

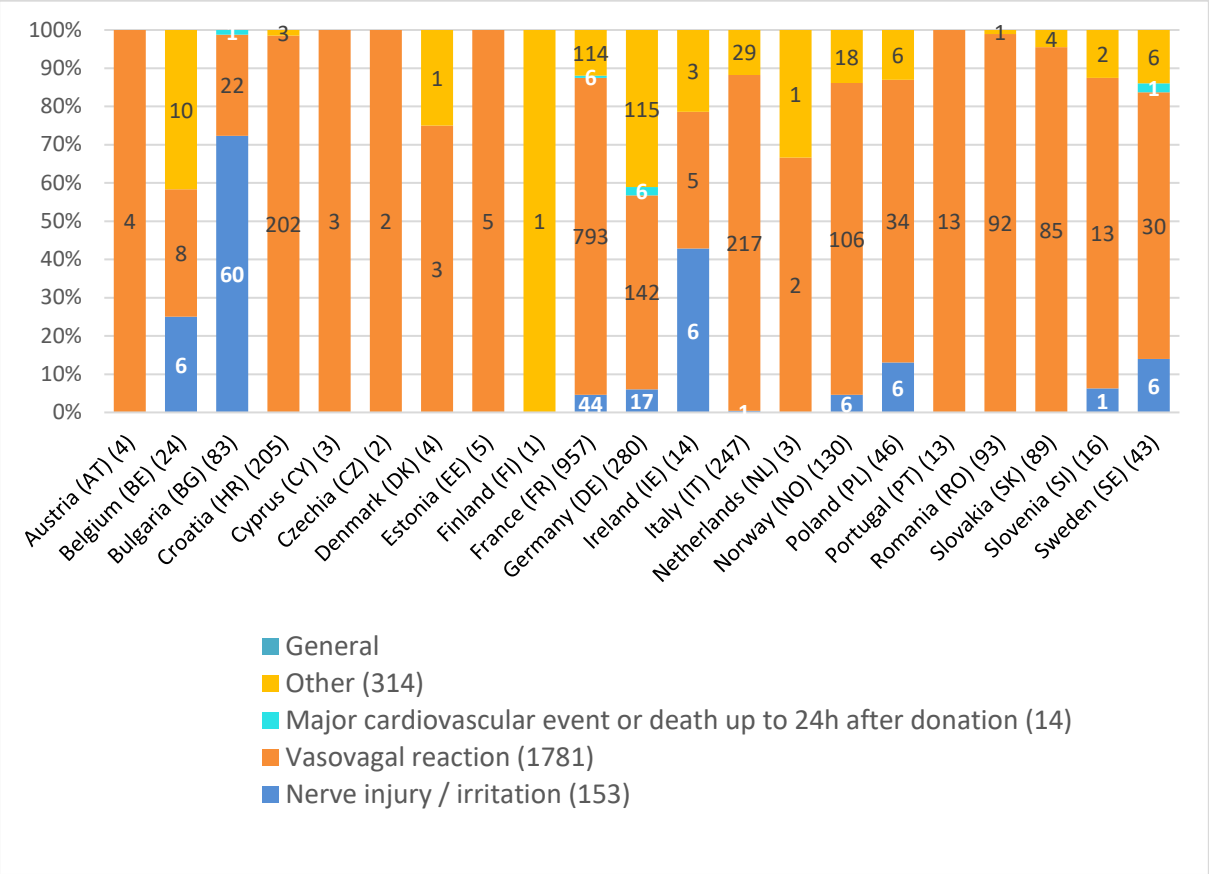


Figure 29. Number of SAR in donors by type (whole blood collection); data 2021

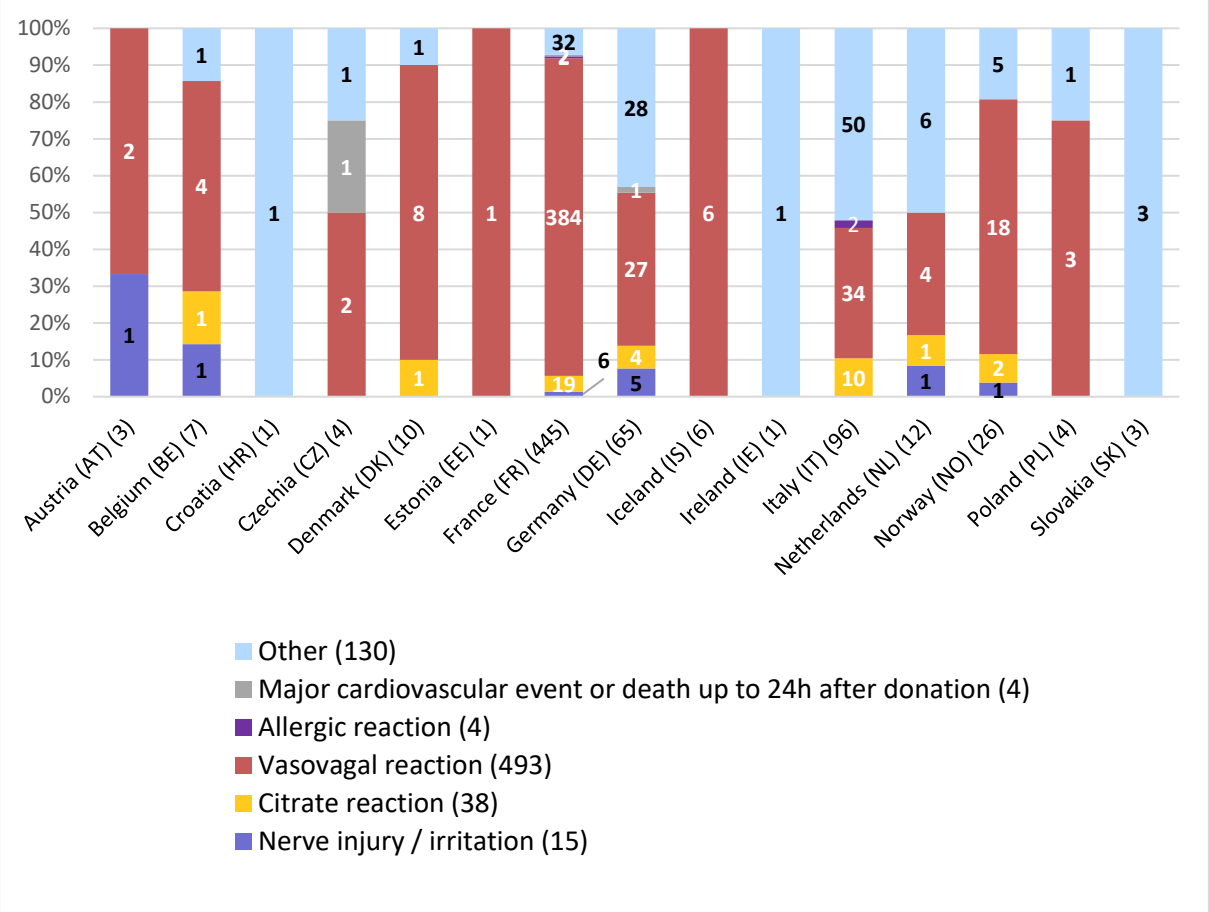


Figure 30. Number of SAR in donors by type (apheresis collection); data 2021

5. CONCLUSIONS

The SARE reporting exercises completed to date have resulted in a gradual improvement in the quality and accuracy of the data reported. In 2021, as many as 30 European countries representing a total of 3 307 transfusion facilities submitted reports, which indicates commitment to the initiative. However, as mentioned throughout this report, there is still a significant degree of inconsistency between countries in terms of data reporting rates, data completeness, classification and management of events.

Significant discrepancies between national reporting policies was also identified during the EU legislation evaluation indicating that "the requirements for national surveillance are not sufficiently specific and sufficiently robust, leading to divergent approaches to surveillance, reduced mutual trust and thus barriers to trade in and access to such treatments."[10][10]

In general, the major findings in this report indicate that European haemovigilance data are consistent with known effects and expected trends, with no new safety concerns regarding blood and blood components identified from national vigilance and surveillance programmes. However, it should be noted that, for the reasons mentioned above, the results of analysis presented in this report should be interpreted with caution.

