

SUMMARY OF THE 2017 ANNUAL REPORTING OF SERIOUS ADVERSE REACTIONS AND EVENTS FOR TISSUES AND CELLS

(DATA COLLECTED FROM 01/01/2016 TO 31/12/2016)

EXECUTIVE SUMMARY

Human tissues and cells for human application and assisted reproduction programmes provide important benefits for thousands of EU citizens every year. Despite this, the use of any substance of human origin carries some risks, such as the possible transmission of disease from the donor. These risks can be controlled and minimised by the application of safety and quality measures as laid down in EU legislation. Vigilance and surveillance programmes allow the identification and detection of risks and the application of corrective and preventive measures, making them essential tools for the system.

According to the legislation¹, EU Member States must submit to the European Commission (henceforth referred to as 'the Commission') an annual report on the notifications of Serious Adverse Reactions (SAR) and Serious Adverse Events (SAE) received by each Competent Authority. For this purpose, definitions of SAR and SAE are provided in the EU legislation². The Commission, in turn, annually publishes a summary of the reports received, which are available to the Competent Authorities and the general public.

Since 2008, the reporting countries (EU Member States, Liechtenstein and Norway) have submitted to the Commission annual vigilance reports on the notification of SAR occurring in recipients of tissues and cells, and SAE which can occur at all of the different stages from donation to the clinical application of tissues or cells.

The Commission has been working with the relevant Competent Authorities for several years to standardise data collection procedures and to improve both the accuracy and the comparability of the information submitted. The consistency and completeness of the data collection and submission to the Commission have improved over time. Discussions of the results between experts demonstrate that the SAR/SAE (henceforth collectively referred to as 'SARE') reporting exercise works well, and assists countries across Europe in pinpointing and improving safety and quality in this field.

This report summarises the data collected by the reporting countries (25) for the year 2016 and assesses them in light of the information submitted in previous years. Some key findings of the reporting exercise are the following:

- The overall number of tissues and cells distributed in 2016 amounted to 2,133,341 units (345,817 non-reproductive, reported by 24 countries and 1,787,524 reproductive tissues and cells, reported by 15 countries). As to the number of recipients, 21 countries reported 317,970 patients. Nineteen countries reported the total number of tissues and cells processed, which reached 1,775,082 units (18 countries reported 267,300 tissues processed

¹ Article 7 and Annexes III, IV and V of Directive 2006/86/EC

² Article 3 of Directive 2004/23/EC

within the non-reproductive category and 13 countries reported 1,507,782 within the reproductive category).

- A total of 221 SAR were reported by 16 countries, of which 97 were related to non-reproductive and 124 to reproductive tissues and cells. Data show that 26% of the SAR associated with the transplantation of non-reproductive tissues and cells were infections, mostly of bacterial or fungal origin. The majority of the reported SAR for reproductive cells were related to the transmission of genetic diseases.
- A total of 769 SAE were reported (482 related to non-reproductive tissues and cells by 16 countries and 287 to reproductive tissues and cells by 16 countries), most of which occurred during procurement or processing stages and were mainly attributed to human error or tissue or cell defects.
- Recognising the importance of protecting donors, the Commission continues to collect details of donor adverse reactions on a voluntary basis. It is notable that the 2017 exercise showed an increase in the voluntary reporting of SAR in donors, with 700 cases reported by 19 countries. Of those, 70 were related to non-reproductive and 630 to reproductive tissues and cells.

Before publication, the data contained in this report was presented at the Tissues and Cells Competent Authorities meeting in June 2018, allowing the reporting countries to verify their national data and to share experience and knowledge.

1. DATA COLLECTION METHODOLOGY

This report provides a summary of the data reported to the Commission in 2017 by 24 Member States and Norway (Cyprus, Greece, Liechtenstein, Luxembourg and Slovakia did not provide data) pertaining to the reporting period from 1 January to 31 December 2016. It also includes comparisons with the data from previous years and general conclusions.

The Commission provided the following tools to the participating authorities to promote a standardised approach to data reporting:

- 1) An electronic reporting template (template version 2.6.1) to be sent to a DG SANTE hosted database.
- 2) The common approach document (henceforth referred to as the “Common Approach”) for definitions of reportable serious adverse events and reactions (version 2.6). The aim of this document is to provide guidance to the reporting countries when filling out the electronic reporting template³.

In December 2017 a service contract agreement was signed between the Commission and the European Directorate for the Quality of Medicines & HealthCare (EDQM), Council of Europe, to carry out the verification and analysis of the 2017 SARE exercise and to draft the summary report. Early in 2018, the EDQM began contacting reporting countries in order to clarify and verify the accuracy of the reported data and then performed the analysis of the information presented in this report.

³ Over the years, the Common Approach has been regularly updated. This has resulted in a gradual increase in the quality of the data collected from the Member States.

2. MAIN FINDINGS OF THE 2016 DATA COLLECTION

2.1. Activity data (denominators)

As part of the reporting exercise, Member States are requested to provide data not only on SAR and SAE but also concerning their national activity. Although not legally binding, providing data on the number of tissues distributed, the number of recipients and the number of tissues processed at national level facilitates a better overview and understanding of the different activities in the Member States and helps to put the data on SARE into context. In particular, as stated in the common approach document, the number of tissues and cells distributed and the numbers of recipients are used as denominators in the analysis of SAR and the number of tissues processed is used as a denominator in the analysis of SAE.

As in previous years, many countries acknowledged that accurate activity data for certain types of tissues and cells were difficult to collect and some provided incomplete numbers for SAR denominators. A few countries could not provide data as the measurement units collected at national level were not harmonised with those requested during the EU exercise (e.g. in the field of assisted reproduction, they collect data in number of cycles, as opposed to number of oocytes distributed as requested in the current version of the reporting template).

For non-reproductive tissues and cells, 24 countries reported data on *units distributed* (AT, BE, BG, CZ, DE, DK, EE, ES, FI, FR, HR, HU, IE, IT, LT, LV, MT, NL, NO, PL, PT, SI, SE and UK) and 21 (AT, BE, BG, CZ, DE, DK, EE, ES, FR, HR, HU, IE, IT, LT, MT, NL, NO, PL, PT, SE and UK) on *recipients*. For reproductive tissues and cells, 15 countries (AT, BE, BG, CZ, DE, DK, EE, HR, HU, IE, LV, MT, NL, SI and SE) and 13 countries (AT, BG, CZ, DK, EE, ES, HR, IE, MT, NL, PT, SE and UK) reported data on units distributed and number of recipients, respectively.

The overall number of *distributed* tissues and cells in 2016, as submitted by the reporting countries, amounted to 2,133,341 units (345,817 non-reproductive tissues and 1,045,606 oocytes delivered for IVF, 466,607 sperm delivered for insemination or IVF and 273,944 embryos delivered for transfer. Additionally, 74 ovarian tissues and 1293 testicular tissues were distributed.

The main types of non-reproductive tissues and cells distributed were skeletal tissues⁴ (210,241 units), Haematopoietic Progenitor Cells (HPC; 55,717 units) and ocular tissues (37,246 units). Please, refer to Figure 1 for further details.

⁴ The “general” category is used by Member States that do not collect data separately for each type of tissue or cell in some categories (i.e. musculoskeletal tissues vs bone, cartilage, tendons/ligaments and other musculoskeletal tissues such as meniscus or ear ossicles).

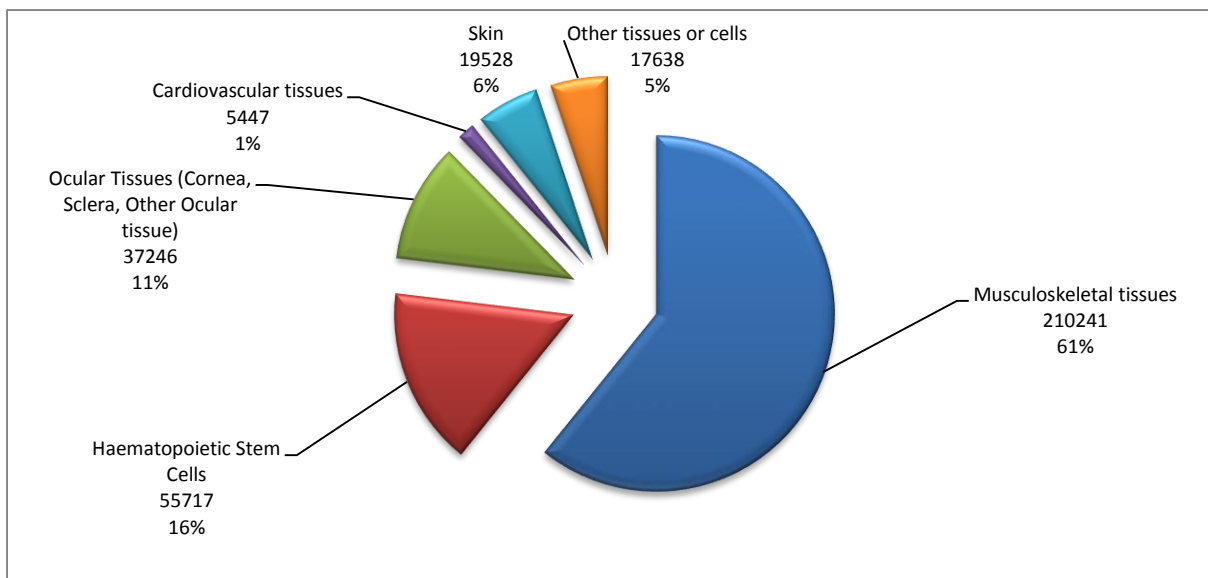


Figure 1. Total number of non-reproductive tissues and cells distributed (units); data 2016.

