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Directorate D - Health systems and products

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SUMMARY OF THE 2014 ANNUAL REPORTING OF SERIOUS ADVERSE EVENTS AND REACTIONS (SARE) FOR BLOOD AND BLOOD COMPONENTS (DATA COLLECTED FROM 01/01/2013 TO 31/12/2013)

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.

This document intends to provide a summary report of the data collected during 2013 (from 1st January to 31st of December) received from the Member States, including preliminary conclusions.

1. DATA COLLECTION METHODOLOGY

The first SARE reporting exercise for blood and blood components was launched in 2008. Since then DG SANCO has worked together with groups of national experts to refine the SARE reporting exercise. More recently a Working Group on haemovigilance, whose members are nominated by the national Competent Authorities, has met on a yearly basis to discuss improvements to the SARE reporting tools. These are:

1) An electronic reporting template to be filled in by Member States with the data collected in the previous year (1st January to 31st December). Once completed by Member States this is sent in html format to a DG SANCO hosted database. The template used in 2014 (for 2013 data) was version 2.4.

2) A common approach document which, although it is not legally binding, provides guidance to Member States when filling out the electronic SARE reporting template as required by Directive 2005/61/EC. First published in 2008, the Common Approach has been regularly updated to clarify points of ambiguity and inconsistency. This has in turn resulted in a gradual increase of the quality of the data collected from the Member States. In 2014, version 5 of the Common Approach document was available to those reporting SARE 2013 data.

2. MAIN FINDINGS OF THE 2013 DATA COLLECTION

2.1. General comments

For the 2014 exercise (data reported in 2013), the PDF reporting template was not changed. A revised version of the 'Common approach for definition of reportable serious adverse events and reactions' was developed by the Commission, together with the Haemovigilance Working Group. This new version updated Annex II by splitting activity step definitions and examples of SAE specifications.

Responses were received from all 28 EU Member States, Liechtenstein and Norway, with 4,017 reporting facilities. All countries reported SARs and most reported SAEs, but in many cases not all denominators were reported, raising questions about the availability/accuracy of data. The data was presented at the November 2014 meeting of the competent authorities on blood and blood components.

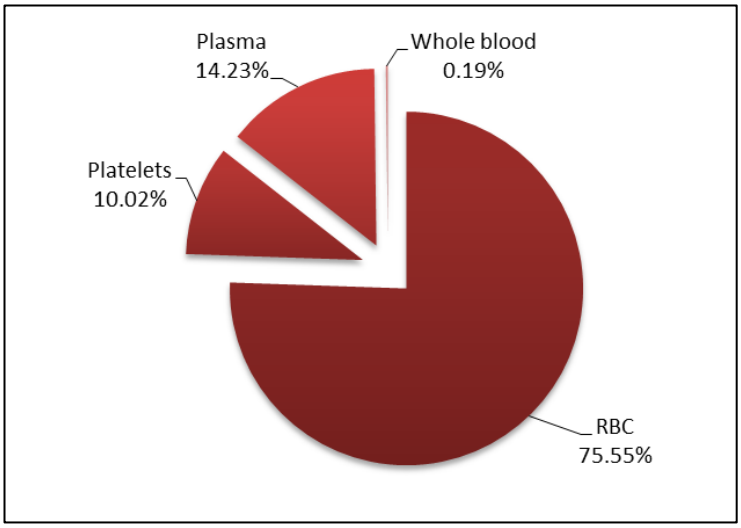
Although data quality has continuously improved (18 countries reported receiving complete data), the data presented here is considered partial and should therefore be interpreted with caution (a further 9 countries received at least 80% of the expected data, two less than 60% and one did not report this figure).

2.2. Denominators

All Member States, Liechtenstein and Norway submitted replies to the questionnaire, thereby complying with the annual report submission established by Article 8. It should be noted that that in the following sections, as well as in the analyses, data from two countries comes from less than 60% of facilities (hospitals or blood establishments).

