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Survey of European Vigilance & Surveillance Systems

(Work Package 4)

This project is supported by the EU Public Health Programme
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EXECUTIVE SUMMARY

This report presents the results of a survey regarding the Vigilance & Surveillance (V&S) systems for tissues and cells used in transplantation and in assisted reproduction in the European Union. The survey was conducted as part of the SOHOV&S project (Vigilance and Surveillance of Substances of Human Origin) co-funded under the European Union Public Health Programme.

All EU Member States (MS) except two participated in the survey. All those that responded indicated that they have a V&S system in place. The number of EU MS with a V&S system in place for tissues and cells has increased from 15 countries (56%) in 2009 to 23 countries (96%) in 2010.

In summary, the survey results describe the general characteristics of these V&S systems. They are nationally organised systems, mostly based on the 2004 and 2006 EU Directives, usually with a common programme for reporting Serious Adverse Reactions and Events (SARE) for all types of tissues and cells, often overlapping with blood and drug vigilance and with multiple ways to send/receive SARE reports. The majority of national systems incorporate some or all of the vigilance tools developed in the EU-funded EUSTITE project. Member States report annually to the European Commission, as required by the Directives, and half of them publish the results of their V&S programmes. Almost half of the Competent Authorities always participate in SARE investigation and 46% participate in some investigations. Nearly 80% are interested in the development of an international SARE investigation team that would be available to all MS for conducting particularly challenging investigations.

Sixty one percent of MS have dedicated vigilance officers and practically all countries are interested in an EU training course on this topic. Sixty eight percent of MS have the requirement to report SARE in living donors, while nine countries have a registry of these donors. Finally, there do not appear to be significant differences between the programmes run by Competent Authorities which are specialised in ART and those which are not.

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INTRODUCTION



This survey was conducted as part of the SOHOV&S project (Vigilance and Surveillance of Substances of Human Origin) which is funded under the European Union Health Programme (see www.sohovs.org). The general aim of the project is to support EU Member States (MS) in the establishment of effective Vigilance & Surveillance systems for tissues and cells used in transplantation and in assisted reproduction (ART). The survey was conducted as part of work-package 4 which was led by the Spanish Transplantation Organisation (ONT).

OBJECTIVES

The survey aimed to gather detailed information on the systems in place in MS for V&S in the field of tissues and cells for transplant and for assisted reproduction. The questionnaire focused on the details of the Competent Authority's role in Vigilance for tissues and cells. It also addressed general aspects of V&S, such as responsibilities for the investigation of serious adverse reactions or serious adverse events (SARE), the vigilance of living donors and, finally, it aimed to gather recommendations of good vigilance practices.

METHODOLOGY

The questionnaire survey was designed by representatives from ONT, the Human Fertilisation and Embryology Authority in the UK (HFEA) and the Italian National Transplant Organisation (CNT), in collaboration with the partners of SOHOV&S and the European Commission, which provided the current list of Competent Authority Representatives. ONT sent the questionnaire in the third week of July, 2010. The blank questionnaire is shown at Annex I. The completed questionnaires were reviewed and the responses compiled in a Microsoft Excel worksheet. The data were analysed with the SPSS software and tables and graphics were developed.

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RESULTS

RESPONSE RATE:

The questionnaire was sent to 32 countries, including the 27 Member States of the EU and 5 Non-EU European countries. The following are the countries that responded:

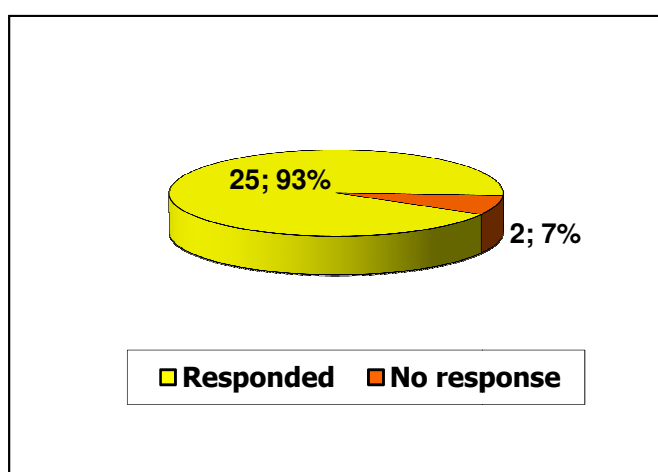
EU MEMBER STATES
Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, <u>France*</u> , Germany, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, <u>Portugal*</u> , Romania, Slovenia, Spain, Sweden, the Netherlands and the <u>United Kingdom*</u> .
NON-EU COUNTRIES
Croatia, Iceland, Lichtenstein, Norway

* Three EU member states answered 2 questionnaires each, one for tissues and cells for transplantation and one for tissues and cells for ART. This reflected the fact that these countries have separate Competent Authorities for these sectors.



The results of the non-EU countries are summarised in Annex II.

RESULTS FOR EU MEMBER STATES

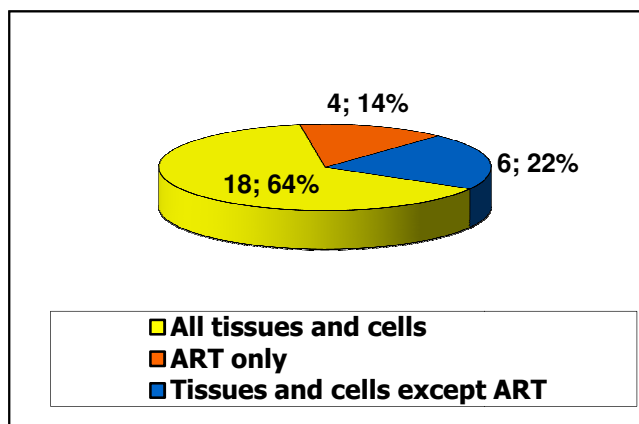
25 of 27 countries completed the questionnaire, **a response rate of 93%.**



The 25 countries that answered sent a total of 28 completed questionnaires, because three countries sent 2 questionnaires. The breakdown of the 28 questionnaires was as follows: 18 were unspecific covering all

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types of tissues and cells (ART and non-ART), 4 were specific for ART (Bulgaria, France, Portugal and UK) and 6 were specific for all tissues and cells except for ART (Austria, France, Hungary, Portugal, Spain and UK).

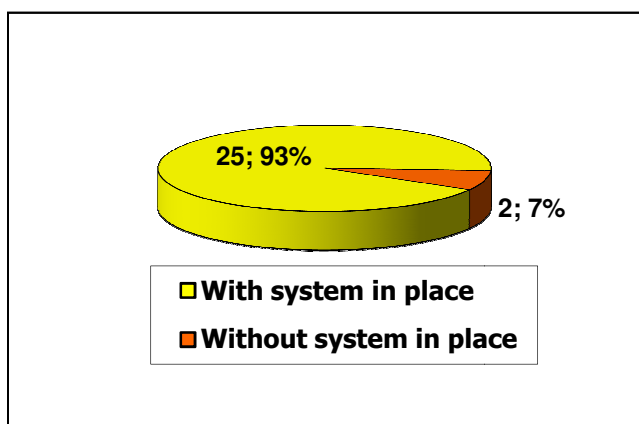


Section 1: General



Countries with or without a system in place for the reporting of Serious Adverse Events and Reactions for tissues and cells.

All countries responding to this survey report that they have a system in place, while 10 of these countries did not in 2009 according to the European Commission report for that year.

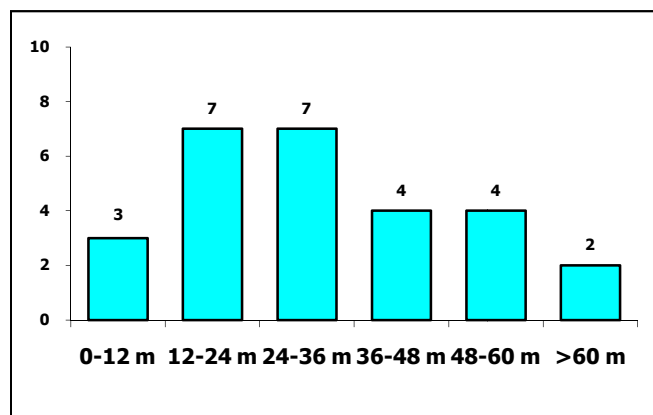
If it is assumed that the countries that have not answered do not have a system in place, 25 of 27 (93%) MS have a system in place. In 2009 only 15 of 27 (56%) EU countries declared to have a system in place.



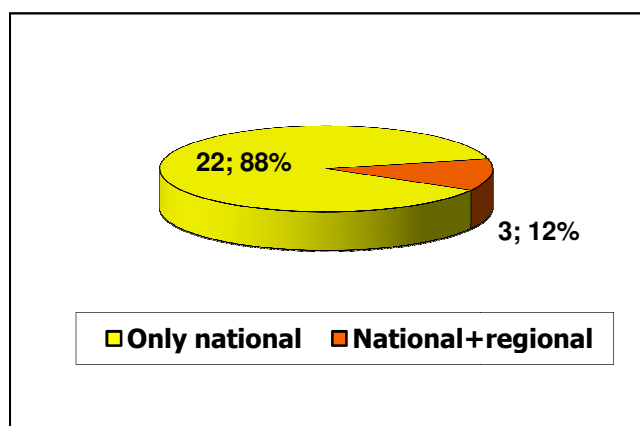
1. If you have a V&S system in place, how long has it been operational? (N=27)

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All countries except one (Romania) answered this question. The V&S systems are in place for an average of 36.22 months (SD: 24.35). The following graph shows the time distribution:



2. If you have a system in place, is it national or both national and regional? (N=25*)





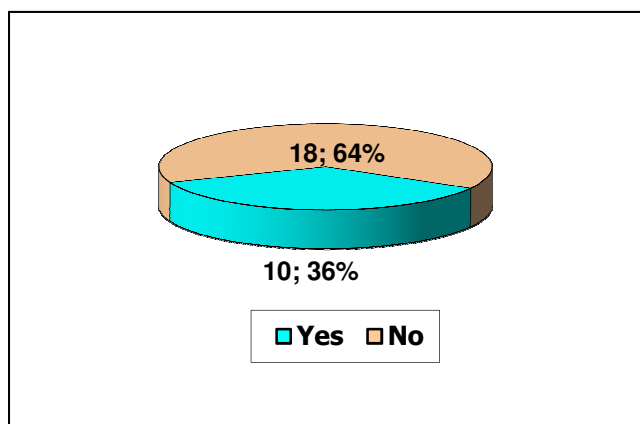
Only Germany, Italy and Spain have a system with both national and regional elements.

*Countries, rather than questionnaires are considered here.

3. All responders except one (France Non-ART) have based their system on the EU Directives.

3.1 Is there additional national legislation relating to V&S that goes beyond the EU Directives? (N=28)



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The questionnaires that reported additional legislation are: Belgium, Estonia, France, Germany, Italy, Poland, Sweden, the Netherlands and UK-ART.