In 2016, 21 countries reported a total of 317,970 recipients (*patients*) having received tissues or cells. Of these, 94,323 were recipients of non-reproductive tissues or cells. Figure 2 shows the total number of patients that received each type of non-reproductive tissue or cell.

For *reproductive cells*, 223,647 patients underwent an assisted reproduction procedure involving partner or non-partner sperm, oocytes or embryos.

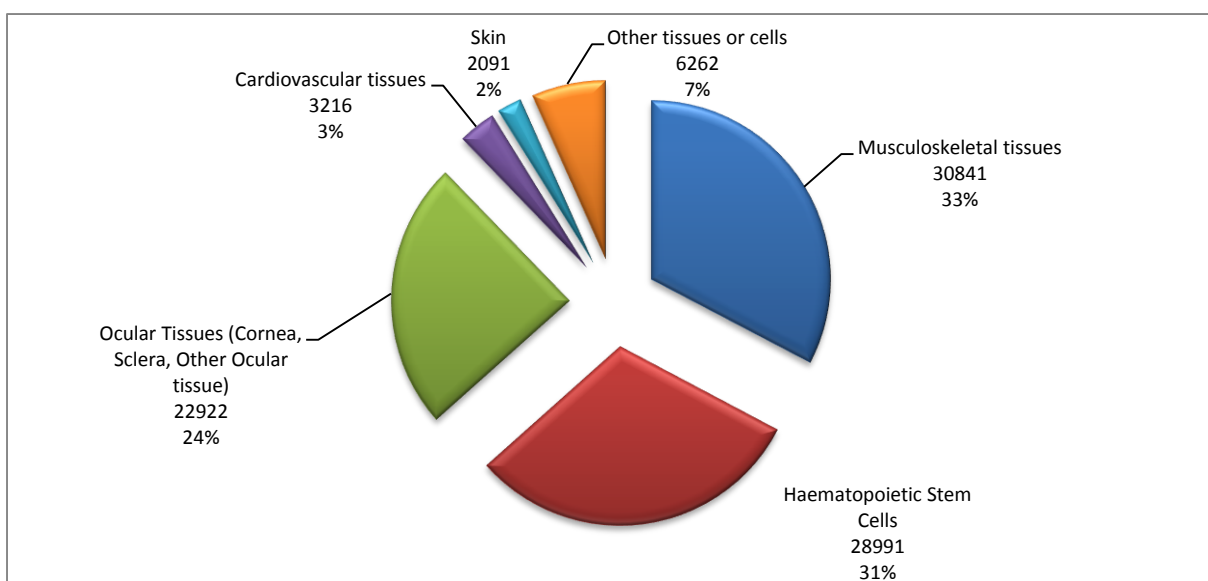


Figure 2. Total number of recipients per type of non-reproductive tissues and cells; data 2016.

An overview of the data for the SAR denominators for non-reproductive and reproductive tissues and cells provided by countries in the period between 2011 and 2017 (data pertaining to 2010-2016) are presented in Figures 3 and 4, respectively.

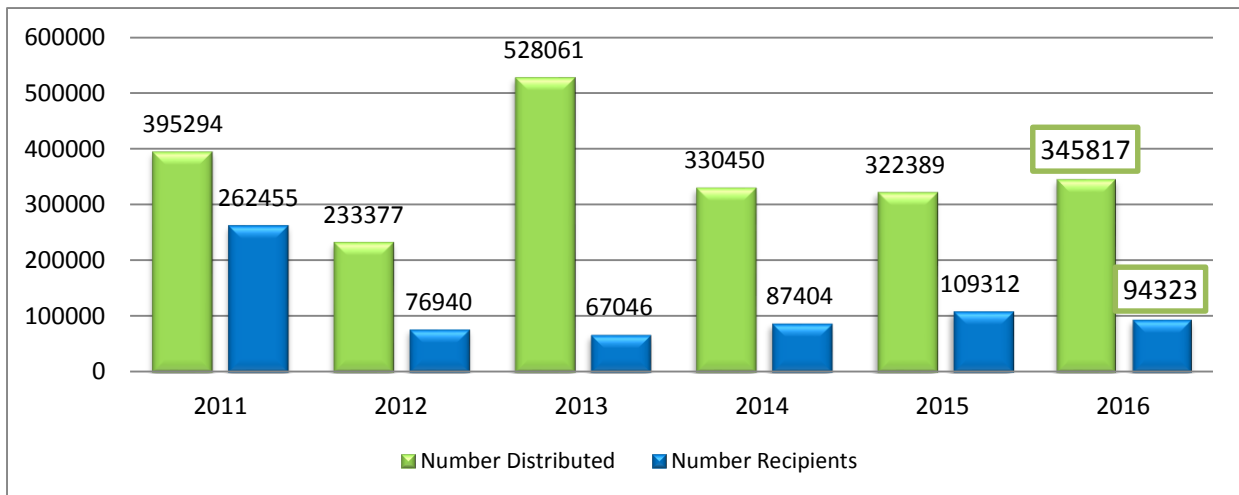


Figure 3. Total number of non-reproductive tissues and cells distributed (units) and number of recipients of human tissues and cells: 2010-2016 comparative data.

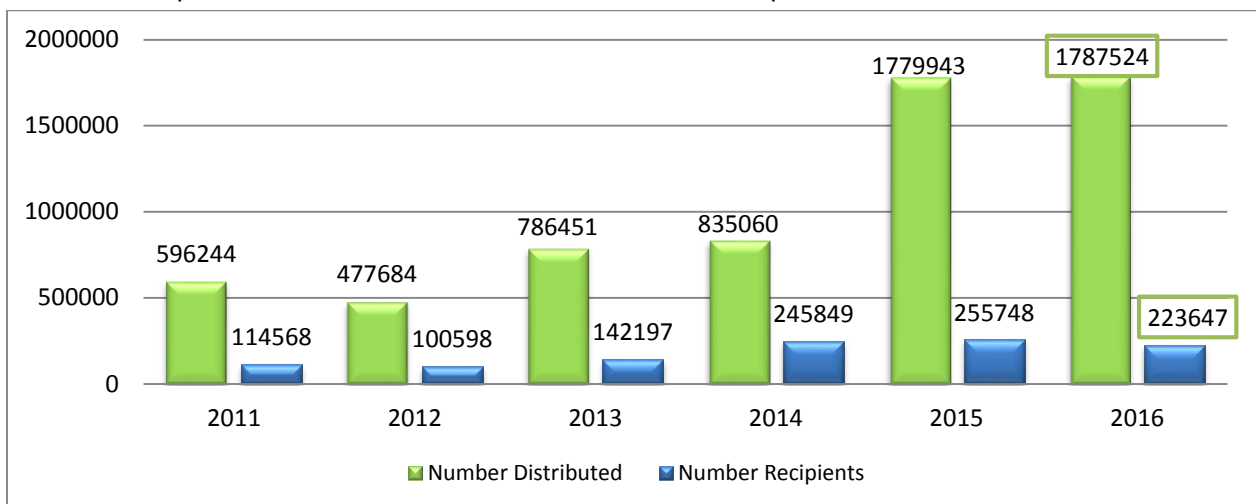


Figure 4. Total number of reproductive tissues and cells distributed (units) and number of recipients of human tissues and cells: 2010-2016 comparative data.⁵

Nineteen countries (AT, BG, DE, DK, EE, ES, HU, HR, IE, IT, LT, LV, MT, NL, PL, PT, SI, SE, UK) provided data regarding the number of tissues and cells *processed* in 2016. For the purpose of this reporting exercise, the term “tissues and cells processed” refers to tissues and cells processed in tissue establishments, but not necessarily distributed to end users. Overall a total of 1,775,082 tissues and cells were reported as processed in 2016.