In total, 16,564,817 units of blood components were reported as transfused by facilities in EU and EEA countries. It should be noted that this is not the total number of units transfused, as only 22 countries (AT, BE, BG, CZ, DK, EE, EL, ES, FR, HR, IE, IT, LI, LT, MT, NL, NO, PT, RO, SE, SK and UK) reported this figure for at least three blood components. The breakdown by component is shown below.

Figure 1: Units transfused (per blood component).

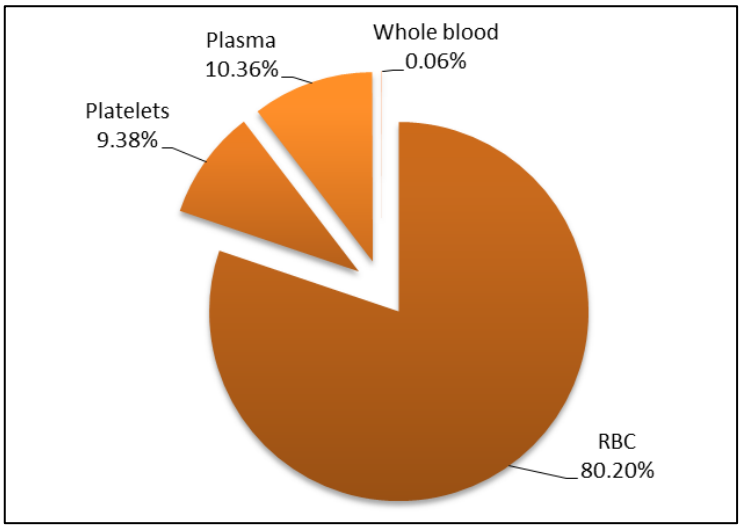


Component	Units Transfused (100,000)
Red blood cells	125.1
Platelets[1]	16.6
Plasma	23.6
Whole blood	0.3
Total	**165.6**

[1] Please note that one platelet unit is normally prepared from several donations.

According to the reports, 3,216,938 recipients (patients) were transfused in 2013. As above, these are partial figures, only 20 countries (AT, BE, BG, CZ, DK, EE, ES, FR, HR, IE, IT, LI, LT, MT, NL, NO, PT, RO, SE and UK) provided data on both units transfused and the number of recipients of blood. Two countries (EL and SK) only provided data about units of blood components transfused. The eight remaining countries (CY, DE, FI, HU, LU, LV, PL and SI) did not provide any data for units transfused or the number of recipients. The breakdown by component is shown below.

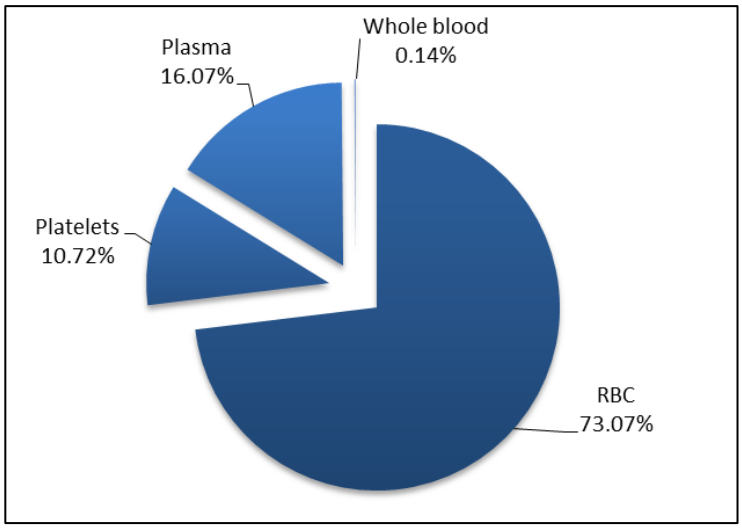
Figure 2: Recipients (per blood component) (AT, BE, CZ, DK, ES, HR, IE, IT, LI, LT, MT, NL, NO, PT, SE and UK provided per component data, totalling 2,499,328 recipients).