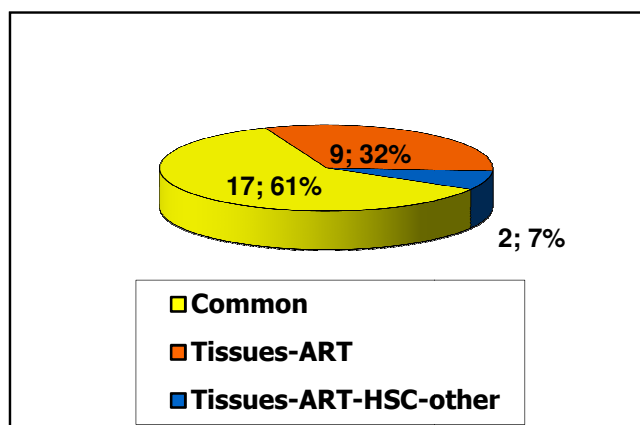
3.2 If yes, please describe briefly:

- Reporting of serious adverse donor complications. (Belgium)
- Currently vigilance and surveillance of organ transplantation is also covered by the Handling and Transplantation of Cells, Tissues and Organs Act. (Estonia)
- Report to the Ministry of Health. Appointment of local ART vigilance correspondents (CLAs). Local correspondents kept informed. National Commission of ART Vigilance. (France-ART)
- The definitions used in the French biovigilance context for the terms adverse event and adverse reaction are slightly modified as compared with those given in the EU legislation. In France, an adverse event is a failure of an element at one step of the process (procurement, processing, testing, storage) that can entail an adverse reaction for the living donor or for the patient/recipient. An adverse reaction is an expected (or not) and serious (or not) clinical and/or biological manifestation that happens to the living donor (including increased risk for living donor) or to the recipient (including loss of chance). Furthermore our system includes also the V&S related to organs. (France-Non ART)
- According to the updated German Drug Law, Tissues and Cells are treated as medicinal products. (Germany)
- The decree covers HPC from peripheral blood and requires send a notification in case of an adverse reaction in the donor, in the recipient or an adverse event in a step of the process from collection to distribution. (Italy)
- The Act of 1 July 2005 on procurement, storage and transplantation of cells, tissues and organs. The Act of 17 July 2009 amending the act on procurement, storage and transplantation of cells, tissues and organs and amending the act - Introducing the Penal Code. (Poland)
- A national directive concerning "Use of Tissues and Cells in health care and Clinical research". (Sweden)
- The existing regulation for the safety and quality of T&C is adjusted in 2007 with the obligations of the EU Directives. (the Netherlands)

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- The HFE Act 1990 (as amended) has adapted the definitions to include ART. We have a Code of Practice that provides guidance recommending the reporting of less serious incidents, near misses and OHSS and an HFEA Directive that makes the reporting of less serious incidents, near misses and OHSS mandatory. (UK-Non ART)

4. Is reporting of serious adverse reactions and events (SARE) common for all types of tissues and cells or separate for different types? (N=28; Multiple choice)

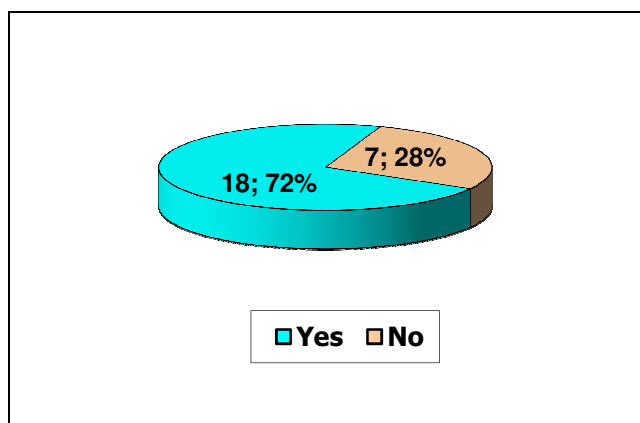


Countries with a common system are Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, Hungary, Ireland, Latvia, Luxembourg, Malta, Poland, Romania, Slovenia, Sweden and the Netherlands.

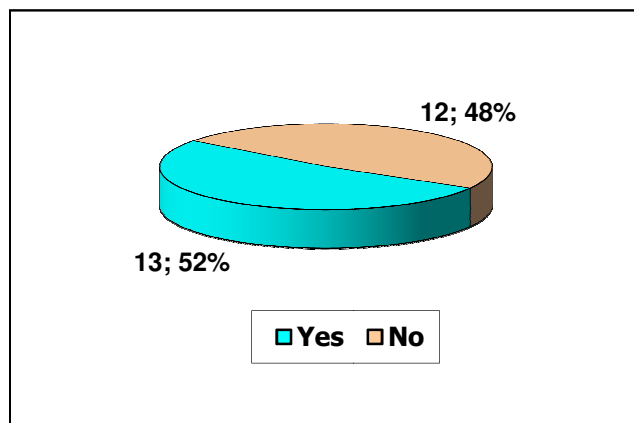
Countries with different reporting systems for tissues and cells for transplantation and for ART are Bulgaria, France, Germany, Italy, Lithuania, Portugal, Spain, France and UK.



5. Is there overlap/interaction/co-operation with other reporting systems? (Multiple choice)

Haemovigilance: (N=25)



Pharmacovigilance: (N=25)

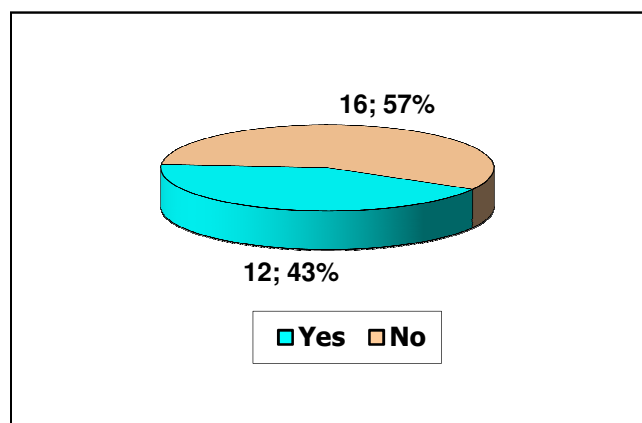


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Countries that have overlap with haemovigilance are: Austria, Belgium, Cyprus, Czech Republic, Denmark, France, Finland, Germany, Hungary, Ireland, Italy, Latvia, Luxembourg, Malta, Slovenia, Sweden, the Netherlands and UK.

Countries that have overlap with pharmacovigilance are Austria, Belgium, Cyprus, Czech Republic, Denmark, France, Finland, Ireland, Luxembourg, Malta, Slovenia, Spain, UK.


Other: (N=28)



Countries that have overlap with other are Austria, Belgium, Czech Republic, Denmark, Estonia, France, Ireland, Malta, Portugal and UK-ART.

The 'other' overlaps or interactions are with:

- Medical Devices. (Austria)
- Hemovigilance, pharmacovigilance and materovigilance systems are informed regarding notifications that might concern them. (Belgium)
- The Pharmacovigilance Department is responsible for vigilance of human pharmaceuticals, blood and HTC SARE. (Czech Republic)
- Medical Devices. Note: Cooperation exists with colleagues of other sectors in the Agency, when interface matters arise. (Denmark)
- The reporting system also covers organ transplantation. (Estonia)
- Biovigilance (medical devices such as culture media), Materiovigilance (medical device), Nosocomial infections. (France-ART)
- Ancillary product vigilance, medical devices vigilance, in vitro diagnosis medical devices vigilance. (France-Non ART)
- Medical devices. (Ireland)
- Medical devices. There is interaction (co-operation in the a V&S system and alert systems of all substances of human origin including blood, pharmaceuticals in the case of advanced medicinal therapies and medical devices). (Malta)
- The system is autonomous but CNPMA's interacts with general directorate for health. (Portugal-ART)

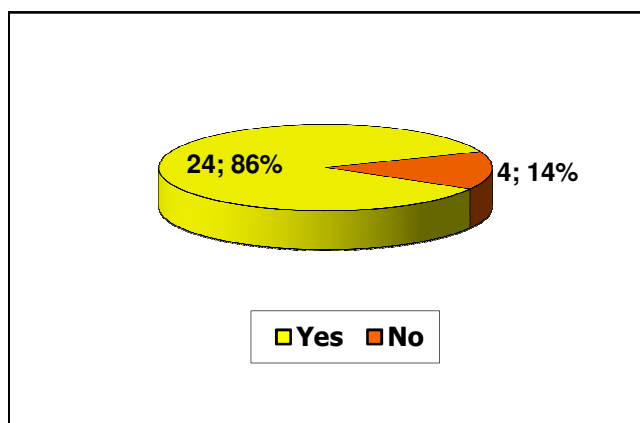
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- This is an independent system, but there is cooperation between pharmaceuticals and Direcção Geral da Saúde (for infectious diseases). (Portugal-Non ART)
- Not really. Very occasionally we will suggest that a centre also reports an incident involving a medical device to the MHRA (UK Pharmaceutical regulator) but it is an informal system. (UK-ART)

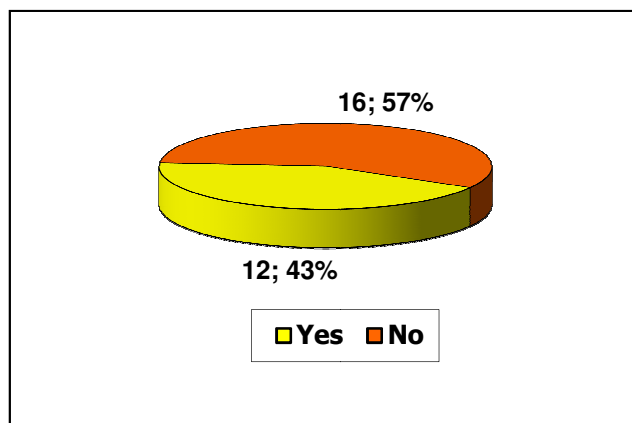
6. How are reports received? (N=28)

Only four countries (Bulgaria, Hungary, Portugal-ART and UK-ART) have a single method of report submission. The other countries have a multiple options, as follows:

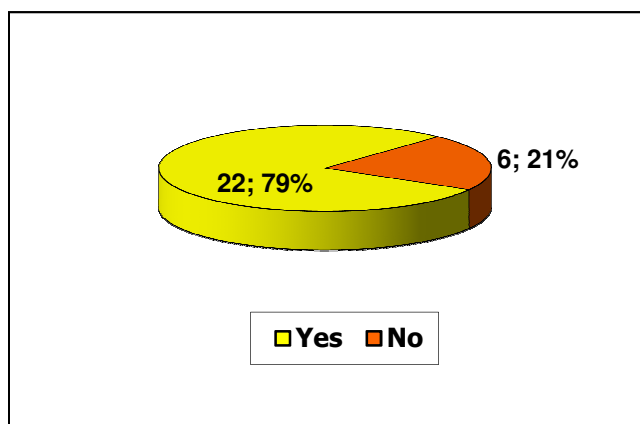
Paper:



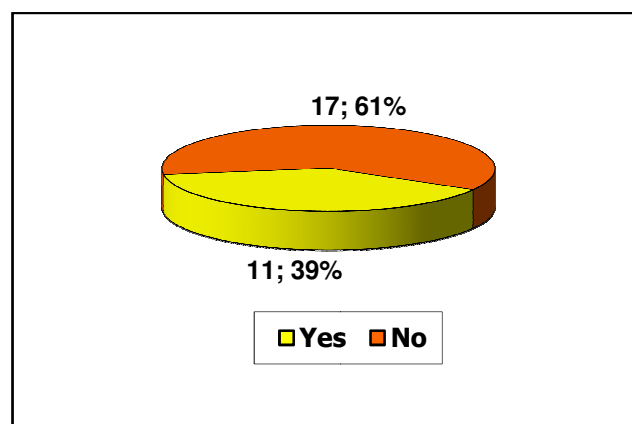
Software:





Email/fax:



Telephone:



Countries that use paper are Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Estonia, France, Finland, Germany, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal-Non ART, Romania, Slovenia, Spain, Sweden and the Netherlands.

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Those that reported use of a software system are Denmark, Estonia, France-ART, Germany, Ireland, Italy, Malta, Portugal-Non ART, Slovenia, Spain, the Netherlands and UK-Non ART.