Comparative data from previous exercises is presented in Figure 5.

⁵ As written in the Common Approach this data includes the number of sperm delivered to a clinic for insemination or to a laboratory for IVF, the number of oocytes delivered to a laboratory for IVF and the number of embryos delivered to a clinic for transfer to patients.

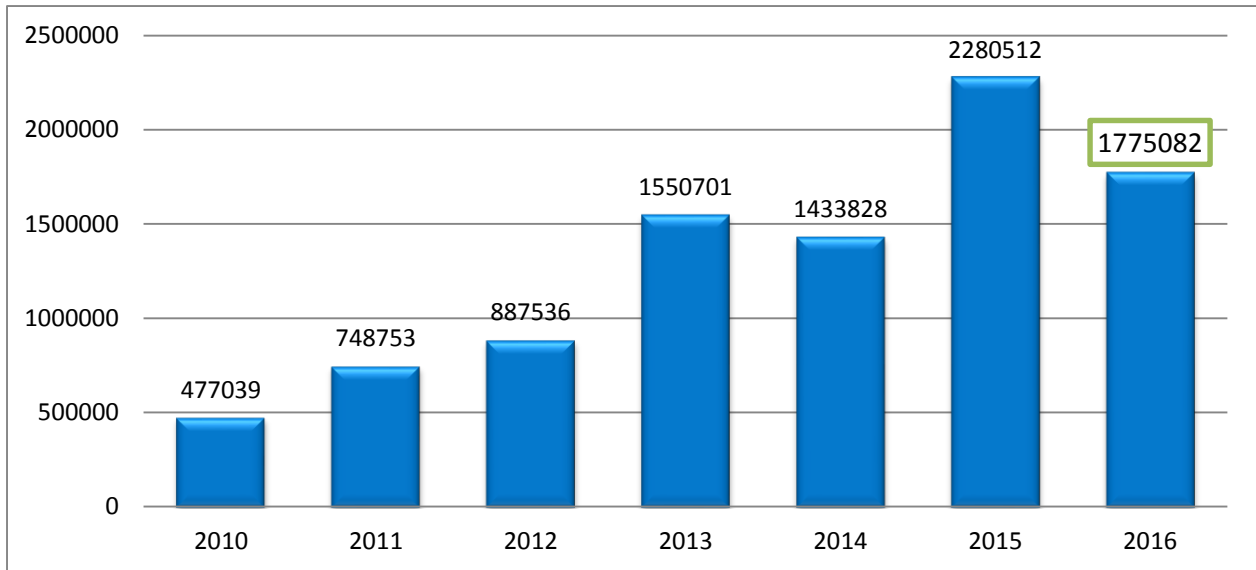


Figure 5. Total number of tissues and cells processed (units): 2010-2016 comparative data.

2.2. Serious adverse reactions

A total of 221 SAR were reported in 2016. Of these, 97 SAR were related to non-reproductive and 124 to reproductive tissues and cells. Of the SAR reported for non-reproductive tissues and cells, at least 6 led to death⁶ and this is explored further in section 2.2.4 of this report.

The number of SAR reported by countries over the years for both categories (non-reproductive and reproductive tissues and cells) is presented in Figure 6.

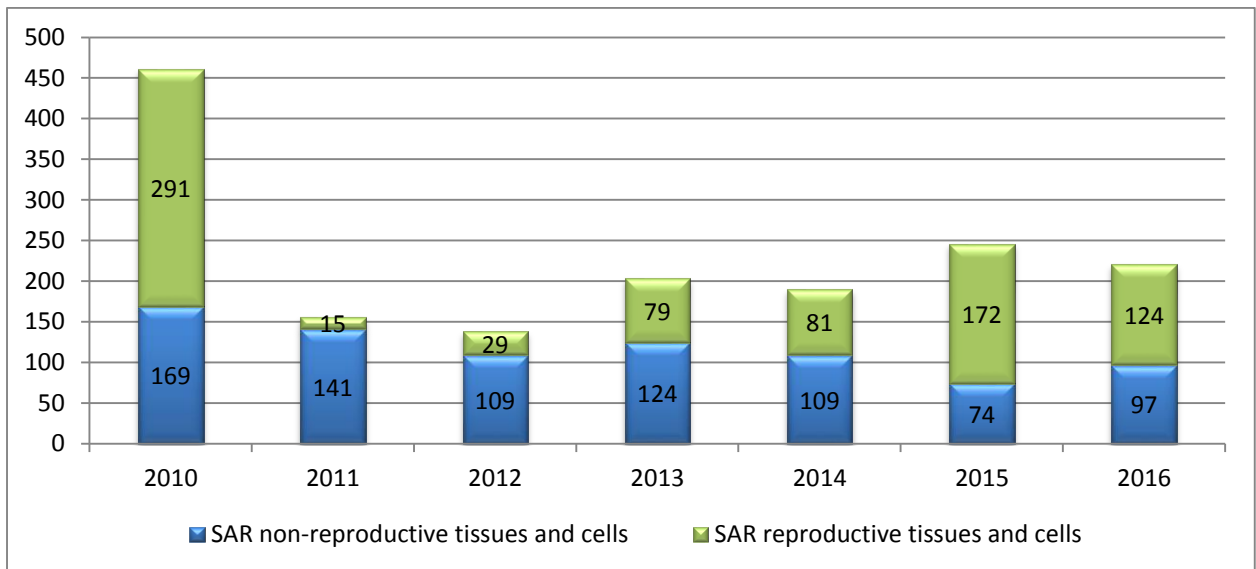


Figure 6. Total number of serious adverse reactions: 2010-2016 comparative data⁷.

⁶ For the first time this year, the Commission has included this specific, non-mandatory section for the reporting of deaths. This is a result of the experience gained in the previous blood SARE exercises, as this information was considered as paramount by all countries involved.

⁷ 2010 SAR data also include 209 cases of ovarian hyperstimulation syndrome (OHSS) reported under SAR, which should have been reported as SAR in donors.

2.2.1. Information by country

Fifteen Member States (AT, BE, CZ, DE, DK, ES, FI, FR, IE, IT, NL, PL, PT, SE, UK) and Norway reported SAR related to the clinical application of tissues or cells. In contrast, 9 Member States (BG, EE, HU, HR, LT, LV, MT, RO, SI) reported no SAR in recipients in 2016. As highlighted in previous exercises, this data suggests that reporting of SAR may still need to be improved at national level.

Ten Member States (AT, DE, ES, FR, IE, IT, NL, PT, SE and UK) reported SAR related to the transplantation of non-reproductive tissues or cells, and 11 Member States (BE, CZ, DE, DK, ES, FI, NL, PL, PT, SE, UK) and Norway reported SAR following the clinical application of reproductive tissues or cells.

The frequency of SAR can be put into context by calculating percentages in relation to national activity data. Based on the data submitted, the percentage of SAR related to the use of non-reproductive tissues and cells among the reporting countries ranged from 0.009-0.381% SAR/# tissues and cells distributed and from 0.019-0.787% SAR/# of recipients. For reproductive cells, this range was 0.0002-0.290% SAR/# tissues and cells distributed and 0.004-2.86% SAR/# of recipients.

However, these percentages should be interpreted with caution as they may not so much reflect the incidence of SAR and the improvement of quality and safety measures but rather the effectiveness and completeness of the national vigilance and reporting systems. Percentages calculated individually for each country having reported denominators have been made available to Member States during meetings of the Competent Authorities, allowing them to benchmark their results against their own previous national exercises and against other Member States.

2.2.2. Data by type of tissue or cell

Out of 221 SAR reported:

- 97 SAR (43.9%) were related to the transplantation of non-reproductive tissues or cells (see Figure 7). Of these:
 - 50 were related to the transplantation of HPC (9 bone marrow, 35 peripheral blood stem cells, 5 cord blood and 1 related to other haematopoietic progenitor cells).
 - 47 were related to transplantation of replacement tissues (1 general⁴ musculoskeletal tissues, 6 bone, 2 tendons/ligaments, 2 cartilage, 2 other skeletal tissues (meniscus and/or ear ossicles), 24 ocular tissue, 6 heart valves, 1 skin and 3 other tissues (1 pancreatic islets, 1 amniotic membrane and 1 adipose tissue).
- 124 SAR (56.1%) were related to the clinical application of reproductive tissues and cells (38 sperm, 22 oocytes, 56 embryos and 8 other reproductive tissues); see Figure 8).