Component	Recipients Transfused (100,000)
Red blood cells	20.0
Platelets[1]	2.3
Plasma	2.6
Whole blood	0.01
Total	**25.0**

Twenty-five EU Member States (AT, BE, BG, CY, CZ, DE, EE, EL, FI, FR, HR, HU, IE, IT, LT, LU, LV, MT, NL, PL, PT, RO, SE, SI and UK), Liechtenstein and Norway provided data regarding units of blood components issued in 2013. Overall, a total number of 24,043,766 units of blood were reported as issued in 2013.

Figure 3: Units issued (per blood component).



Component	Units Issued (100,000)
Red blood cells	175.7
Platelets[1]	25.8
Plasma	38.6
Whole blood	0.3
Total	**240.4**

Twenty-six EU Member States (AT, BE, BG, CY, DK, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LU, LV, MT, NL, PL, PT, RO, SE, SI, SK and UK), Norway and Liechtenstein provided data regarding total blood collections in 2013. Overall, there were 15,353,382 whole blood collections and 1,596,067 apheresis collections reported in 2013.

Sixteen countries (AT, BE, BG, EE, FR, HR, IE, IT, LI, LT, MT, NL, NO, PT, RO and UK) reported all denominators (units issued, units transfused, recipients transfused and figures on collections) with at least 87% reports received (10 reported complete data). For this subset of countries, there were 13,251,287 units issued, 12,487,228 units transfused, 2,525,924 recipients transfused, 10,337,650 whole blood collections and 1,433,609 apheresis collections reported.

2.3. Serious Adverse Reactions (SAR)

2.3.1. Information by country

In 2013, a total of 1,739 SAR with a likely or certain attribution to the blood or blood component transfused (i.e. at imputability level 2-3) were reported by the 28 Member States, Liechtenstein and Norway. For the 22 countries that provided data for the number of SAR and units transfused per blood components, there were 9.8 SAR per 100,000 units transfused and 10,231 units transfused per SAR. Where SAR and units transfused were both reported, the number of units transfused per SAR (level 2-3) ranged from 2,802 to 336,141 across countries.

Three countries (BG, LI and LU) did not report any SAR (level 2-3) attributed to blood and blood components in 2013. These figures should also be interpreted with caution as many reports are still partial and differences between countries do not necessarily indicate a safer system. In fact, a higher number of SAR reported may indicate a more reliable and accurate reporting system, and a lower number of SAR may indicate under-reporting.

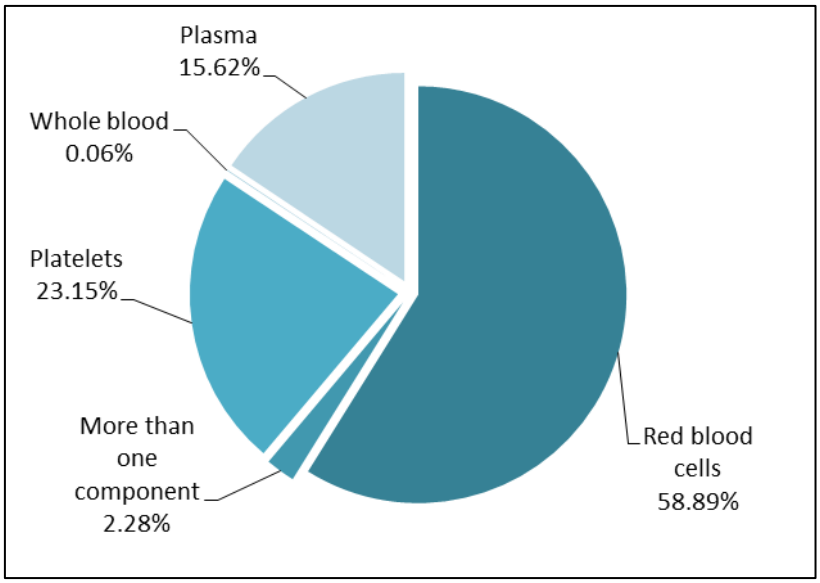
2.3.2. Information by blood component

Of the 1,739 level 2-3 SAR reported:

- 1,015 SAR were related to **red blood cells**,
- 410 SAR were related to **platelets**,
- 268 SAR were related to **plasma**,
- 1 SAR was related to **whole blood, and**
- 45 SAR were related to **more than one blood component.**

Figure 4 shows the number of units transfused of each component per SAR for the 22 countries that reported per unit transfused figures.

Figure 4: Percentage of SAR per blood component and units transfused per SAR (for those 22 countries which report units transfused and SAR for at least three blood components).



Component	Units transfused SAR^{-1}
Red blood cells	13,118
Platelets	4,428
Plasma	9,319
Whole blood	32,297

2.3.3. Information by category of SAR

The 1,739 SAR (level 2-3) reported were classified as follows:

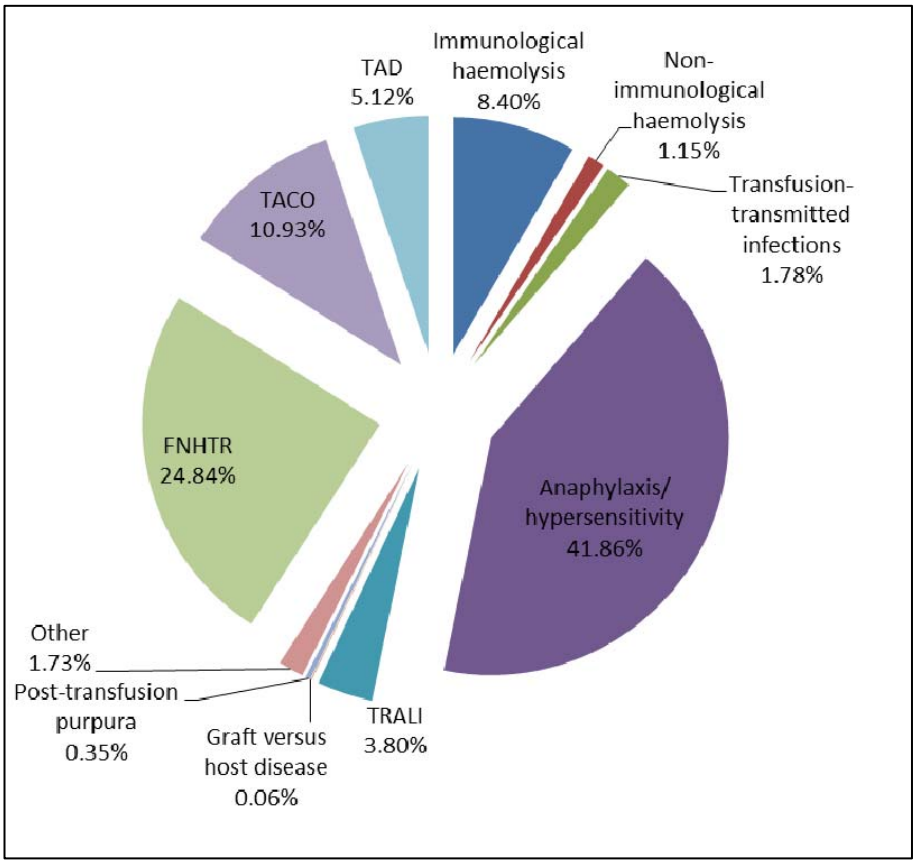
- **Immunological haemolysis**: 146 cases (8.4% of reported SAR), of which
  - 52 cases due to ABO antibody (2.99%), and
  - 94 cases due to other allo-antibodies (5.41%),
- **Non-immunological haemolysis**: 20 cases (1.15% of reported SAR),
- **Anaphylaxis/hypersensitivity**: 728 cases (41.86% of reported SAR),
- **Transfusion related acute lung injury** (TRALI): 66 cases (3.8% of reported SAR),
- **Transmitted infections**: 31 cases (1.78% of reported SAR), of which:
  - 16 cases of bacterial infections (0.92%),
  - 14 cases of viral infection (3 HBV, 3 HCV, 4 HEV, 3 HIV-1/2 and 1 unspecified) (0.81%), and
  - 1 case of parasitical infection (*Trypanosoma cruzi*) (0.06%),