Only Bulgaria, Germany, Hungary, Latvia, Spain and UK-Non ART don't use email/fax.



Countries that use telephone are Denmark, Finland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal-Non ART and Spain.

7. Are mandatory reporting times-frames defined? (N=28)

Seventeen countries (61%) have mandatory reporting times; these are Austria, Bulgaria, Czech Republic, Estonia, Finland, France, Germany, Hungary, Lithuania, Portugal, Slovenia, Spain, Sweden, the Netherlands and UK-ART.

7. 1 If yes, please describe briefly:

- The reports of SARE should be submitted without delay. (Austria)
- According to ORDINANCE N° 10 dated March 30, 2007 the responsible person has to send within 7 days period a report to the CA. (Bulgaria)
- Regulation No.81 of the Minister of Social Affairs of 19/12/08. "Conditions and procedure for biovigilance and recall applicable to cells, tissues and organs and formats for notification of serious adverse events and serious adverse reactions" stipulates that a competent person of the handler shall notify the state Agency of Medicines electronically within 24 hours of the SAE or SAR and of the measures taken on the formats presented in Annexes 1 and 4 to the Regulation. (Estonia)
- Without delay. (Finland)
- Without delay. (France-ART)
- Without delay or at the latest within 48 hours for serious reaction. No more than 15 days for others. (France-No ART)
- According to the updated German Drug Law, SARE should be reported immediately, at the latest within 15 days after discovery. (Germany)
- According to the Ministerial Decree 18/1998 on tissue and cell establishments the CA gets the data of the annual report every year until 30th of April from the county-based policy administration services of public health. (Hungary)
- Under the Lithuanian law, in accordance with the Order of the Minister of Health No V-401 dated 22 May 2007,, regarding serious adverse events and reactions...", the responsible person must: 9.3, immediately verbally" inform the National Transplant Bureau and other relevant establishments; 9.4. during 24 hours must fill in,, Rapid notification for suspected SARE" and send it to Bureau and other relevant establishments. 9.5. during 2 weeks perform the investigation of the cause of SARE; 9.6 to send the conclusions of SARE investigation to National Transplant Bureau and other relevant establishments. (Lithuania)
- If there is a suspicion that the occurrence may have impact on another ART center (either national or abroad) the alert must be sent within 48 hours of the finding. If there is no suspicion that the occurrence may have an effect on other centres, meaning that it only affected the context of the ART center, the form must be sent by the day 15 of the month after the finding. (Portugal-ART)
- For severe SARE /in 24 hours. (Slovenia)
- We have a specific time (24 h) for the notification of urgent and serious adverse reactions. (Spain)

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- The report form constitutes of two parts: part 1 should be used "in conjunction" with the SAR and part 2 when the investigation and possible actions have been taken. (Sweden)
- 'Non calamities' must be reported before closure of reporting year. 'Calamities' must be reported immediately to the CA/inspection of healthcare. (the Netherlands)
- 12 hours if verbal (this would then be followed up by submission of an electronic form) or 24 hours electronic. (UK-ART)



8. Is a requirement to report SARE extended to third parties? (N=28)

Fifteen countries (54%) have requirements for reporting SARE extended to third parties.

These countries are Bulgaria, Cyprus, Czech Republic, Estonia, Finland, France-Non ART, Ireland, Italy, Lithuania, Malta, Portugal-Non ART, Slovenia, the Netherlands and UK.

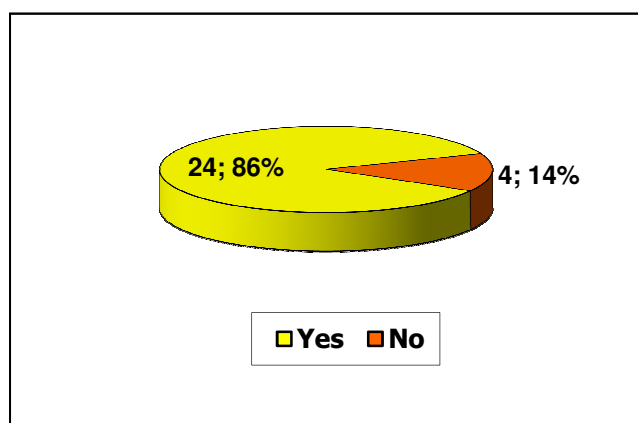
8. 1. If yes, please describe briefly:

- According to ORDINANCE N° 10 dated March 30, 2007, the head of the hospital is required to report immediately to all TEs that have contracts to provide these tissues and cells in the case of suspected SARE. (Bulgaria)
- Third parties report to TE and TE is responsible for reporting to CA. (Cyprus)
- There is a requirement for infection case reports into the System of the Public Health Institution. (Czech Republic)
- Regulation No.81 of the Minister of Social Affairs of 19/12/08. "Conditions and procedure for biovigilance and recall applicable to cells, tissues and organs and formats for notification of serious adverse events and serious adverse reactions" stipulates that a health care provider performing transplantation shall notify the handler who issued the cell, tissue or organ transplanted to the recipient immediately after the occurrence of a serious adverse reaction after transplantation (§ 1 (5)). Regulation No.83 of the Minister of Social Affairs of 19/12/08 "Rules for handling cells, tissues and organs" stipulates that a handler shall enter into written contracts with other handlers and the specialized medical care providers who will carry out transplantation and to whom cells, tissues and organs will be issued. The abovementioned contract shall set out the rights and obligations of the parties and the procedure for notification of serious adverse reactions and events (§ 21 (7)). (Estonia)
- TE should report SARE detected in its third party. (Finland)
- All the reports are also sent for information to the Agence de la Biomedecine. (France-Non ART)
- Responsible person (or designee) at TE submits reports. Other organizations (e.g. procurement organization or organization responsible for human application) should report SARs/SAEs that have occurred at their facility to the associated TE, who will report on to the IMB. A report submitted directly to the IMB from a procurement organization or organization responsible for human application will also be accepted. Reports submitted from other sources will be accepted e.g. Medical device section, other CAs etc. (Ireland)
- Third parties have to communicate SARE to the bank with which they have a contract. (Italy)
- In accordance with the above referred Order No V-401, the Reporting institution (e.g. Procurement Organisation) must report about SARE not only to National Transplant Bureau, but also to TE and to organization responsible for human application of T&C. (Lithuania)
- To centres where clinical application occurs. (Malta)
- All TE are requested to include in the contracts with third parties the SARE and haemovigilance. This aspect is inspected. (Portugal-Non ART)
- Third parties who could be involved must be informed. (Slovenia)

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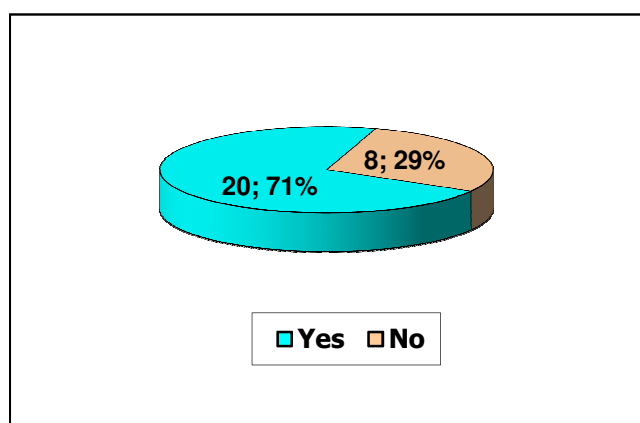
- All SARE must be reported to TRIP, who collects all reports for the annual report. (the Netherlands)
- Third parties are required to report to a licensed establishment who in turn report to the HTA. (The same applies to end users). (UK-Non ART)
- They would do so through the primary centre specified as part of their third part agreement. (UK-ART)

9. Has your system incorporated/adapted any of the EUSTITE V&S Tools? (N=28)





9.1. If yes: (N=28; multiple choice)

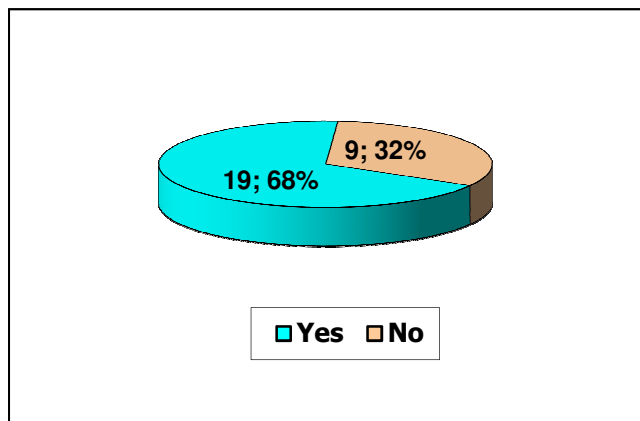
EUSTITE definitions:



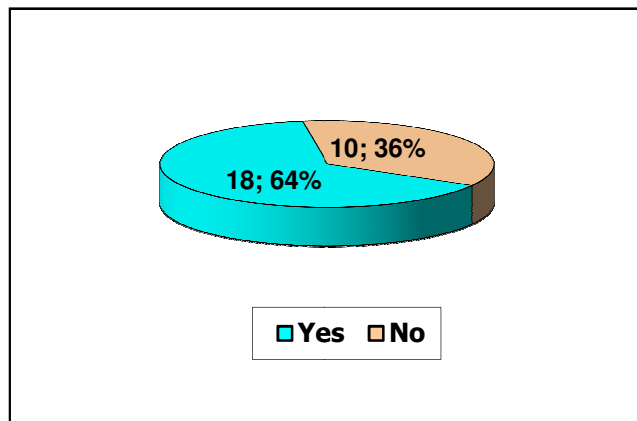
Systems that have incorporated EUSTITE definitions are: Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, Germany, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Poland, Portugal-Non ART, Slovenia, Spain, Sweden, the Netherlands and UK-Non ART.

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SAE reporting criteria:



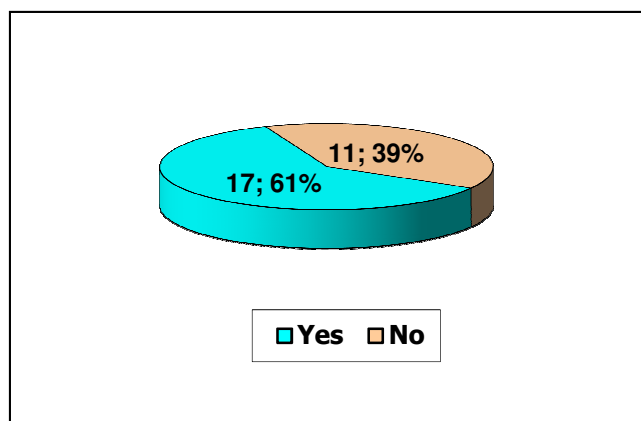
SAR severity scale:



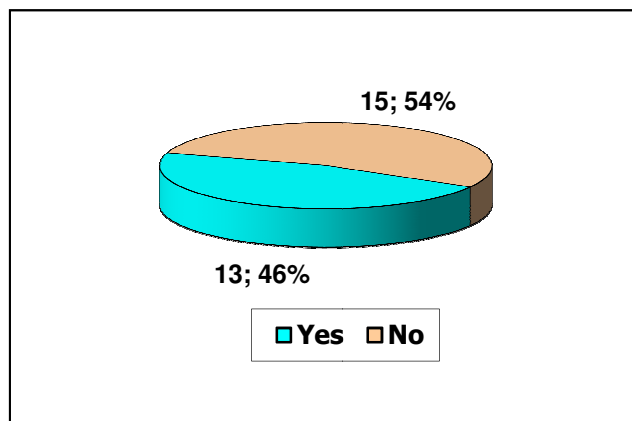
Systems that have incorporated the EUSTITE SAE reporting criteria are: Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Estonia, Finland, Germany, Ireland, Italy, Latvia, Malta, Poland, Portugal-Non ART, Slovenia, Spain, Sweden, the Netherlands and UK-Non ART.