No SAR were reported for Donor Lymphocyte Infusions (DLI), other cardiovascular tissues, hepatocytes or ovarian and testicular tissues.

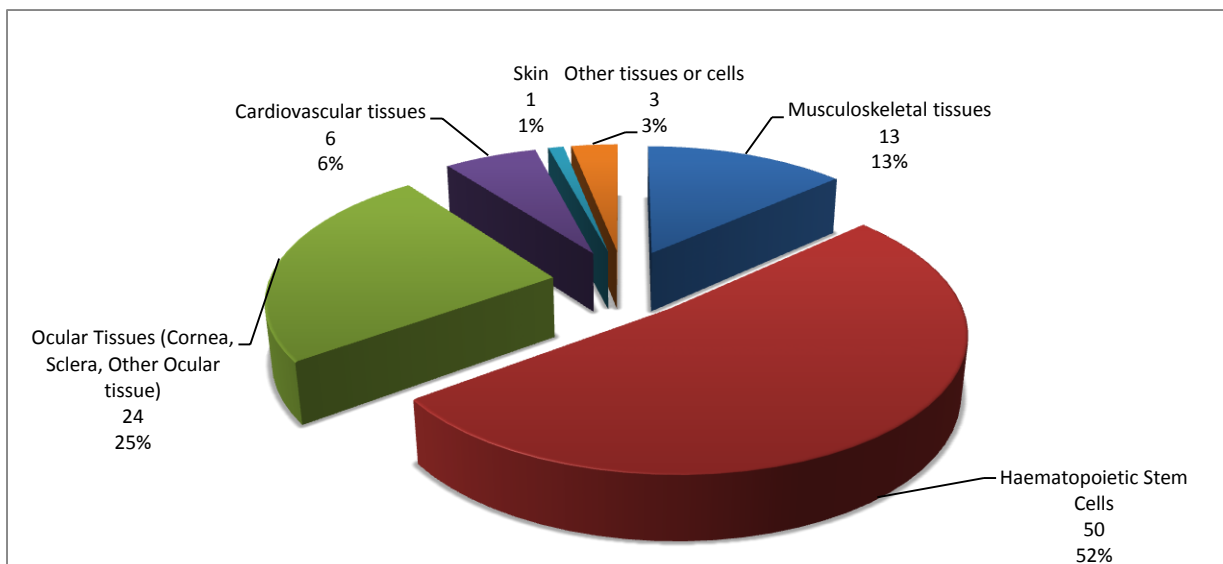


Figure 7. Number of SAR for each type of non-reproductive tissues and cells (absolute values and percentages of total recipient SAR); 2016 data.

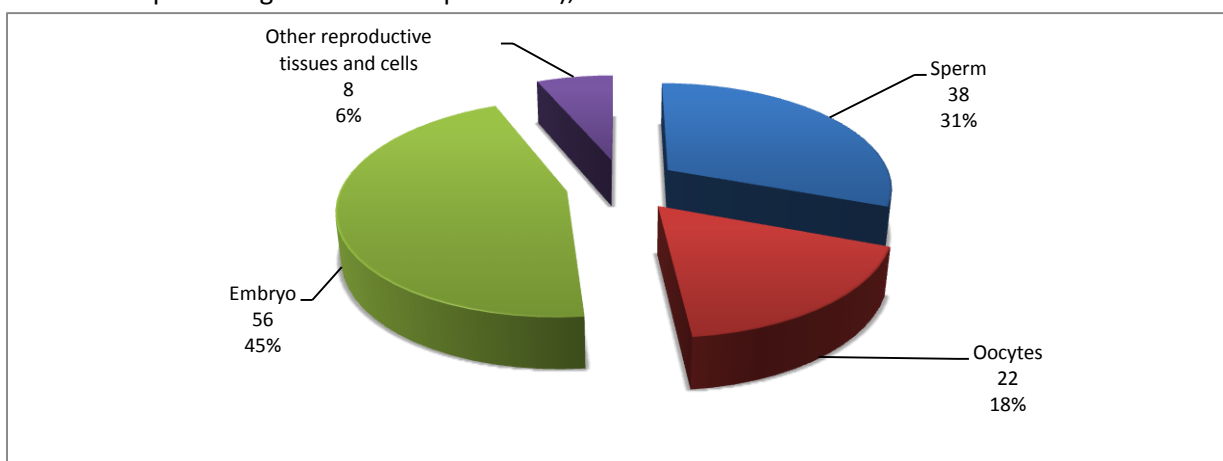


Figure 8. Number of SAR for each type of reproductive cells (absolute values and percentages of total recipient SAR); 2016 data.

2.2.3. Data by type of serious adverse reaction

The 97 SAR related to the transplantation of **non-reproductive** tissues and cells were categorised as follows:

- Transmitted infections: 25 cases (26% of all reported SAR for non-reproductive tissues and cells; see Figures 9 and 10), divided as follows:
 - 12 cases of bacterial infections, reported for the following transplanted tissues/cells: 2 ocular tissues, 4 HPC, 3 musculoskeletal tissues and 3 cardiovascular tissues.
 - 13 cases of other transmitted infections, reported for the following transplanted tissues/cells: 9 ocular tissues (all fungal infections), 2 musculoskeletal tissues (1 fungal and 1 other transmitted infection), 1 cardiovascular tissue (other transmitted infection), 1 pancreatic islets (fungal infection).
- Transmitted malignant disease: 1 case (1% of all reported SAR for non-reproductive tissues and cells) following peripheral blood stem cell transplantation.

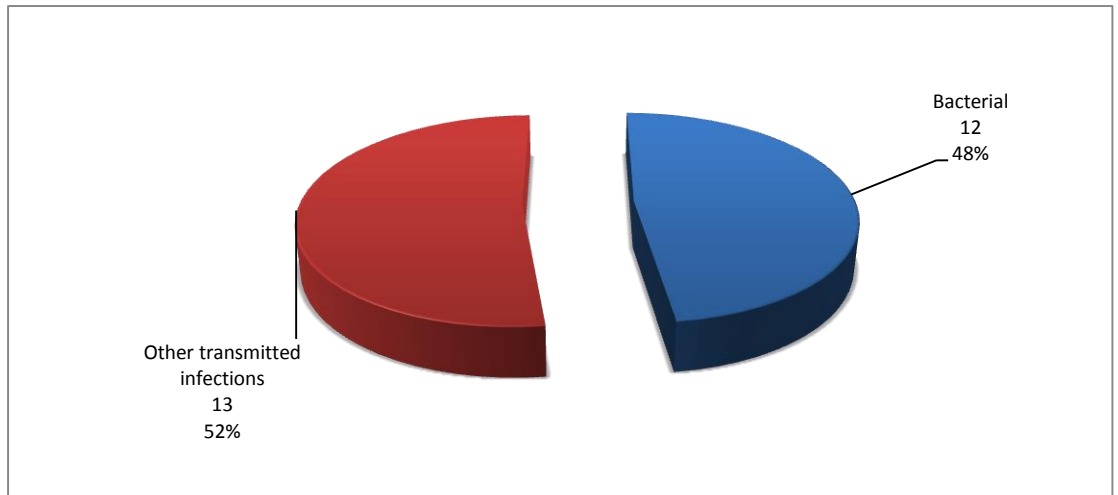


Figure 9. Transmitted infections in non-reproductive tissues and cells; data 2016.

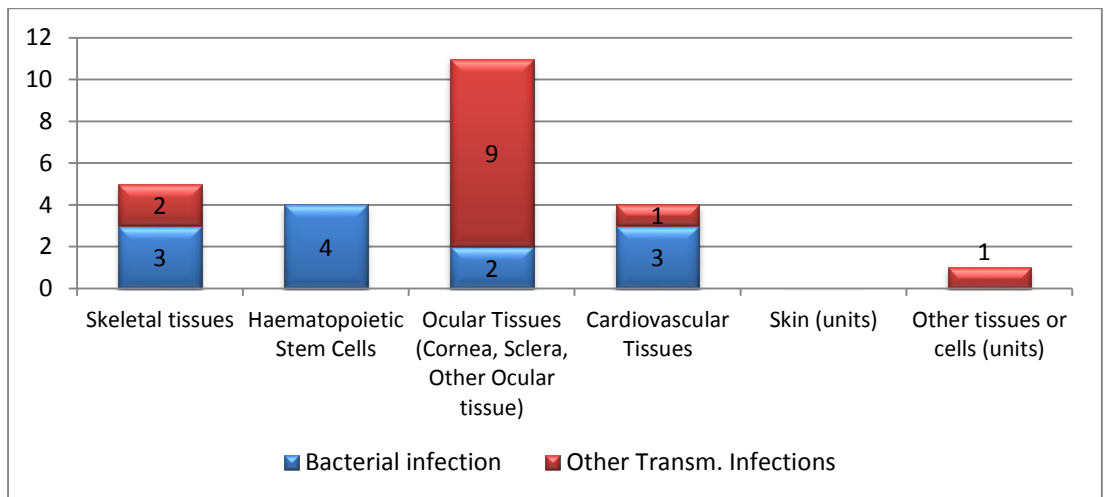


Figure 10. Transmitted infections per type of non-reproductive tissues and cells; data 2016.