  This number concerns infectious agents that were present in the final preparation, that were transfused to the patient and caused infection. It should be noted that safety and quality measures from donation to transfusion eliminate the vast majority of infectious agents at earlier stages.
- **Post transfusion purpura**: 6 cases (0.35% of reported SAR),

- **Graft versus host disease**: 1 cases (0.06% of reported SAR),
- **Other SAR**: 741 cases (46.88% of reported SAR). This category includes:
    - 432 cases of febrile non-haemolytic transfusion reaction (FNHTR) (24.84%),
    - 190 cases of transfusion associated circulatory overload (TACO) (10.93%),
    - 89 cases of transfusion associated dyspnea (TAD) (5.12%),
    - 5 cases of delayed serologic transfusion reaction (DSTR) (0.29%),
    - 4 cases of haemosiderosis (0.23%), and
    - 3 cases of hypotension (0.17%).

Of the 1,739 cases of SAR reported, there were 22 deaths from: immunological haemolysis (5 cases), non-immunological haemolysis (1 cases), bacterial infections (2 cases), anaphylaxis (1 case), post-transfusion purpura (1 case), TRALI (5 cases), TACO (6 cases) and unclassifiable complication of transfusion[2] (1 case).

Figure 5: Percentage of SARs per category.



[2] ISBT definition: An unclassifiable complication of transfusion (UCT) is an occurrence of an adverse effect or reaction temporally related to transfusion, which cannot be classified according to an already defined ATE and with no risk factor other than transfusion and no other explaining cause.

2.3.1. SAR in donors

Twenty-three countries (AT, BE, BG, CZ, DE, DK, EE, EL, FI, FR, HR, IE, IT, LI, LT, LU, MT, NL, PL, PT, RO, SE and UK) reported a total of 2,470 SAR in donors (on a voluntary basis). This equates to 14.6 SAR per 100,000 collections or 6,862 collections per SAR in those countries which reported both SAR in donors and figures on collections.

A subset of countries also provided additional information to the Commission on SAR in donors. Based on these reports, it can be seen that many of the reactions in donors were related to blood vessel injuries, nerve injuries, vasovagal episodes, or cardiovascular reactions.