Systems that have incorporated the EUSTITE SAR severity scale are: Bulgaria, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Ireland, Italy, Latvia, Malta, Poland, Portugal-Non ART, Slovenia, Sweden, the Netherlands and UK-Non ART.

SAR imputability scale:





SARE impact assessment tools:



Systems that have incorporated the EUSTITE SAR imputability scale are: Bulgaria, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Ireland, Italy, Latvia, Malta, Poland, Portugal-Non ART, Slovenia, the Netherlands and UK-Non ART.

Systems that have incorporated the EUSTITE impact assessment tool are: Cyprus, Czech Republic, Finland, France-Non ART, Germany, Ireland, Italy, Latvia, Malta, Poland, Portugal-Non ART, Slovenia and UK-Non ART.



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10. Does your CA report to other agencies? (Multiple choice)

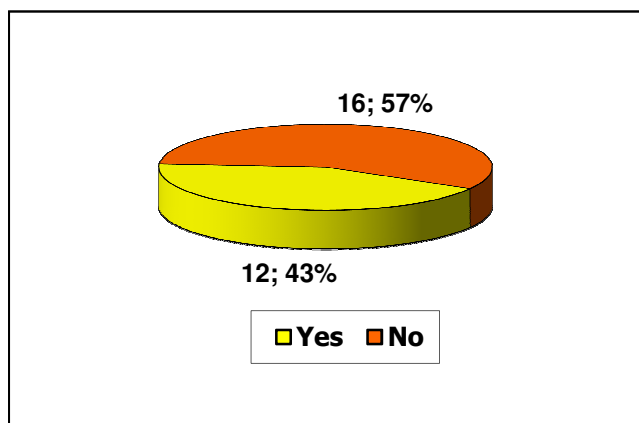
Apart from reporting to the European Commission as required in Directive 2006/86/EC, fourteen (61%) countries report to others. These countries are: Austria, Denmark, Finland, France, Germany, Hungary, Ireland, Lithuania, Luxembourg, Malta, Portugal, Romania, Slovenia and UK (N=25).

The agencies to which these countries report are:

- Government (Ministry for Health). (Austria)
- National Board of Health and the Ministry of Interior & Health. (Denmark)
- Depending on the case different agencies will be informed. (Finland)
- AFSSAPS, government, Public Health Agency. Individual ART vigilance event can be reported if needed, according to the typology and the seriousness of the event. (France-ART)
- Agence de la Biomedecine for each report and to other public health agencies monthly with the "coordination des vigilances" meetings. (France-Non ART)
- Federal Ministry of Health. (Germany)
- Liaise with other National Government/Public Health Agencies as required e.g. Department of Health and Children (DoHC), Health Service Executive (HSE), The Health Protection Surveillance Centre (HPSC), Ireland's, agency for the surveillance of communicable diseases. Patient Safety and Quality Assurance Agency, The Health Information and Quality Authority (HIQA). (Ireland)
- Ministry of Health. (Hungary)
- Health Care Ministry and the State Medical Audit Inspectorate. (Lithuania)
- Reports to WHO by providing data for the blood safety database and also provides a report to the International Haemovigilance Network. (Malta)
- We report to Ministry of Health and whenever an incident occurs CNPMA articulates with IGAS (General Inspectorate of Health-related Activities), since we do not have and inspectorate body. (Portugal-ART)
- Government, Public Health Agencies. (Portugal-Non ART)
- National Transplant Agency. (Romania)
- Public Health Agency, Ministry of Health. (Slovenia)
- Medicines and Healthcare Products Regulatory Authority (MHRA) on an informal basis. (UK-Non ART)
- Depending on the nature of the incident. They may report to the MHRA (pharmaceuticals) Patient Safety agency. (UK-ART)

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11. Do you collaborate with Scientific and Professional Societies, registries run by professionals or other non-governmental organizations for vigilance reporting, evaluation, investigation or outcome dissemination? (N=28)



Competent Authorities that collaborate with Scientific Societies are Belgium, Denmark, France, Germany, Italy, Latvia, Malta, Slovenia, Sweden, the Netherlands and UK-Non ART.

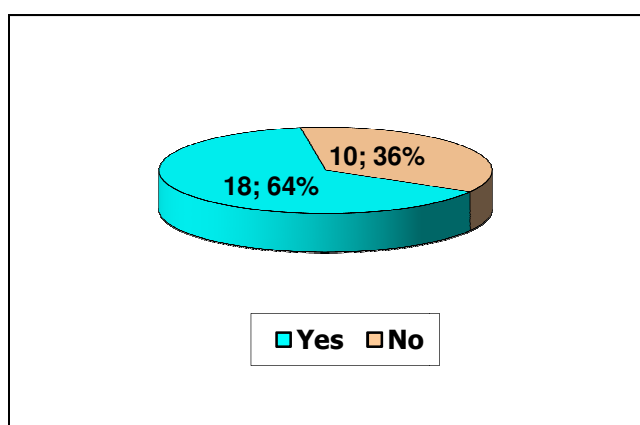
11.1 If yes, please describe the collaboration:

- Collaboration with Superior Health Council for advice. (Belgium)
- For example, the Dansk Fertility Society and the Danish Orthopedic Society are advised on their reporting obligations. (Denmark)
- Professional societies: CAGOF (National College of French Gynecologists and Obstetricians); Turner syndrome and pregnancy: clinical practice recommendation, GEDO (study group on oocyte donation), CECOS, etc.
http://www.agence-biomedecine.fr/uploads/document/RPC_Syndrome_de_Turner_et_grossesse_anglais.pdf
<http://www.agence-biomedecine.fr/uploads/document/DOC290710-29072010111318.pdf>
- Turner syndrome association (AGAT); Scientific congresses; Working groups. (France-ART)
- The national commission of biovigilance meets at least twice a year and it is composed of representatives from all healthcare professional groups (scientists, Professional Societies, representing patients' associations, registries run by professionals governmental organization for vigilance reporting). Many working groups with professional representatives. (France-Non ART)
- The Paul-Ehrlich-Institute has already participated in the EUSTITE pilot V&S and is collaborating partner of the SOHO V&S project. (Germany)
- The Italian Bone Marrow Donor Registry receives the notifications of SARE and communicates them to the Competent Authorities (CNT/CNS) and to the World Marrow Donors Association (WMDA). (Italy)
- Lectures. (Latvia)
- As above: Reports to WHO by providing data for the blood safety database and also provides a report to the International Haemovigilance Network. (Malta)
- Expert meeting to clarify difficult medical cases and prepare strategy for further work. (Slovenia)
- We exchange information and collected data at meetings and seminars. (Sweden)

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- HTA has contacts that are relevant with a number of professional organizations, but contacts are currently on an informal and 'as required' basis. Organizations include the Health Protection Agency, the Ocular Tissue Advisory Group and the UK's largest public tissue bank, NHSBT. HTA is also represented on the several advisory boards of National Health Service committees related to vigilance and surveillance and donor selection for blood tissue and organ donors. These are called SaBTO and JPAC. (UK-Non ART)


12. Do you disseminate learning points arising from your vigilance system to the professional field or more widely? (N=28)



Responders that answered that they disseminate learning points are: Belgium, Czech Republic, Finland, France, Germany, Ireland, Italy, Latvia, Lithuania, Malta, Portugal-Non ART, Slovenia, Spain, Sweden, the Netherlands and UK.

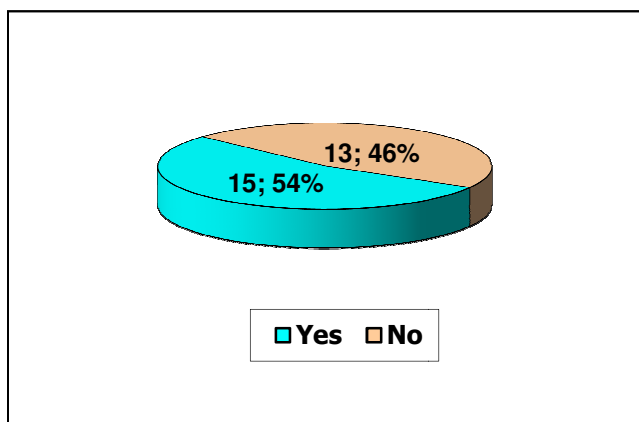
12.1. If yes, please describe how this is done:

- Recommendations made in the annual report. (Belgium)
- An important view to maintain the legislation requirements if provided as a part of each inspection. (Czech Republic)
- It is possible to present consolidated report and discuss about these cases with TEs and other authorities during congresses or other common events (without center identification). (Finland)
- *Regionally with ARS (regional health agencies) *meetings with local ART vigilance correspondents (CLAs) *Information spread via the CA's website, e-mail, information letter and public annual report *newsletter. (France-ART)
- Through: -meeting with the professionals in the field; -Afssaps website; -congress and meetings; -newsletters for vigilance. (France-Non ART)
- Presentations at national and international meetings. (Germany)
- In a consolidated report without center identification provided to the responsible person in each Tissue Establishment. (Ireland)
- Through periodical communication, it is used also for revision of the protocols (for HPC). Through courses, reports to the Regional CAs, during inspections (for tissues). (Italy)
- Training courses. (Latvia)
- We try involving TEs, POs and Transplant Centers into EUSTITE V&S Pilot project, encouraging them to use the EUSTITE tools to report about SARE. (Lithuania)

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- In the case of haemovigilance, a full detailed report is compiled with an analysis of the most common and serious adverse reactions and events and near misses and with recommendations for preventive and corrective actions. (Malta)
- Dissemination of information concerning the vigilance, 2 workshops were organized (2009 and 2010). (Portugal-Non ART)
- Until now we did not organize special training for our inspectors. We intend to provide special trainings in this field through EU projects. (Romania)
- This September it will be organized 1st national meeting of all responsible persons in preparation of TEs with CAs in Slovenia. (Slovenia)
- Dissemination of Annual Report of National Biovigilance System. (Spain)
- See Q 11.1 and with individual tissue establishments we discuss and follow up the reported SAR's during inspection at the site. (Sweden)
- There is an online reporting system in place with a link-possibility to CA or TE's. (the Netherlands)
- The HTA publishes an annual report for establishments licensed under the EUTCD, which includes findings from inspections, licensing and also a summary of the submitted annual SAEs and SARs. (UK-Non ART)
- As alerts. (UK-ART)

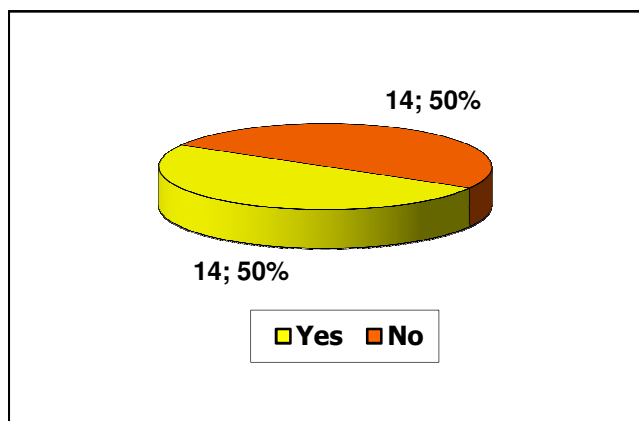
13. Do you publish the results of your vigilance system? (N=28)





Over of 50% publish the results of their vigilance programmes. These are: Belgium, Bulgaria, Finland, France, Germany, Ireland, Latvia, Malta, Portugal-Non ART, Spain, Sweden, the Netherlands and UK.