- Other SAR: 71 cases (73% of all reported SAR for non-reproductive tissues and cells; see Figure 11). In this broad and heterogeneous category:
 - 45 SAR concerned HPC transplantation (7 bone marrow, 33 peripheral blood cells and 5 cord blood);
 - 13 SAR concerned ocular tissue;
 - 8 SAR concerned musculoskeletal tissue;
 - 2 SAR concerned heart valves;
 - 1 SAR concerned skin tissue and;
 - 2 SAR related to the transplantation of other tissues (1 amniotic membrane and 1 adipose tissue).

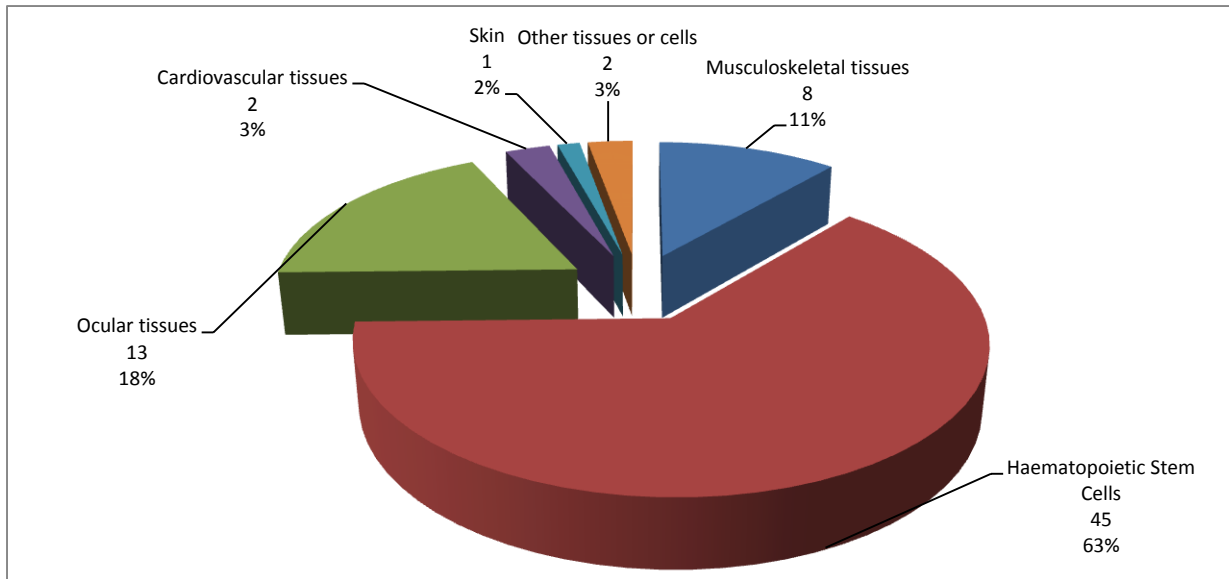


Figure 11. SAR in “Other category” within non-reproductive tissues and cells; data 2016 (absolute values and percentages of total).

The 124 SAR associated with the application of **reproductive cells** were classified as follows (see Figure 12):

- Transmitted infections: 5 SAR (4.03% of all reported SAR for reproductive tissues and cells) related to bacterial infections following the clinical application of sperm in 2 cases and embryos in 3 cases.
- Transmitted genetic conditions: 53 SAR (42.74% of all reported SAR for reproductive tissues and cells) following assisted reproduction treatments using sperm in 34 cases, oocytes in 16 cases and embryos in 3 cases.
- Other SAR: 66 SAR (53.22% of all reported SAR for reproductive tissues and cells) related to the clinical application of embryos in 50 cases, oocytes in 6 cases and sperm in 2 cases, with 8 cases related to other reproductive tissues.

Of these 124 SAR, 56 (45% of all SAR reported for reproductive tissues and cells) were related to non-partner donation (35 sperm and 21 oocytes).

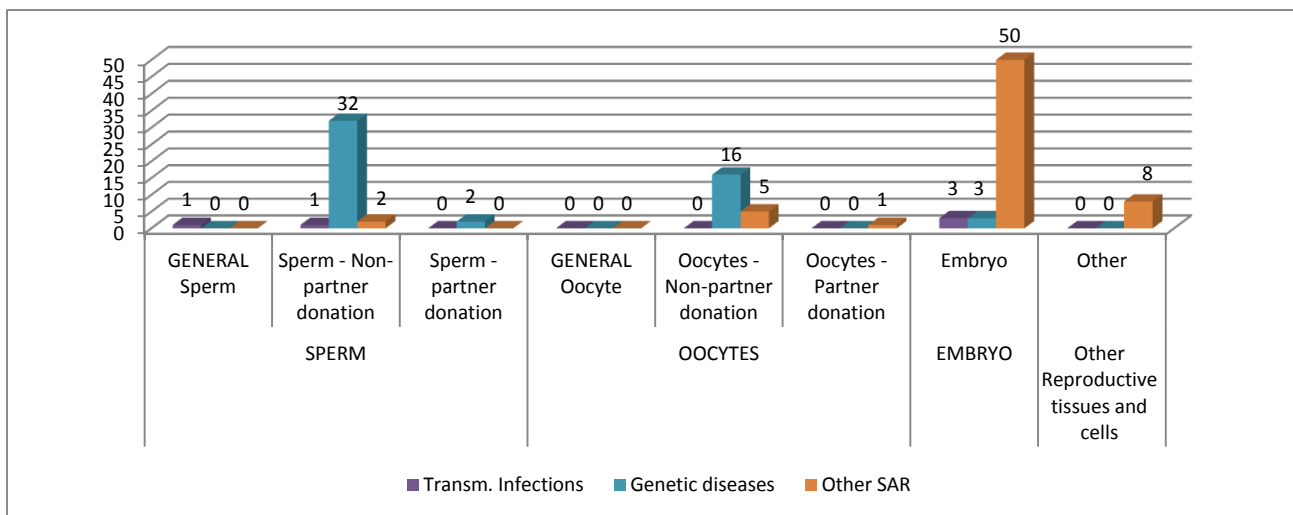


Figure 12. SAR related to the application of gametes and embryos; 2016 data.

2.2.4. Serious adverse reactions that resulted in recipient death

As vigilance systems are in place to protect donors and recipients, the Commission and Member States had deemed it appropriate to include a specific field for reporting deaths in this exercise.

Seven recipient deaths were reported in 2016. Of those, 6 deaths were reported within the non-reproductive category. All of these deaths were related to the transplantation of haematopoietic stem cells: 3 related to peripheral blood stem cells (2 related and 1 non-related PBSC respectively), 2 to autologous peripheral blood stem cells and 1 to bone marrow transplantation. It should be noted that the deaths were not directly attributable to the quality and safety of the tissues or cells transplanted, but rather to unforeseeable clinical complications related with the underlying conditions of the recipients.

Regarding the reproductive category, one death was reported: that of a child born with a transmitted genetic disease. Further investigations determined that this was caused by a possible mix-up of samples in the genetics laboratory located in a third country. The investigation concluded that an embryo which was diagnosed as inconclusive carrier of the genetic disease in the original report could have been transferred, and that would potentially explain the outcome of the pregnancy. Nonetheless, given its importance, the Commission and Member States considered that the case should be mentioned in this report.

2.3. Serious adverse events

The total number of SAE reported for 2016 was 769, showing that such events occurred for 0.043% of tissues and cells processed during this period. As mentioned above for SAR, the percentage of SAE in relation to the total number of tissues and cells processed should be interpreted with caution as not all countries reported these data. The total number of SAE reported in 2016 represented an increase when compared to previous exercises, as presented in Figure 13.