2.4. Serious Adverse Events (SAE)

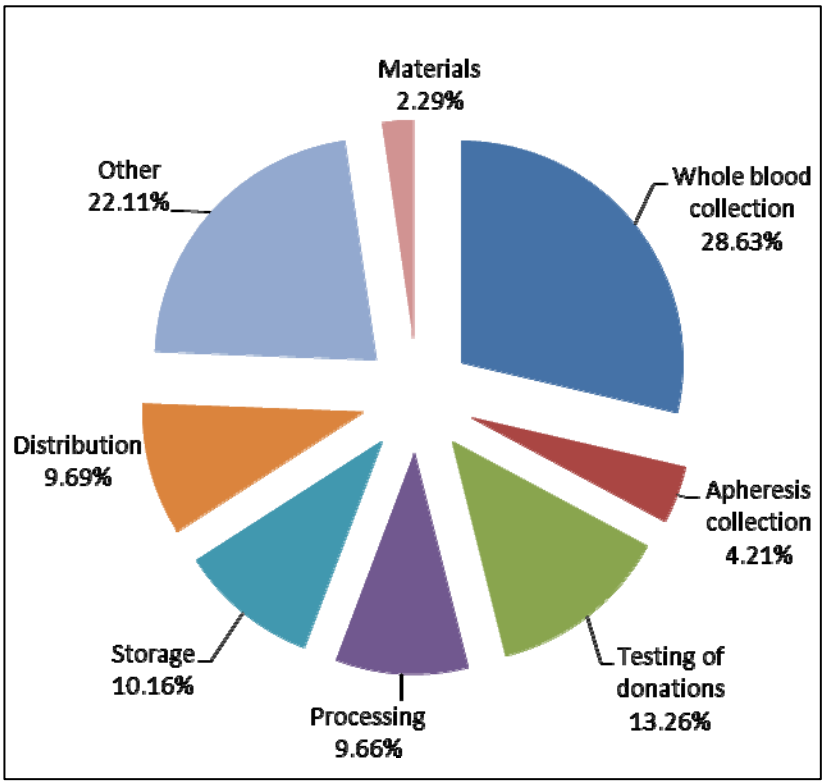
2.4.1. Information by country

SAE were reported by the 28 Member States, Liechtenstein and Norway. The total number of SAE reported for 2013 was 2,972. Although it should be noted that seven countries (CY, HU, LI, LT, LU, LV and MT) reported that there had been no reportable SAE in 2013.

2.4.2. Information by type of SAE

The 2,972 SAE reported were linked to the following activity steps:

Figure 6: Serious adverse events by activity step.



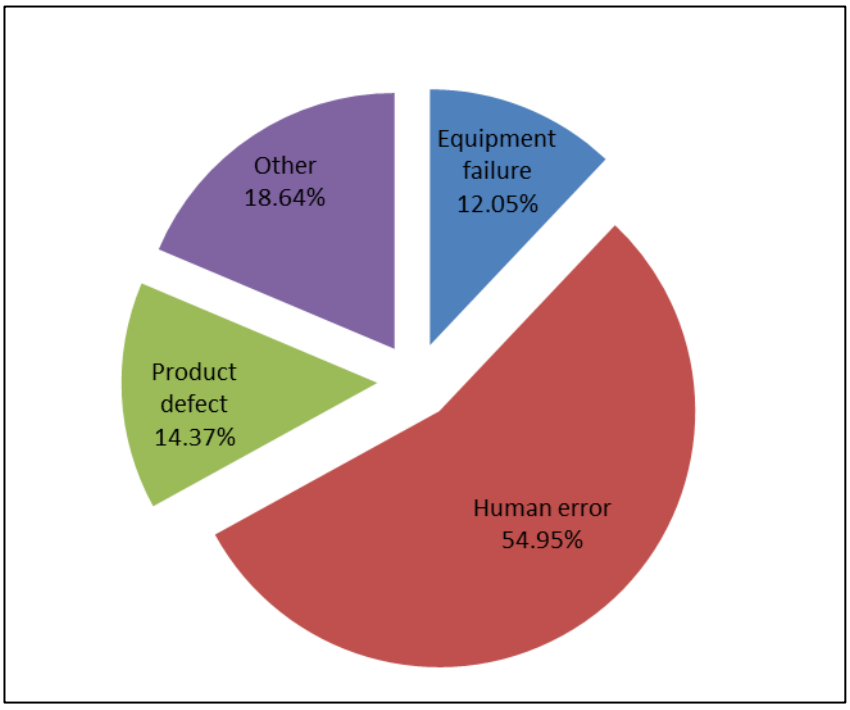
- **Whole blood collection**: 851 SAE (28.63%),
- **Apheresis collection**: 125 SAE (4.21%),
- **Testing of donations**: 394 SAE (13.26%),
- **Processing**: 287 SAE (9.66%),
- **Storage**: 302 SAE (10.16%),
- **Distribution**: 288 SAE (9.69%),
- **Materials:** 68 SAE (2.29%), and
- **Other activity steps:** 657 events (22.11% of reported SAE). This category includes 'compatibility testing', 'transport', ‘IT system errors’ and ‘microbial safety'.