13.1. If yes: (N=28; Multiple choice)

Published Report without centre identification:



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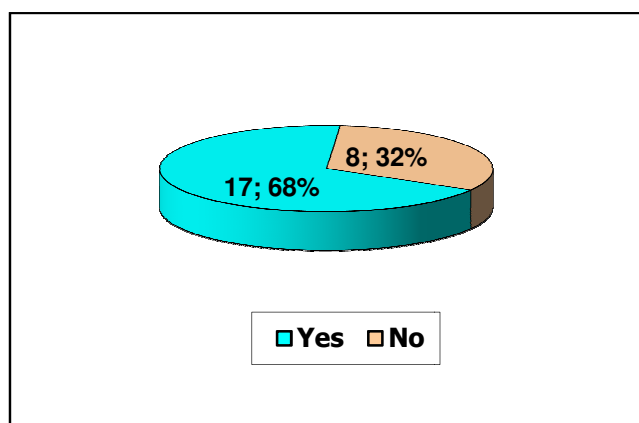
Countries that answered “yes” are Belgium, Finland, France, Germany, Ireland, Latvia, Malta, Portugal-Non ART, Spain, Sweden, the Netherlands and UK.

No country answered that they publish the results of the **system as individual reports with centre identification** but **three responders** answered that they publish the result ‘**in other ways**’: Bulgaria, France-Non ART and UK-ART.

The ‘other ways’ were described as follows:

- In a consolidated report on CA web site. (Bulgaria)
- Healthcare professionals recommendations. (France-Non ART)
- The minutes relating to Serious (grade A) incidents that are considered by the License Committee are published on our website (anonymously). (UK-ART)



14. Do you have a formal system for alerting professionals regarding new risks (e.g. emerging diseases or particularly serious incidents)? (N=25)



The responders that answered “yes” are: Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, France, Germany, Ireland, Latvia, Lithuania, Malta, Portugal, Romania, Slovenia, Sweden and UK.

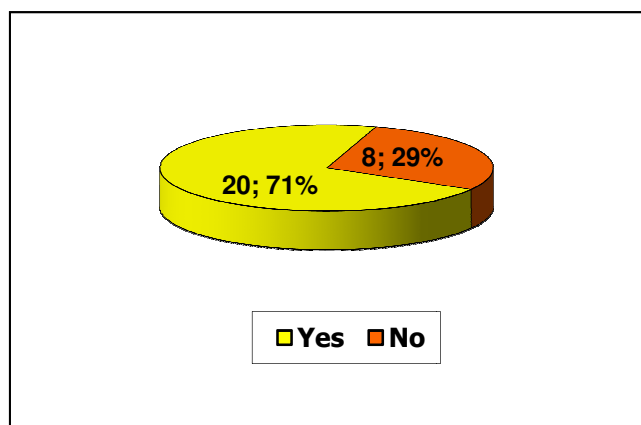
14.1. If yes, please describe briefly:

- The Austrian Federal Office for Safety in Health Care alerts by mail to the tissue establishments. (Austria)
- Circulars and information notes send to the responsible persons of the tissue and cells establishments. (Belgium)
- All RPs are notified by official letter. (Cyprus)
- Same as for pharmaceuticals. (Czech Republic)
- Targeted communications might be sent to all or selected tissue establishments, to selected national professional societies or the information may be publicly announced at the Agency website. (Denmark)
- Estonian Health Board provides this service. (Estonia)
- Emails, network of local ART vigilance correspondents (CLAs), website, mail. (France-ART)
- Through specific Afssaps's departments (depending on the nature of the risk) i.e. emerging agents, viral safety; -through biovigilance mailing lists if needed, in link with the Agence de la Biomédecine if necessary. (France-Non ART)

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- All professionals who require an authorization and the Länder authorities will be alerted by the Paul-Ehrlich-Institute. All professionals who do not require this authorization will be then notified by the Länder Authorities. (Germany)
- Alerts can be issued on the IMB website and/or disseminated via email to the responsible persons in tissue establishment, either as a rapid alert or information sharing communication. (Ireland)
- E-mail. (Latvia)
- The Order of the Minister of Health No V-657 dated 23 July 2010 for the exchange of information about extreme situations, extreme events and other events causing risks to the health or life of population. Here we have described institutions, responsible persons, their duties and ways how to alert and manage serious incidents. (Lithuania)
- Malta has a formal alerting system whereby all stakeholders are alerted. This includes dissemination of alerts received through RATC and CIRCA. (Malta)
- By now, mailing list. We are working on an intranet platform that enables rapid and efficient communication between CA and ART centers. (Portugal-ART)
- By e-mail and regular mail to all TE, as well as to the retrieval and transplantation units, when applicable; Information is also available at the CA website. (Portugal-Non ART)
- E-mail list of Te´s responsible persons whom alertly information are delivered. (Slovenia)
- An updated mailing list (e-mail) and through our website. (Sweden)
- The HTA may issue regular alerts in respect of risk identified via submitted events and reactions. We can also issue general communications to the sector. (UK-Non ART)
- Alerts. (UK-ART)



15. Do you have a formal system for alerting professionals regarding RATC alerts from the European Commission? (N=28)





Responders that answered yes are Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, France, Germany, Ireland, Latvia, Lithuania, Malta, Portugal, Romania, Slovenia, Sweden, the Netherlands and UK-Non ART.

If yes, please describe briefly:

- The Austrian Federal Office for Safety in Health Care alerts by mail to the tissue establishments. (Austria)

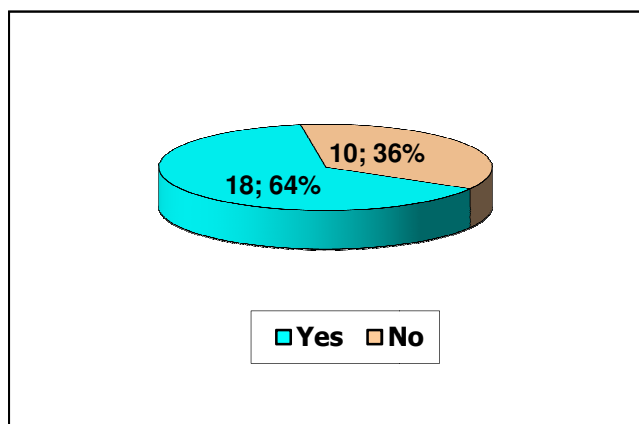
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- Circulars and information notes sent to the responsible persons of the tissue and cells establishments. (Belgium)
- We have a contact person for CIRCA. (Bulgaria)
- RPs in TEs likely to be affected are notified of the risks and are required to take measures. (Cyprus)
- RA system same as for pharmaceuticals. (Czech Republic)
- Targeted communications (only summaries of RATC's) may be sent to all or selected tissue establishments, or to selected national professional societies. (Denmark)
- *Urgent system department in the ministry of health (emails) *Network of local ART vigilance correspondents (CLAs). (France-ART)
- The RATC alerts from EC arrived in a specific mail box raised every day and the alert is transmitted to recipient by mail or mailing list and/or by a specific subscription to the Afssaps's alerts. (France-Non ART)
- The Section Pharmacovigilance II of the Paul-Ehrlich-Institute has access to the CIRCA platform. (Germany)
- Alerts can be issued on the IMB website and/or disseminated via email to the responsible persons in tissue establishment, either as a rapid alert or information sharing communication. (Ireland)
- Collaboration with European Commission. (Latvia)
- According the above referred Order No V-657, Health Emergency Situations Centre of the Ministry of Health ensures receipt of the information from RATC system about SARE outside business hours and on holidays. National Transplant Bureau is responsible for this matter during business hours. "Further processing of alerts is carried out as described in answer to Question 14.1 above." (Lithuania)
- Malta has a formal alerting system whereby all stakeholders are alerted. This includes dissemination of alerts received through RATC and CIRCA. (Malta)
- By now, mailing list. We are working on an intranet platform that enables rapid and efficient communication between CA and ART centers. (Portugal-ART)
- By e-mail and regular mail to all TE, as well as to the retrieval and transplantation units, when applicable; Information is also available at the CA website. (Portugal-Non ART)
- We put all relevant e-mails and addresses of TE's responsible persons in RATC list for quick rapid alert. (Slovenia)
- Someone is always on call for the mailbox "RATC". (Sweden)
- Described in a procedure in the Quality Systems manual of the Health Care Inspectorate. (the Netherlands)
- The HTA may issue regular alerts in respect of risk identified via submitted events and reactions. We can also issue general communications to the sector. (UK-Non ART)

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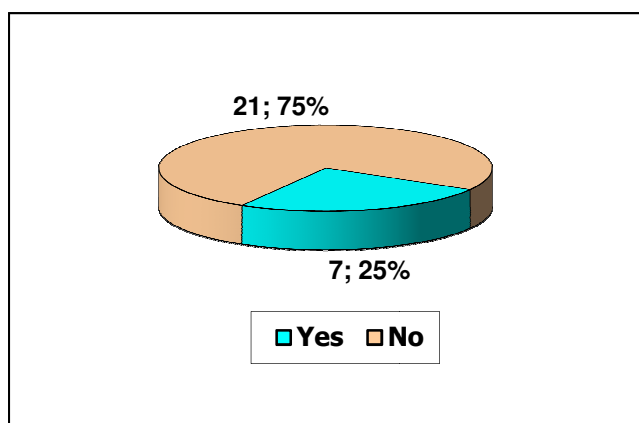
16. When new disease transmission risks are identified (e.g. Q-fever, West Nile Virus) how are donor selection criteria modified to reduce risk? (N=28; Multiple choice)

a. New exclusion/testing criteria set nationally by the CA?




The responders that answered “yes” are: Austria, Belgium, Cyprus, Czech Republic, Finland, France, Germany, Italy, Lithuania, Malta, Poland, Portugal, Romania, Spain, Sweden and UK-Non ART.

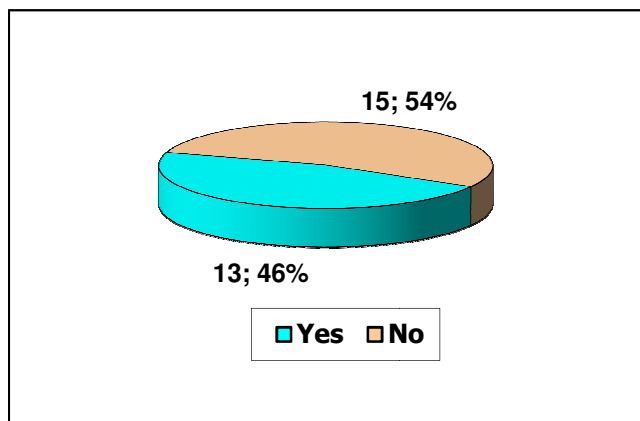
b. New exclusion/testing criteria set by other national organization?



Responders that answered “yes” are: Czech Republic, Denmark, Estonia, France-Non ART, Latvia, Slovenia and UK-Non ART.

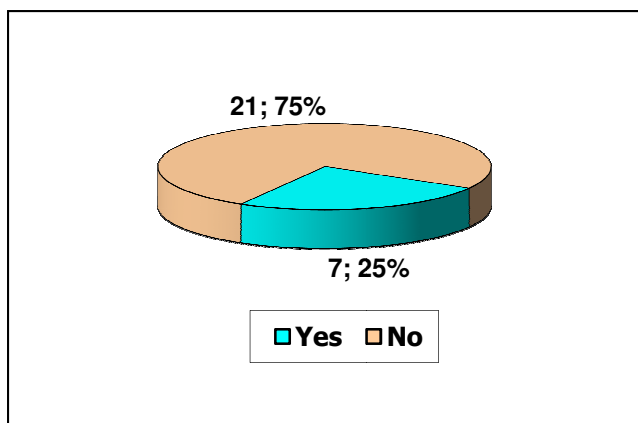
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c. New exclusion/testing criteria set at Tissue Establishment level?