[10] COMMISSION STAFF WORKING DOCUMENT EXECUTIVE SUMMARY of the Evaluation of the Union legislation on blood, tissues and cells {SWD(2019) 375 final}, Brussels, 10.10.2019 available at https://health.ec.europa.eu/system/files/2019 10/swd_2019_375_summary_en_0.pdf

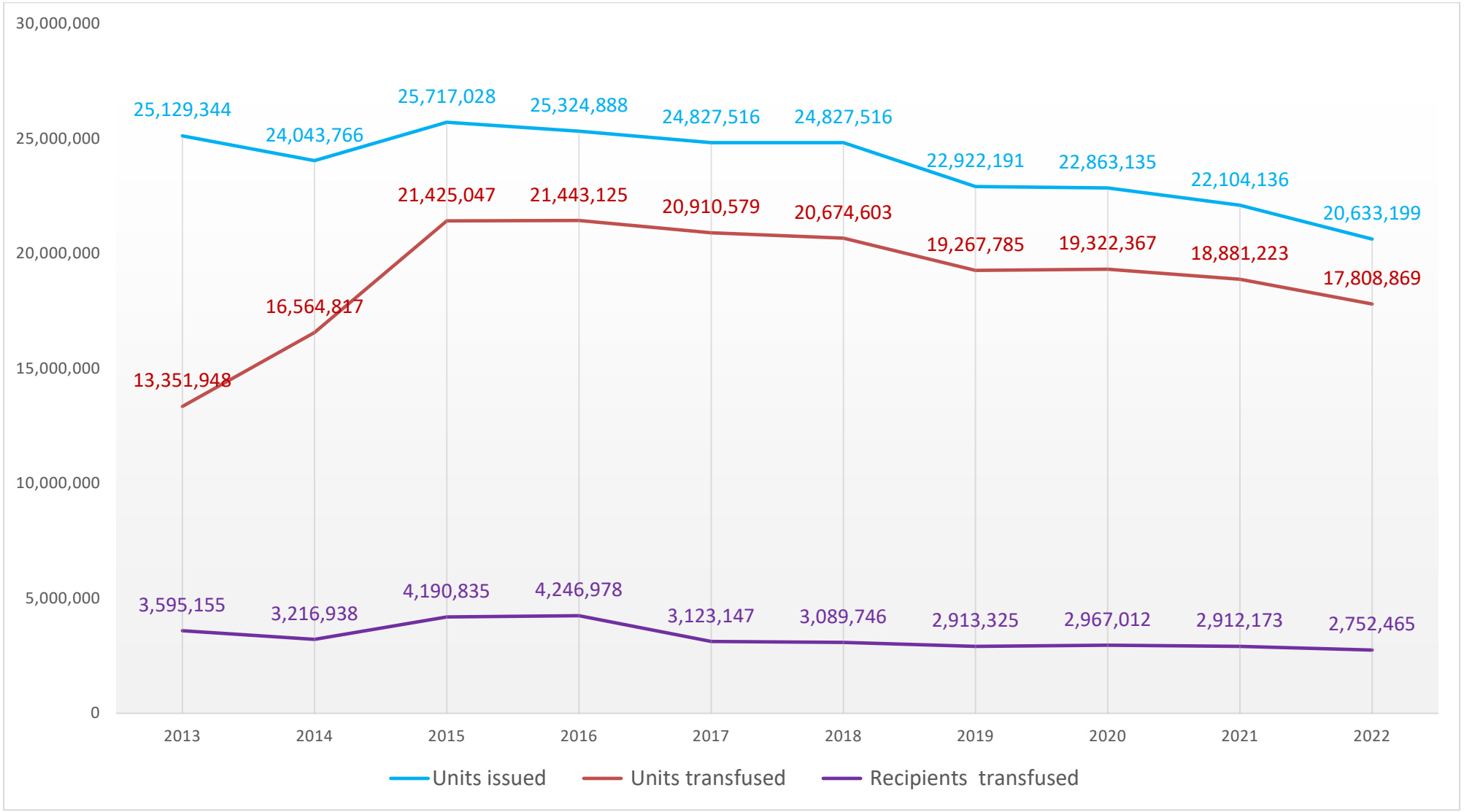
Annex 1. Case reports on fatalities (findings of investigation)