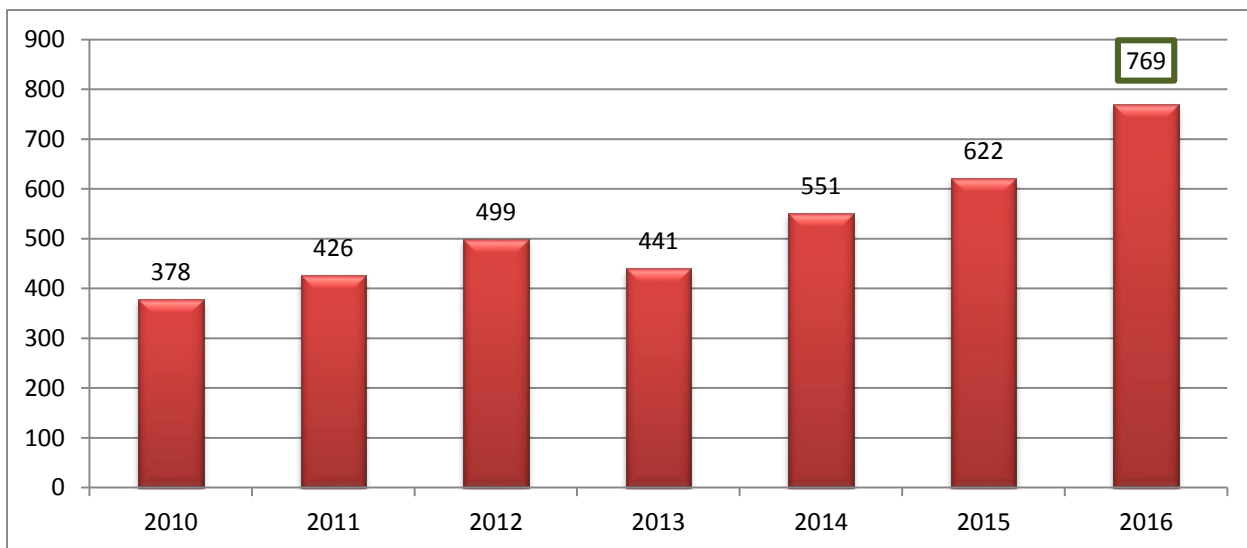


Figure 13. Total number of SAE reported: 2010-2016 comparative data.

The largest single cause of SAE was “human error” during the processing and procurement stages, as was the case in previous exercises. An overview of SAE types reported over the years is presented in Figure 14.

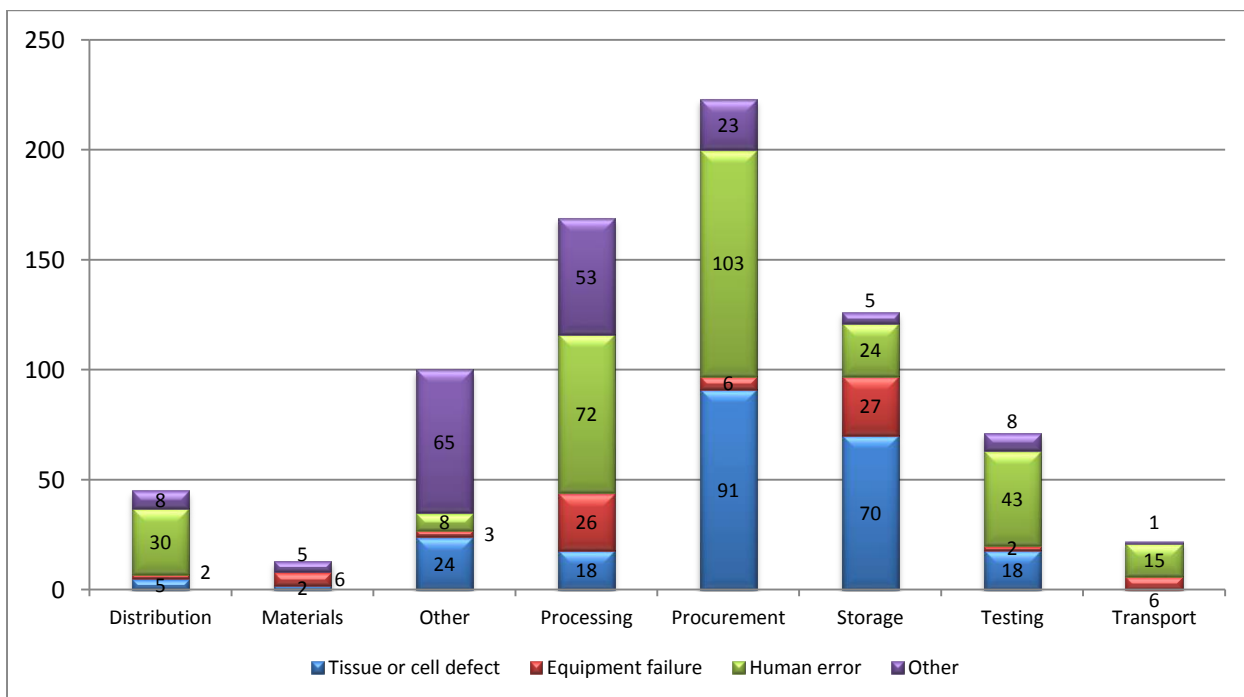


Figure 14. Total number of SAE reported categorised by origin: 2010-2016 comparative data.

2.3.1. Information by country

Sixteen countries reported SAE for non-reproductive tissues and cells (AT, BE, DE, DK, ES, FI, FR, HU, IE, IT, NL, PL, PT, SE, UK and NO) and 16 countries for reproductive cells (BE, CZ, DE, DK, ES, FI, FR, HU, IE, IT, MT, NL, PT, SE, UK and NO).

2.3.2. Information by activity

An overview of the SAE reported by type of activity is presented in Figure 15.

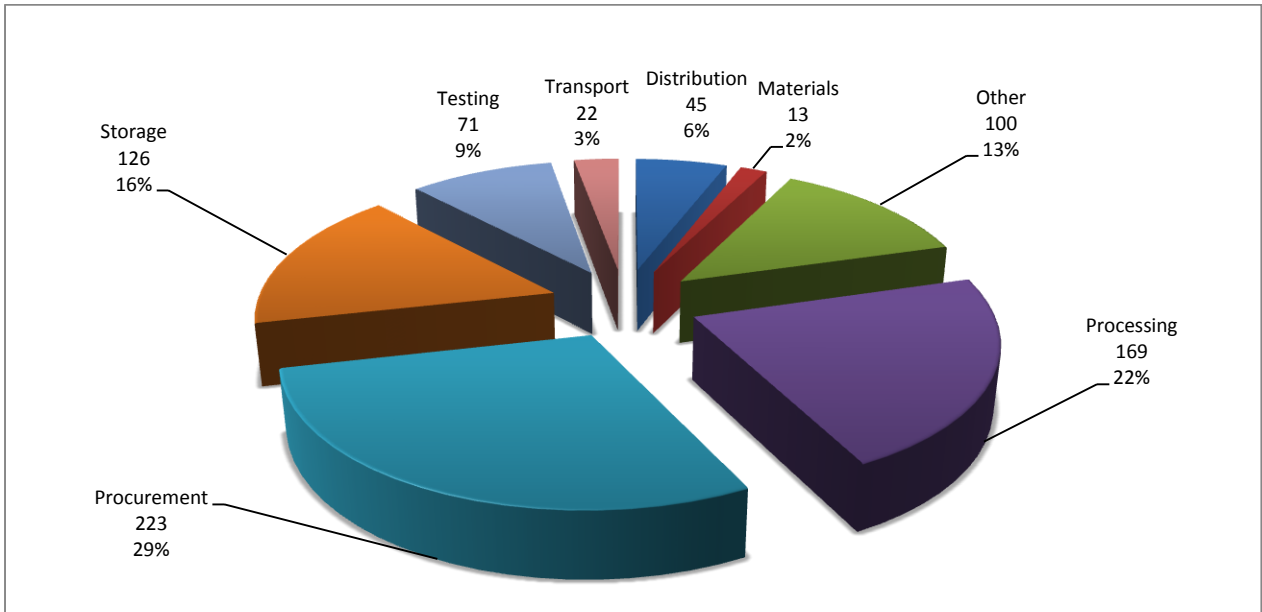


Figure 15. Number of SAE and percentage of total SAE reported by type of activity (absolute values and percentages of total).

2.3.3. Information by type of serious adverse event

The 769 SAE were classified as tissue or cell defects, human error, equipment failure and other types of events. The distribution by type is presented in Figure 16.