Responders that answered “yes” are: Bulgaria, Czech Republic, Denmark, Finland, Hungary, Ireland, Luxembourg, Malta, Poland, Portugal-Non ART, Slovenia, the Netherlands and UK-Non ART.



d. Other:



Responders that answered “yes” are: Denmark, Finland, France-Non ART, Malta, Portugal-Non ART, Slovenia and UK-ART.

Other (describe):

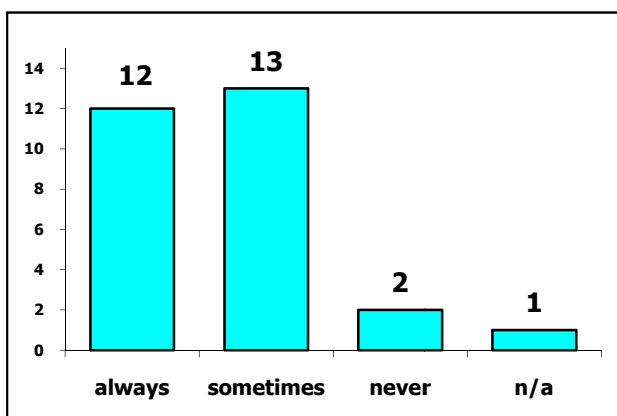
- Selection criteria are defined and maintained by our sister Agency, the National Board of Health, which is also a designated Competent Authority for Tissues & Cells. (Denmark)
- When needed we co-operate with Public Health Agencies as well as TEs. (Finland)
- Criteria as established and recommended by expert institutions such as ECDC. (Malta)
- CA prepares recommendations for TEs. (Slovenia)

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- Our legislation requires that center's adapt their screening when new risks emerge; we would expect this to happen without our intervention but may issue an alert to notify them of the new risk. (UK-ART)

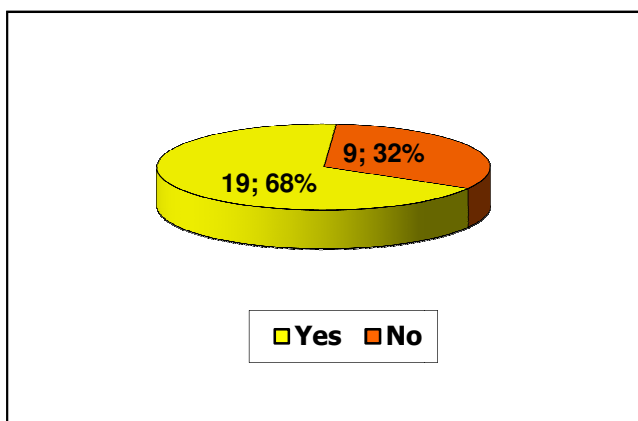
Section 2: Investigation

17. Does your CA participate actively in SARE investigations (site visits, participation in analysis of the cause, interviewing of those involved, review of TE findings, etc.)? (N=28)




Only two CAs report that they do not participate in investigations.

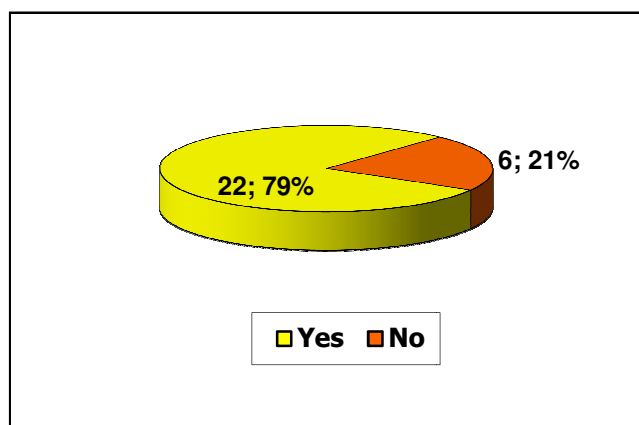
18. Do you use experts in the field to assist in investigation and evaluation of SARE? (N=28)



Responders that answered "yes" are Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Ireland, Italy, Latvia, Poland, Portugal-Non ART, Slovenia, Spain and Sweden.

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19. Would your CA be interested in participating in an international team/pool of investigators which would be available to EU MS? (N=28)



Responders that answered “no” are Belgium, Denmark, Finland, France-Non ART, Hungary and Luxembourg.

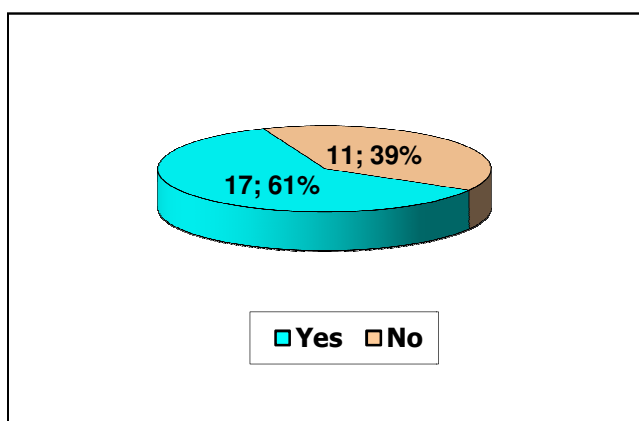
Austria, Bulgaria, Cyprus, Czech Republic, Estonia, France-ART, Germany, Ireland, Italy, Latvia, Lithuania, Malta, Poland, Portugal, Romania, Slovenia, Spain, Sweden, the Netherlands and UK answered “yes”.



Additional comments:

- At the moment we have limited resources. (Finland)
- Subject to establishment of the arrangements for such work and depending on the availability of resources. (Ireland)
- Good idea but lack of personnel. (Italy)
- Yes, the Maltese CA would be interested in participating in an international team/pool of investigators which would be available to EU MS. (Malta)
- We are interested in collaboration in the international expert group / EU MS. (Slovenia)

Section 3: Responsible individuals

20. Do you have dedicated vigilance officer(s) in the CA? (N=28)





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The responders that answered “yes” are: Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Ireland, Latvia, Lithuania, Malta, Portugal-Non ART, Slovenia, Sweden, the Netherlands and UK-Non ART.

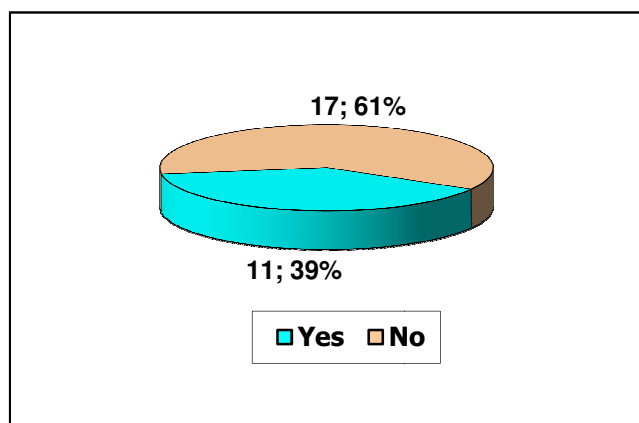
20.1. The number of vigilance officers is 1 (median) with a range of 1-3.

20.2. The qualification and training of these vigilance officers were described as follows:

- Participation at EUSTITE training courses and TPM online tissue banking course provided by the University of Barcelona. (Austria)
- MD, PhD, clinical pathology, training in blood banking and transfusion and tissue and cell banking. (Belgium)
- Senior Pharmacovigilance assessor in the field of human pharmaceuticals, medical doctor. (Czech Republic)
- Scientifically qualified and with experience/knowledge of the technical regulatory aspects of the tissues & cells sector. (Denmark)
- Qualified inspector (TEs), Microbiologist, PhD. Regular training. (Finland)
- Medical, inspection, scientific, regulatory background. (France-ART)
- Medical biologist doctor specialist in microbiology and hygiene (full time), Pharmacist specialist in tissue and cells (half time). (France-Non ART)
- 8 vigilance officers are medical doctors, 1 officer holds a PhD in biology. (Germany)
- Nursing Qualifications (General / Midwifery / Intensive Care). Haemovigilance training and experience. Over four years working in the National Haemovigilance Office and in the area of transfusion medicine. Completed 2 haemovigilance stand alone modules for professional development. Understanding and management of blood transfusion practice in a haemovigilance context and blood transfusion practice. CAPA training course completed. (Ireland)
- Trained as inspectors. (Italy)
- Doctor, senior expert. EUSTITE, Residential course, Wien, Austria, 2008. (Latvia)
- MD graduate, having completed international Tissue banking course; Training course for Tissue and Cell Inspectors" (EUSTITE project); participating in V&S Pilot Project. (Lithuania)
- Specialized in Public Health, further training though EUSTITE and other sources e.g. International Haemovigilance Network. (Malta)
- MD and biologist. (Portugal-Non ART)
- Medical clinicians, other biomedical staff, TPM and other. (Slovenia)
- Their qualifications are medical training as background and thereafter internal and external training in the special issues regarding Quality and Safety in donation, processing and use of Blood, Tissues and Cells. (Sweden)
- Inspectors, additional training. (the Netherlands)
- All have medical or science qualifications, some with a specific background in microbiology. All have experience in quality management. It is a multidisciplinary team, where input of staff with relevant qualifications (also from outside the team) is sought where necessary. (UK-Non ART)
- Registered nurse. Diploma in Risk Management. (UK-ART)

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20.3. If yes, do they also inspect TEs? (N=28)





The responders that answered “yes” are: Finland, France-Non ART, Germany, Italy, Latvia, Malta, Portugal-Non ART, Sweden, the Netherlands and UK.

20.3.1. Twelve of the 17 (71%) that answered “no” have some interaction with the inspectors.

20.4. All responders except France-Non ART, Hungary, Luxembourg (the latter two did not reply) are interested in **sending** their Vigilance Officers to an **EU Training Course**.