2.4.3. Information by Specification of SAE

The 2,972 SAEs were attributed to one of the following specifications:

- **Human Error**: 1,633 SAE (54.95%)
- **Equipment failure**: 358 SAE (12.05%)
- **Product defect**: 427 SAE (14.37%)
- **Other:** 554 SAE (18.64%), including 'organisational errors' or unclassified SAE.

Figure 7: Serious adverse events per specification.



3. SARE REPORTING 2011-2014

The table below gives an overview of SARE reporting for the last four years (data from 2010 to 2013). As we can see, the number reporting denominators has increased slightly over the past four years (although fewer reported units issued than in 2012). In general, the numbers for denominators have fluctuated between years (23-25 million units issued, 12-17 million units transfused and 2-3.5 million recipients transfused), which is partly explained by the number of countries reporting.

The number of SAR (at imputability level 2-3) reported has increased from 2011 to 2014, but the number of deaths has remained relatively stable (around 20). For SAEs, the numbers reported are much lower than in 2011, which is probably the result of improved reporting by establishments.

Table 1: Overview of the 2011 to 2014 SARE reporting exercises (2010-2013 data).

	2011		2012		2013		2014	
	Countries reporting	Number	Countries reporting	Number	Countries reporting	Number	Countries reporting	Number
Units issued	26	22817166	29	24821809	27	25129344	27	24043766
Units transfused	19	16718258	17	12311691	20	13351948	22	16564817
Recipients transfused	11	2298304	16	2964839	19	3595155	20	3216938
SAR (1-3)	30	2449	30	3133	30	3519	30	2831
SAR (2-3)	30	1259	30	1574	30	1831	30	1739
SAR death (2-3)	30	20	30	14	30	22	28	22
SAE	28	16360	25	4113	28	2953	30	2972
SAR in donors					18	2494	23	2470

4. DISCUSSION AND CONCLUSIONS

The number of SAR in recipients (imputability level 2-3) reported for 2013 is low (1,739), especially in relation to the number of units of blood components transfused in the EU (9.8 SAR per 100,000 units transfused and 10,231 units transfused per SAR for the 22 countries that reported SAR and per component transfusion figures). This figure is similar to that reported in 2012 and 2013. However, considering that the data reported is partial, year on year comparisons should be interpreted with caution.

The results also show that the number of deaths resulting from blood transfusion is low (0.115 deaths per 100,000 units transfused or 872,297 units transfused per death overall

for those countries that report per component transfusion figures). It is, however, important to note that of the 22 deaths reported, the majority were not attributable to the quality and safety of the blood component, but rather to clinical practice or to unforeseen reactions (such as immunological haemolysis, anaphylaxis, TACO, TAD).

The voluntary reporting on donors, added during the last two exercises, highlights a significant number of SAR (around 2,500). It is important to have these data and to further assess the underlying reasons, in order to better protect those persons who make transfusion medicine possible.

For SAE, the reported figures are very similar to last year, but significantly decreased since 2010 (16,360 in 2010, 2,953 in 2012 and 2,972 in 2013) (12.4 SAE per 100,000 units issued or 8,062 units issued per SAE for the 25 countries that reported units issued and SAE). This is due to general improvements in data collection, which have resulted in only 'serious' adverse events being reported. It should be noted, however, that on an individual Member State basis a higher number of SAE reported may indicate a more reliable and accurate reporting system and a lower number may indicate under-reporting. The large number of SAE reported as due to human error highlight the importance of root cause analysis to determine the ultimate cause of serious adverse events.

Overall, the available data indicate that reporting is consistent with known effects and expected trends, with no new safety concerns regarding blood and blood components identified from national monitoring programmes. At the European level the exercise has allowed Member States to share experience and knowledge on haemovigilance, supporting the development of their national systems. Individual countries should continue to use this exercise to evaluate the safety of their national blood sectors and identify where quality issues occur and should be addressed to improve the safety and quality of blood in the entire EU.