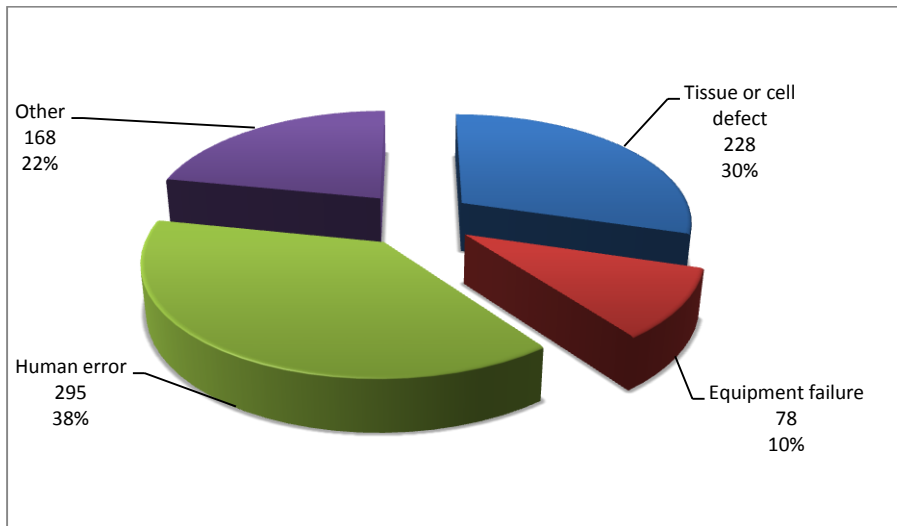


Figure 16. SAE types; 2016 data (absolute values and percentages of total).

Taking into account the type of SAE and the stage at which they occurred during the donation-distribution chain, SAE were categorised as shown in Figures 17 and 18, divided into non-reproductive and reproductive categories, respectively.

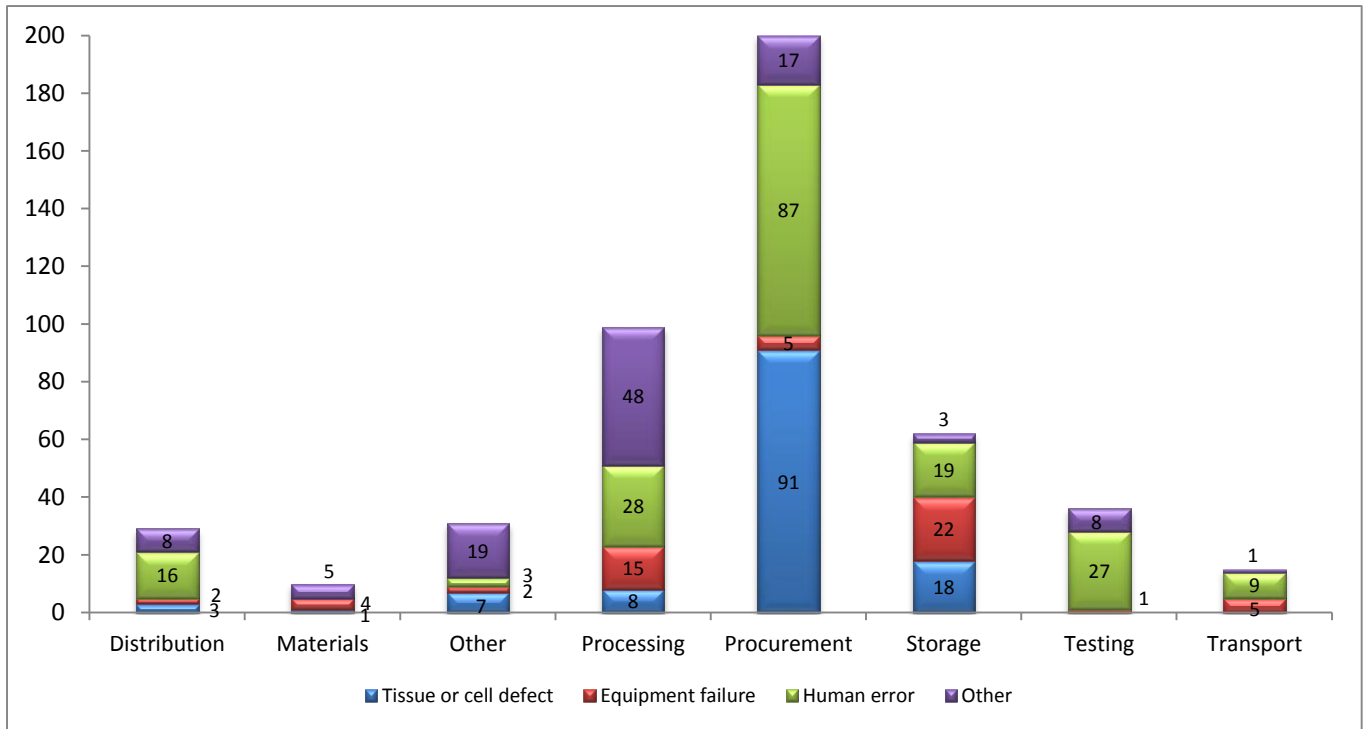


Figure 17. SAE in the non-reproductive category per type and stage at which they occurred during the donation-distribution chain; data 2016.

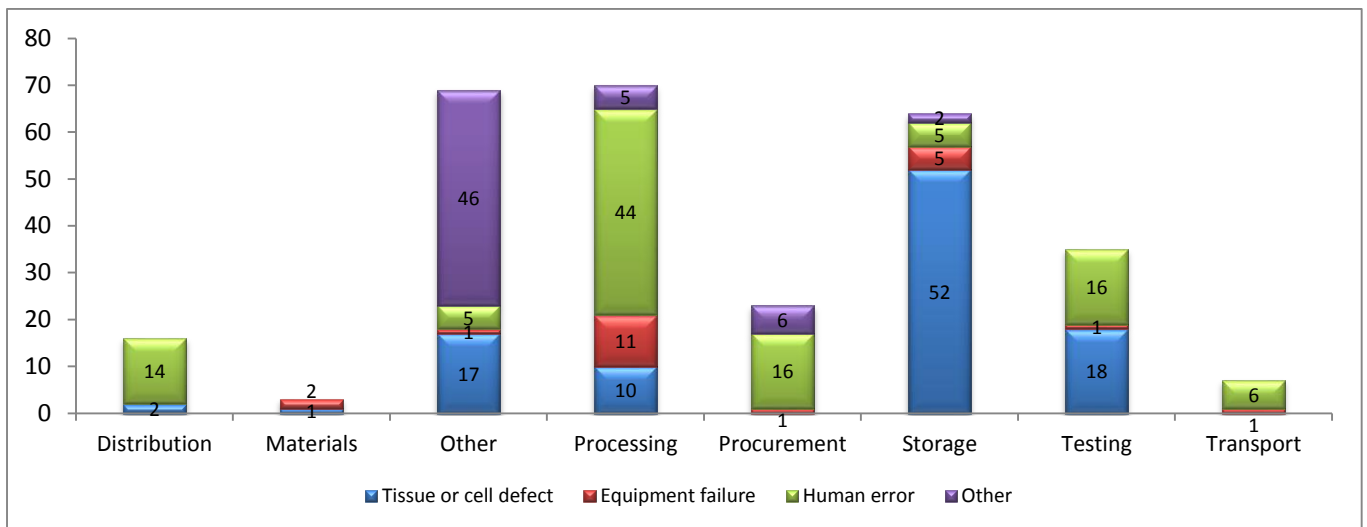


Figure 18. SAE in the reproductive category per type and stage at which they occurred during the donation-distribution chain; data 2016.

The non-reproductive SAE (482 cases) occurred mostly during the procurement and processing stages, mainly due to human error and tissue or cell defects, whereas the reproductive SAE (287 cases) occurred primarily during processing and storage, followed by the “other category”; these were mainly due to human error, tissue or cell defects and “other” reasons.

2.4. Serious adverse reactions in donors

Recognizing the importance of all donor adverse reactions, including those not directly impacting the quality and safety of tissues and cells, which are reported in pharmacovigilance systems (e.g. Ovarian

Hyper-Stimulation Syndrome [OHSS] following oocyte donation, reactions subsequent to the administration of granulocyte colony-stimulating factor [GCSF] for collection of peripheral blood HPC, etc.), the Commission continues to collect such data on a voluntary basis in agreement with the Member State Competent Authorities.

In 2016, 19 Member States (AT, BE, BG, CZ, DE, DK, EE, ES, HR, IE, IT, FI, FR, NL, PL, PT, SI, SE, UK) reported a total of 700 SAR in donors. Of those, 70 cases were related to the donation of non-reproductive tissues or cells (10 % of all SAR in donors) and were reported by 8 Member States (DE, ES, FI, FR, IT, NL, PT, UK). Overall, 68 cases were associated with donation of HPC and 2 cases with other non-reproductive tissues.