20.4.1. The topics that should be covered in the training course were identified as follows:

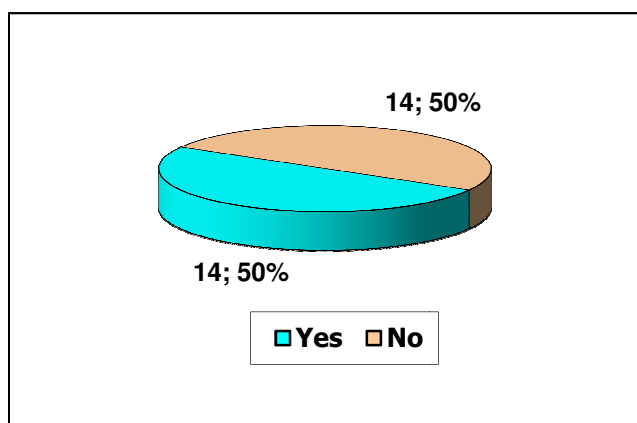
- Definitions: when reactions or events need to be reported, discussion about reports on SARE from other countries, showing examples of reported SARE. (Austria)
- Detailed training for SAR Severity Scale. (Bulgaria)
- E.g. assessment of SARE in HTC. (Czech Republic)
- Develop & evaluate standardized report formats for epidemiological matters. (Denmark)
- V&S in special cases like ATMP, hospital exemption. Utilizing classification system for SAE and SAR. How to provide vigilance training to cells and tissues handlers. (Estonia)
- Reporting systems. Examples of SAE/Rs. Evaluation of SAE/Rs (severity and impact assessments). Responses to SAE/Rs reports. (Finland)
- Should cover the whole system including the software, and sharing of experience. (France-ART)
- Regulatory framework, tissue-specific aspects. (Germany)
- Investigation and evaluation of SARs/SAEs to include root cause analysis & CAPA training. Guidance and training for applying grading tools to prevent a variation in scoring (provision of worked examples for reference material). Reporting requirements, what is reportable? ART SAR/E reporting requirements. Non-mandatory reporting / donor reactions. Information flow and interaction with other sectors, internal and external, i.e. pharmacovigilance, medical device, ATMP, other CAs, Commission. Rapid alert reporting responsibilities. Fraudulent activity. Communication /

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Listening skills. Train the trainers i.e. preparation for disseminating this information to others. (Ireland)


- How to conduct investigations involving multiple countries. How to investigate illegal activity. How to prove imputability. (Italy)
- Management of Serious Adverse Events and reactions. Communication with clinical users, other vigilance systems, testing laboratories. Categories of Events and reactions to Notify. (Latvia)
- In principle, the essentials had been covered by previous courses/projects mentioned in 20.2, but refreshment course could be helpful that could focus on newest developments and, in particular, involving practical case studies. (Lithuania)
- All areas of vigilance including the definition of SAREs, the detection of SAREs, SARE electronic reporting systems and national databases, investigation of SAREs. (Malta)
- We are going to appoint VO. (Poland)
- V&S systems and procedure; Accreditation, designation, authorization or licensing systems in the MS; Inspection techniques and procedures, including practical exercises; Identification of, and subsequent actions pertaining to, illegal or fraudulent activity. (Romania)
- Clinical perspective of vigilance; guides to increase safety and quality procedures. (Slovenia)
- Definitions of SAR and SAE ; SAR and SAE criteria; Management of SAR and SAE. (Spain)
- Identifying Events and reactions that require on-site investigation. Conducting an on-site SARE investigation. Long term follow-up. (UK-Non ART)
- Severity grading, information analysis, root cause analysis, collecting evidence/information, making recommendations, using experts... (UK-ART)

21. Do you provide specific vigilance training to individuals in the field (hospital staff, TE staff, Quality Managers, etc.)? (N=28)

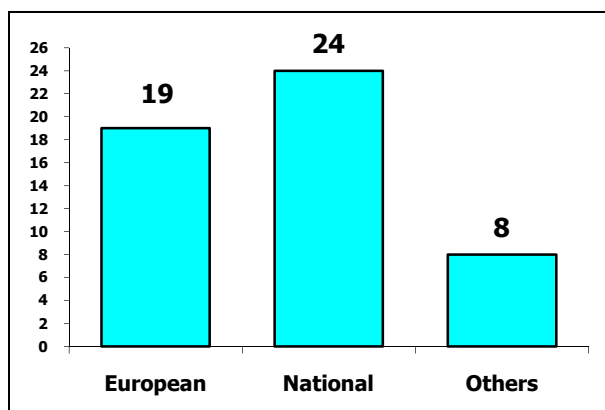


The countries that answered "yes" are: Austria, Bulgaria, France, Ireland, Italy, Latvia, Malta, Poland, Portugal-Non ART, Romania, Slovenia and UK.

21.1. Only two countries (Belgium, Hungary) answered that they **don't consider it necessary to provide specific training.**

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21.2. If yes, how should this be delivered? (N=28; multiple choice)

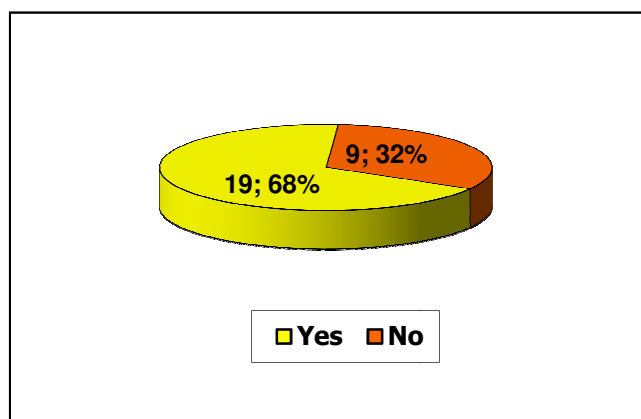




The 'others' were described as:

- Common approach to vigilance is important within the EU so as to ensure that alerts are handled in the same manner by everybody. (Cyprus)
- Scientific consultations. (Czech Republic)
- Both above mentioned would come useful. (Estonia)
- E-learning regionally (ARS + professionals). (France-ART)
- In link with regional safety agencies. At that time, the training is focused on the field of biovigilance with a lot of examples. (France-Non ART)
- Consideration should be given to developing an online training course. (Ireland)
- Through regular seminars organized by the biovigilance section. (Malta)
- CA should participate in National courses, to help the establishments to interpret the national directives. (Sweden)
- In national course delivered by our Vigilance team. (UK-Non ART)

Section 4: Vigilance (Safety) of the Living Donor

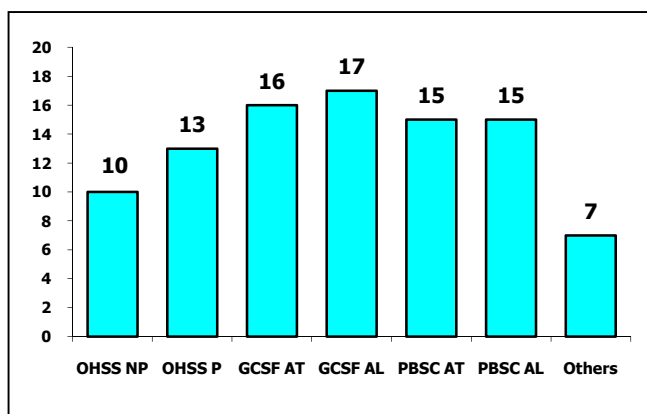
22. Does your CA require reporting of SAR in donors even if the quality and safety of the donated tissues or cells has not been affected? (N=28)



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The countries that answered “yes” are: Belgium, Bulgaria, Cyprus, Czech Republic, France, Germany, Italy, Latvia, Lithuania, Luxembourg, Poland, Portugal-Non ART, Slovenia, Spain, Sweden, the Netherlands and UK.

22.1. If yes, does this include? (N=28; multiple choice)



OHSS NP: Ovarian Hyperstimulation Syndrome in non-partner oocyte donors

OHSS P: Ovarian Hyperstimulation Syndrome in partner oocyte donors

GCSF AT: Reactions to GCSF in autologous patients



GCSF AL: Reactions to GCSF in allogeneic donors

PBSC AT: Toxicity during PBSC collection in autologous donors

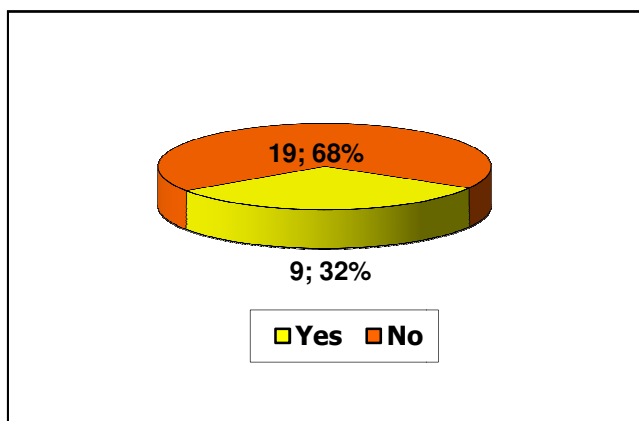
PBSC AL: Toxicity during of PBSC collection in allogeneic donors

The description of “others” is:

- Only in case of suspicious unexpected SAR. (Czech Republic)
- All the clinical complications due to ovarian stimulation and oocyte procurement for oocyte donation even without impact on the quality of gametes (example: hemoperitoneum, ovarian abscess...) (France-ART)
- All adverse reactions related or potentially related to the donation occurring in a living donor. (France-Non ART)
- Reactions resulting in harm to the donor e.g. cardiac or neurological episode. The IMB will collate all donor reactions as per recommendations in the Common approach Document (2.5.2). (Ireland)
- All serious adverse reactions. (Luxembourg)
- Any other SAR in donors. (the Netherlands)
- Any reaction in the donor which causes additional medical intervention or hospitalization, and which may be related to the donation. (UK-Non ART)

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23. Do you maintain a registry of living donors to follow their health in the long term? (N=28)



The countries which maintain a registry are: Cyprus, France-Non ART, Italy, Malta, Portugal, Romania, the Netherlands and UK-ART.



23.1 If Yes, please describe:

- It is the TE's responsibility. (Cyprus)
- The registry is maintained by the Agence de la Biomedicine. (France-Non ART)
- In compliance with Italian Bone Marrow Donor Registry (IBDMR) standards, we require 10 years of follow up for volunteer peripheral blood stem cell donors and 1 year for volunteer bone marrow donors even in the absence of any particular clinical symptom or problem. (Italy)
- Though a National Transplant Register. (Malta)
- Registries are decentralized and kept in centres. We are now working on a national registry for reproductive cells' donors. (Portugal-ART)
- The registry exists up to now at hospital/TE. A national registry is now under development. (Portugal-Non ART)
- We have a national registry of living donors of hematopoietic stem cells, covered by the Government Decision no. 760/2009, published in the Official Journal no. 555 from 10 august 2009. (Romania)
- Registration by donation centres. (the Netherlands)
- It is not to monitor their health but to monitor the 10 family limit, potential risks to off spring (e.g.: if chromosomal abnormalities arise) and to provide donor details to offspring. (UK-ART)



Section 5: Good Practice Recommendations

24. From your experience, do you have any recommendations of good practice principles that should be incorporated in the SOHO V&S guidance on vigilance and surveillance investigation for tissues and cells?