CASE 1 A 26-year-old female patient with SCD received a transfusion of non-matched EC after miscarriage. Evolution to (immunological) hyperhaemolysis with shock and 3 times cardiac arrest despite ICU and administration of Tocilizumab.
CASE 2 A 61-year-old female patient with a history of heart failure, chronic renal failure and adenocarcinoma of the head of the pancreas with hepatic metastasis (under palliative chemotherapy). Hospitalized on an outpatient basis in the morning for her chemotherapy check-up. She complained of great asthenia and dyspnoea. The Hb level was 70 g/L and the renal assessment indicated acutization of her chronic renal failure. It was decided to transfuse with two red cells units. The medical prescriber in charge of the patient prescribed transfusion with slow flow. Weight of patient 78 kg, Blood pressure and heart rate were normal. The 1st red cells unit was transfused in outpatient hospitalisation from 12:00 p.m. to 2:30 p.m. The transfusion of the 2nd red cells unit began at 2:40 p.m. in outpatient hospitalisation and continued in conventional hospitalisation (in Hepatology care unit) from 3:45 p.m. At 3:42 p.m., the patient had an arterial pressure of 150/73 mmHg, and heart rate of 61 beats/min. At the end of the transfusion (5:15 p.m.), blood pressure and heart rate were normal. At 5:30 p.m., the patient was in acute respiratory distress with massive acute pulmonary oedema (disorders of consciousness, 36% desaturation in ambient air). Rapidly unfavourable evolution, no resuscitation advice given the unfavourable short-term prognosis. The patient died at 5:45 p.m.
CASE 3 A 78-year-old patient with COVID-19 (O RhD positive blood type), was hospitalized in a moderately severe state, with dyspnoea at rest and multiple comorbidities, including multiple organ failure. Saturation 80%. Oxygen therapy was in use since the patient's admission to Emergency Room. Transfusion of convalescent plasma was planned and there were no indications for administration of packed RBCs. As a result of human error however, the patient was given 1 unit of packed leukocyte depleted RBCs intended for another patient (incompatible A RhD positive blood type). No symptoms of adverse reaction were observed during transfusion and immediately after the procedure was terminated. According to plan, the patient was then transfused with 1 unit of group-compliant convalescent plasma and no adverse reactions were reported. 2.5 hours after termination of the second transfusion, the patient's condition deteriorated, and blood pressure dropped. Additional tests revealed: strong haemolysis in serum, anaemia, elevated levels of bilirubin. After about 8 hs from the onset of the first symptoms, blood saturation dropped to 70% (intubation, ventilation), followed by cardiac arrest and death an hour later. The patient was resuscitated, to no effect. Acute haemolytic reaction was recognized due to transfusion of incompatible packed RBCs. The hospital physicians and nurses discussed the circumstances of this serious adverse reaction and were instructed to strictly follow all transfusion procedures in order to avoid future errors of the same kind.