All 630 cases with reproductive tissues were related to SAR in oocyte donors (amounting to 90 % of all SAR in donors) and these were reported by 19 Member States (AT, BE, BG, CZ, DK, DE, EE, ES, FR, HR, IE, IT, NL, PL, PT, SI, SE and UK). SAR in donors of reproductive tissues or cells were reported under the following categories: oocytes general (80), oocytes for non-partner donation (19) and oocytes for partner donation (531).

In the case of non-partner donation, the main SAR reported were severe OHSS (6), haemoperitoneum (5), infection (2), adnexal torsion (1) and others (5), as shown in Figure 19.

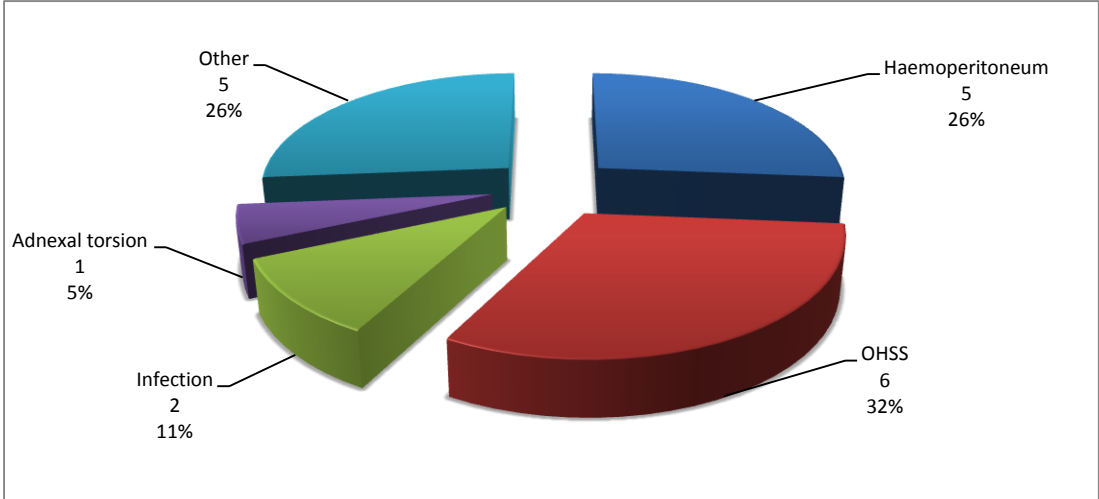


Figure 19. Classification of SAR in donors for oocyte donors in non-partner donation.

Most of the SAR in oocyte donors were critical, severe and moderate-to-severe OHSS cases (451 cases). The remaining cases included infectious complications and other types of SAR; see Figure 20 for further details. This data emphasises the need for Competent Authorities to put in place appropriate follow-up and protection mechanisms for living donors of tissues and cells.

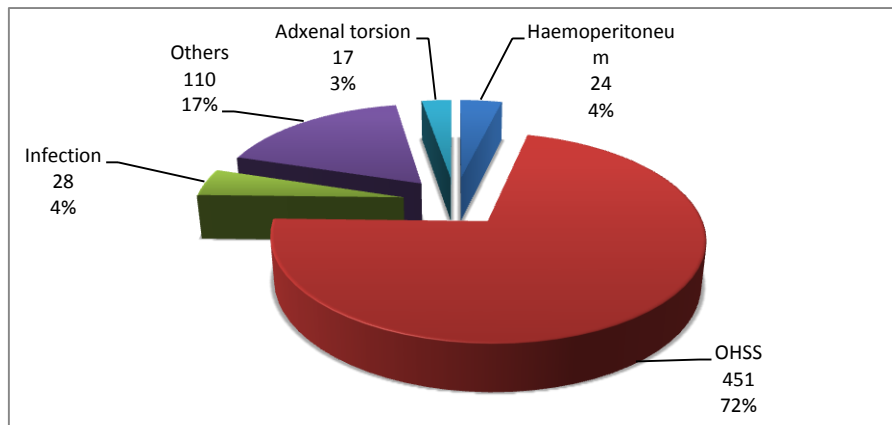


Figure 20. SAR in oocyte donors; 2016 data (absolute values and percentages of total).

It should be noted that no SAR resulting in donor deaths were reported in 2016.

3. Conclusions

The implementation of vigilance requirements and data collection systems in the tissues and cells field has improved over time. However, the fact that most countries report data on the number of tissues and cells distributed, but not all report the number of recipients, suggests that while tissue establishments are gradually improving their data recording and reporting, more work is needed within the organisations responsible for human application, who are the ones ultimately applying those tissues and cells into patients. It is worth noting that the lack of consensus on which units to use for the collection of data for certain tissue and cell types (e.g. units of skin vs cm² vs m², oocytes in units vs number of cycles) may explain why some countries chose not to, or were not able to, report data on activity data (used as denominators for the SARE data analysis). These data are key for providing a clear picture of the activity within the field and for ensuring traceability of tissues and cells.

Health professionals involved in the clinical application of tissues and cells and tissue establishments should be encouraged to submit case reports in order to contribute to greater understanding of the actual situation. This will help to identify preventive and corrective measures taken, so lessons learned can be shared with others to help avoid the unnecessary repetition of SARE.

As in previous exercises, most of the SAR related to the transplantation of non-reproductive tissues and cells were associated with infection – mostly of bacterial and fungal origin. In contrast, the most frequently reported SAR for the clinical application of reproductive cells involved the transmission of genetic diseases. However, it should be emphasised that the likelihood of transmitting a multi-factorial genetic disease from the donor to the offspring is sometimes difficult to assess.

The majority of SAE were reported under the category of “human error”, especially during the procurement and processing steps. This may suggest the need to further clarify the most critical aspects that need to be addressed when revising standard operating procedures in tissue establishments and assessing the training needs and competencies of the personnel.

The reporting exercise also revealed an increase in the number of reported SAR in donors in the year 2016 in comparison with previous years, indicating that Competent Authorities support reporting of these SAR so appropriate follow-up mechanisms for tissues and cells donors are put in place.

Since 2017, through a service grant agreement signed with the Commission, the EDQM is carrying out the verification and analysis of the blood and tissues and cells SARE exercises and drafting the final summary reports. Due to the expertise of the EDQM in the field of biovigilance and with international data collection activities, this collaboration has greatly contributed to improving the EU SARE exercise by helping refine the Common Approach document and reporting templates, increasing the quality of the data reported by the Member States through extensive data curation and verification and going deeper into the data analysis and interpretation. In addition, within the framework of a direct grant agreement between the EC and the EDQM, a technical meeting on the topic “National and EU-level tissue and cell activity data collection and reporting” took place in Strasbourg (France) in March 2018. Fruitful discussions among professional societies and national representatives regarding future steps needed for the harmonisation of data collection exercises in the field were held and will contribute to increasing the quality and harmonisation of future international exercises, as well as enhancing the cooperation among professional societies carrying out similar work, Member States and the Commission.

In addition, since January 2017, a Vigilance Expert Sub-group (a sub-group to the Competent Authorities on Substances of Human Origin (SoHO) Expert Group) was established by the Commission, in agreement with the Member States. This sub-group had agreed Terms of Reference that included supporting the development and improvement of the SARE reporting system. The ongoing work of the sub-group is helping to improve and harmonise the exercise and support the development of national SoHO vigilance systems. In addition, its work will also contribute to the ongoing evaluation of the legal frameworks on blood, tissues and cells⁸.

The Joint Action VISTART⁹, which includes a work package dedicated to vigilance reporting for blood, tissues and cells, finalises in 2018 and its outcomes will be a further source of data for reflection on improving the implementation of vigilance requirements and SARE data collection.

Overall, the implementation of vigilance requirements and data collection in the field is improving over time, as Member States are making efforts each year to improve their vigilance systems and the quality and accuracy of data submitted. However, there is still a significant degree of under-reporting by some Member States; thus data should be interpreted with caution. The Commission, together with the EDQM and Member States, will reflect on the most appropriate solution to these issues, with the support of the established SoHO Vigilance Expert Sub-group and taking into account the work carried in the context of relevant EU-funded projects and joint actions.

⁸ https://ec.europa.eu/health/blood_tissues_organ/policy/evaluation_en

⁹ Vigilance and Inspection for the Safety of Transfusion, Assisted Reproduction and Transplantation is a Joint Action co-funded by the European Union.