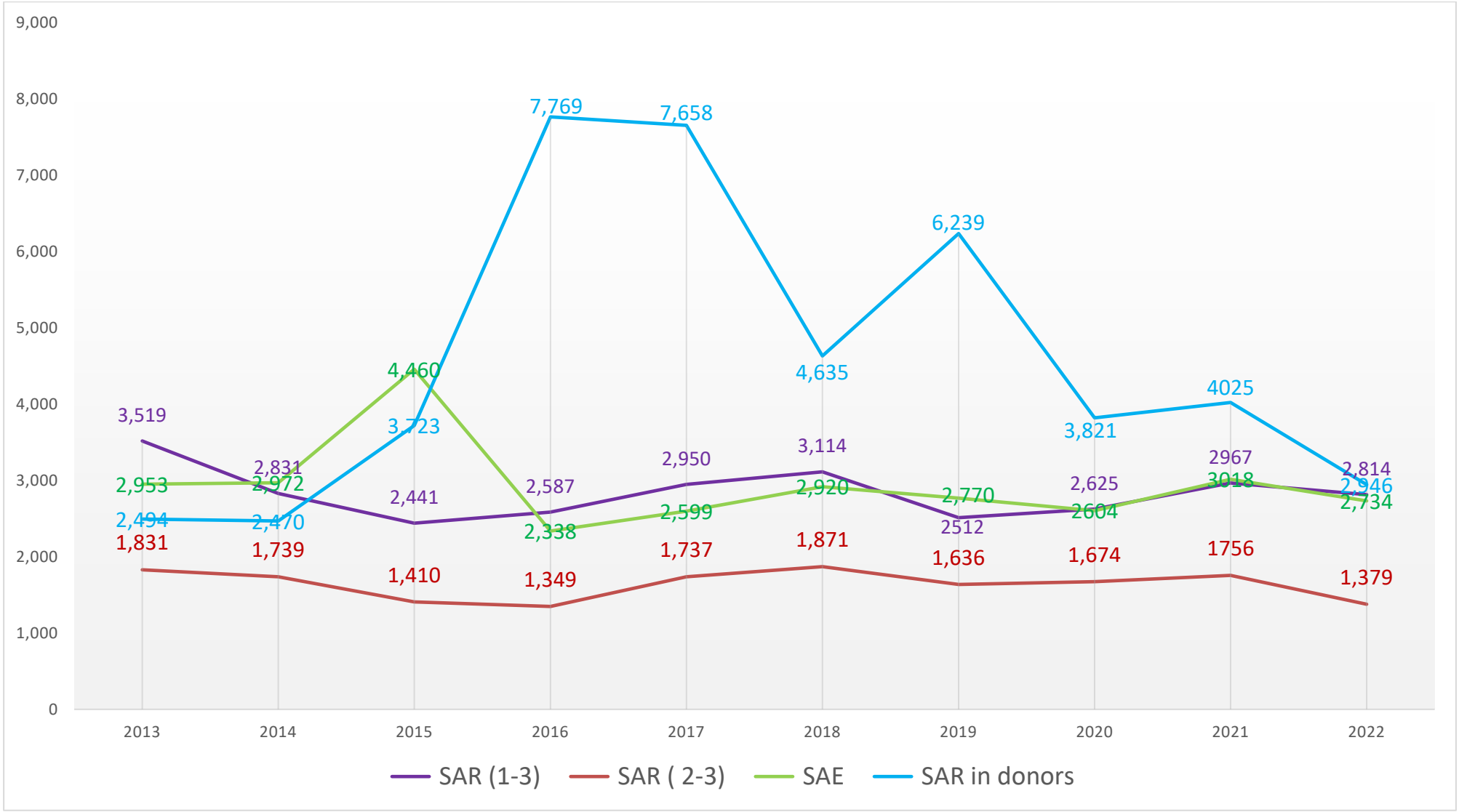
Annex 2. Overview of the 2018 - 2022 SARE reporting exercises (2017 - 2021 data)

Parameter	2018 (data 2017)		2019 (data 2018)		2020 (data 2019)		2021 (data 2020)		2022 (data 2021)	
	Countries reporting	Number	Countries reporting	Number	Countries reporting	Number	Countries reporting	Number	Countries reporting	Number
Units issued	29	25 093 906	28	22 922 191	27	22 863 118	30	22 104 136	25	**20 633 199**
Units transfused	24	20 674 603	23	19 310 224	22	19 334 629	24	18 881 223	26	**17 808 869**
Recipients transfused	19	3 522 623	19	3 262 767	17	3 228 635	15	2 912 173	19	**2 752 465**
SAR (1-3)	28	3 114	27	2 538	27	2 625	28	2 967	27	**2 814**
SAR (2-3)	26	1 871	24	1 687	26	1 674	26	1 756	24	**1 379**
SAR death (2-3)	8	28	7	20	10	26	9	24	11	**25**
SAE	20	2 920	23	2 770	22	2 604	24	3 018	24	**2 734**
SAR in donors	23	4 635	23	6 239	24	3 821	28	4 025	23	**2 946**

Annex 3: Annual comparison (Years of exercises 2013-2022): number of units issued/transfused/recipients



Annex 4: Annual comparison (Years of exercises 2013-2022): SAR (1-3), SAR (2-3), SAE, SAR in donors



Annex 5: Annual comparison (Years of exercises 2013-2022): number of deaths (2-3)