- Common definitions - what needs to be reported. Communication of key messages and recommendations from the European Commission based on the submitted SARE reports of the European countries. (Austria)
- Unfortunately, our experience is too short in investigating (SARE). (Bulgaria)



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- E.G. summary of examples, more detailed classification of SARs (possible risks, assessment of risks for every type of HTC) etc. (Czech Republic)
- As a principle it is beneficial to establish and maintain professional links with national colleagues of the other healthcare sectors (i.e. Medical devices, blood products and medicinal products) to keep up to date with areas of common interest and interface matters. e.g. *corrective actions in the marketplace related to testing kits for infectious markers. *the management and potential implications of recalls related to CE marked culture media used in the ART sector. (Denmark)
- *Guidance for filling out the forms. * Guideline on the implementation of the ART vigilance system. Comment: recommendations should include ART specific recommendations and procurement complications (oocyte donors). (France-ART)
- The inspector(s) should prepare an agenda of the planned inspection and deliver it to the tissue establishment in advance. The inspector(s) should be polite and should try to create a friendly atmosphere. The inspector(s) should be dressed appropriately and behave professionally. (Germany)
- Requirement for a harmonized approach. Establishing national and international communication links. (Ireland)
- Need for good collaboration with professionals in the field, particularly for the investigation of cause. Need for training in "Root Cause Analysis" for professionals and regulators. *Systems should be non-punitive to encourage reporting until there is clear evidence of illegal activity - at this point it should be clear to the practitioner that the investigation is moving from "vigilance" to "enforcement" and appropriate powers should be in place. Results of vigilance should be widely shared in an anonymous way to improve learning and safety for patients. Global vigilance networks should be established to increase communication and learning. Clinicians should be encouraged to suspect that reactions might be caused by the tissues or cells applied and should be encouraged to report. (Italy)
- No, I have little practical experience. (Latvia)
- Co-operation at EU level is highly recommended - this includes initiatives such as EUSTITE. (Malta)
- Our experience in this field is very poor. (Romania)
- Discussion on difficult cases with different points of view (also different experts). (Slovenia)
- For different types of tissues and cells should be individual guidelines for reporting SARE, partly formulated by the professionals who handle and use these types of T&C. (the Netherlands)
- Training of all SARE officers in the use of EUSTITE Tools and the evaluation of initial notifications and follow-up. Training of officers in working together with establishments during their investigation and providing advice and guidance where required. Officers should also be trained to identify cases where more significant regulatory action is required and where there is a wider risk which needs to be communicated to other establishments. Regular meetings of the SARE team to ensure consistent evaluation and follow-up. Minutes are shared with the whole inspectorate for awareness. The inspectorate as a whole should receive some SARE training to ensure they can identify SAREs during inspections and when information is received through other channels. They need to be able to give appropriate advice and guidance to establishments during inspections. (UK-Non ART)



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COMPARISON BETWEEN RESPONSES OF CAs WITH SPECIALIST OR GENERAL COMPETENCIES

QUESTION	ART SPECIALIST (N=4)	ALL TISSUES AND CELLS EXCEPT ART (N=6)	ALL TISSUES AND CELLS INCLUDING ART (N=18)
1. Age of V&S system	49.25 (SD 53) months	41.67 (SD 21) months	31.24 (SD 15) months
2. Type of system	100% National	83% National 17% National/Regional	89% National 11% National/Regional
3. Based on the EU Directives?	100% Yes	83% Yes 17% No (France)	100% Yes
3.1. Based in additional legislation?	50%	17% (France)	39%
5.a. Overlap with haemovigilance?	50%	67%	78%
5.b. Overlap with pharmacovigilance?	50%	67%	50%
5.c. Overlap with other vigilance?	75%	50%	33%
6.a. Reports sent/received by paper	50%	83%	94%
6.b. Reports sent/received by software	25%	50%	44%
6.c. Reports sent/received by email/fax	75%	50%	89%
6.d. Reports sent/received by telephone	None	33%	50%
7. Mandatory Reporting times defined	100%	83%	44%
8. Reporting requirements extended to third parties	50%	50%	56%
9. Integration of any EUSTITE tools?	50%	100%	89%
9.1.a. Definitions	25%	67%	83%
9.1.b. SAE Reporting Criteria	25%	67%	78%
9.1.c. Severity scale	50%	50%	72%
9.1.d. Imputability scale	50%	50%	67%
9.1.e. Impact Assessment Tool	None	50%	56%
10.a. Report to EC	75%	100%	94%
10.b. Report to others	75%	83%	50%
11. Collaboration with Scientific societies	25%	33%	50%
12. Dissemination of learning points	50%	67%	67%
13. Publication of results	75%	67%	44%
13.1.a. Without centre id	50%	67%	44%
13.1.b. With centre id	None	None	None
13.1.c. In other ways	50%	17%	None
14. System for alerting new risks	75%	67%	72%
15. System for alerting RATC	75%	67%	72%
16.a. New Donor Selection set Criteria by CA	50%	83%	61%
16.b. New Donor Selection Criteria set by other national organization	None	33%	28%



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16.c. New Donor Selection Criteria set by TEs	25%	50%	50%
16.d. New Donor Selection Criteria set by 'other means'	25%	33%	22%
17.Participation of CA in SARE investigation	Always: 2 Sometimes: 1 Never: 1	Always: 3 Sometimes: 3	Always: 7 Sometimes: 9 Never: 1
18. Use of experts for SARE investigation	50%	33%	72%
19.Interested in an international SARE investigator team?	100%	67%	78%
20.Dedicated vigilance officers?	25%	67%	67%
20.1.Number?	1.5 (1-3)	1.7 (1-3)	1 (3-6)
20.2. Qualification?	-	-	-
20.3.Do they also inspect TEs?	25%	50%	39%
20.3.1.No interaction with inspectors	50%	50%	39%
20.4.Intested in training course?	100%	67%	94%
21.Does CA provide specific training to vigilance officers?	75%	67%	39%
21.1. Is specific training necessary?	100%	88%	89%
21.2 This training should be delivered at level:	European: 2 National: 4 Others: 1	European: 1 National: 4 Others: 2	European: 16 National: 16 Others: 5
22. Report requirements for SAR in living donors	75%	67%	67%
22.1 Living donor reporting requirements by type:	OHSS NP: 3 OHSS P: 3 GCSF AT: 0 GCSF AL: 0 PBSC AT: 0 PBSC AL: 0 Others: 1	OHSS NP: 0 OHSS P: 1 GCSF AT: 4 GCSF AL: 4 PBSC AT: 4 PBSC AL: 3 Others: 2	OHSS NP: 9 OHSS P: 10 GCSF AT: 12 GCSF AL: 13 PBSC AT: 11 PBSC AL:12 Others: 5
23.Registry of living donors?	50%	33%	28%

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CONCLUSIONS



1. The response rate was good (93%).
2. The number and percentage of EU countries with a V&S system in place has increased from 15 (56%) in 2009 to at least 25 (93%) in 2010.
3. Eighteen (64%) of the responders are CAs that regulate both ART and non-ART tissues and cells, 6 are ART specialist CAs and 4 regulate tissues and cells other than gametes and embryos.
4. The vigilance systems have been in place for an average of three years.
5. In the majority of MS the system is exclusively national. Only three countries have a national and regional system.
6. All MS except one have based their system on the 2004 and 2006 European Directives.
7. Around 61% of EU countries reported SARE in a common way for all types of tissues and cells. Eleven responders have different system for tissues and ART.
8. There is overlap with other reporting systems, from 52% with pharmacovigilance to 72% with haemovigilance.
9. Only four countries have a single method for sending/receiving SARE reports. Paper and email/fax are the most common ways to send/receive these reports.
10. More than half of MS have mandatory reporting times, and also have requirements for reporting SARE extended to third parties.
11. Twenty-four (86%) of the countries that answered have incorporated some or all of the EUSTITE tools in their systems.
12. More than half (54%) of EU countries publish the results of their V&S system.
13. Around 70% of the MS have a system for alerting professionals regarding new risks and for communicating Rapid Alerts received from the Commission's RATC system.
14. In 12 cases (43%) the Competent Authority always participates in SARE investigations, 13 (46%) sometimes do and 2 never do..
15. Twenty-two (79%) of the responders are interested in participating in an international team of investigators which could be made available for EU countries.
16. 61% of the MS have dedicated vigilance officers.
17. All EU countries except three are interested in an EU training course on SARE investigation and reporting.
18. Nineteen (68%) of MS have the requirement to report SAR in donors even if the quality and safety of the tissues or cells procured has not been affected.
19. Nine countries have a registry of living donors.
20. There were differences between ART and non-ART responses only in the following points:
 - a. ART-specialist vigilance is more frequently based on additional legislation than non-ART.
 - b. Non-ART programmes overlap more frequently with other vigilance reporting systems than ART-specialist programmes.
 - c. Non-ART programmes have incorporated EUSTITE tools more frequently than ART-specialist programmes.
 - d. Non-ART programmes disseminate learning points more frequently than ART-specialist programmes.

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ANNEX I

Blank Questionnaire

Responsible Partner Organization	Organización Nacional de Trasplantes (ONT)
Address	C/ Sinesio Delgado 6-8 P. III. 28029 Madrid (España)
Contact Person	Gregorio Garrido & Marina Alvarez
Telephone / Fax Number	+34 91 822 49 13/ +34 902 300 226
E-mail	ggarrido@msps.es & malvarez@msps.es

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<p align="center"> Survey of European Vigilance & Surveillance Systems (Work Package 4) </p>	



PREAMBLE

This survey is being conducted as part of the SOHOV&S project (Vigilance and Surveillance of Substances of Human Origin) which is funded under the European Union Health Programme. The general aim of the project is to support EU Member States (MS) in the establishment of effective Vigilance & Surveillance systems for tissues and cells used in transplantation and in assisted reproduction.

The questionnaire aims to gather detailed information on the systems in place in MS for V&S in the field of tissues and cells for transplant and for assisted reproduction. Information gathered in the EUSTITE V&S System review will not be repeated. This questionnaire is concerned very specifically with the details of the Competent Authority's role in Vigilance of tissues and cells. It should be completed by a person who is directly involved in vigilance in a Competent Authority for Tissues and Cells.

This questionnaire survey was designed by representatives from ONT, HFEA and CNT, with the collaboration of other partners of SOHOV&S.



Competent Authority representatives are invited to fill in and return the present questionnaire, together with any relevant supporting documents, to Marina Alvarez, preferably by e-mail (malvarez@msps.es), before the end of August, 2010.

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PART I: GENERAL DATA



Contact details of the Organization filling the questionnaire:

Country			
Organization name			
Organization role (competencies in relation to the EU tissues and cells directives)			
Full Postal Address			
Contact Person			
Telephone n.		Fax n.	
Email address			
Is there another organization(s) also named as Competent Authority (ies) in your MS that should complete a copy of this questionnaire?	If yes, please provide contact details		



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PART II: QUESTIONNAIRE

Section 1: General		
Is the information shown in Annex a still accurate for your country (and the area of competence of your CA)? If no, please update the information here:		YES/NO (please delete as appropriate)
1.	If you have a V&S system in place, how long has it been operational?	Insert your text here
2.	If you have a system in place, is it: (Multiple choice - delete as appropriate)	a. National b. Regional c. Other
3.	Are the EU Tissue and Cell Directives the basis of your system?	YES/NO (please delete as appropriate)
3.1	Is there additional national legislation relating to V&S that goes beyond the EU Directives?	YES/NO (please delete as appropriate)
3.2	If yes, please describe briefly:	Insert your text here
4.	Is reporting of serious adverse reactions and events (SARE) common for all types of tissues and cells or separate for different types? (Multiple choice - delete as appropriate)	a. One common tissue and cell system b. One system for tissues and cells for transplant and one for ART c. One system for tissues, one system for haematopoietic stem cells and one system for ART d. Other (describe): Insert your text here
5.	Is there overlap/interaction/co-operation with other reporting systems? (Multiple choice - delete as appropriate)	e. Blood f. Pharmaceuticals g. Other: (Describe).....
6.	How are reports received? (Multiple choice - delete as appropriate)	a. Paper system - standardized forms b. Specific software application: (Name)..... c. Email communication/ fax d. Telephone
7.	Are mandatory reporting time - frames defined?	YES/NO (please delete as appropriate)

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7.1	If yes, please describe briefly:	<i>Insert your text here</i>
8.	Is a requirement to report SARE extended to third parties?	YES/NO (please delete as appropriate)
8.1	If yes, please describe briefly:	<i>Insert your text here</i>
9.	Has your system incorporated/adapted any of the EUSTITE V&S Tools?	YES/NO (please delete as appropriate)
9.1	If yes: (Multiple choice - delete as appropriate)	a. EUSTITE Definitions b. SAE Reporting Criteria c. SAR Severity Scale d. SAR Imputability Scale e. SARE Impact Assessment Tool
9.2	If no, do you apply other tools? If yes, please describe briefly:	YES/NO (please delete as appropriate) <i>Insert your text here</i>
10.	Does your CA report to other agencies? (Multiple choice - delete as appropriate)	a. European Commission b. Other (e.g. Patient Safety Agency, Government, Public Health Agencies...) Please describe: <i>Insert your text here</i>
11.	Do you collaborate with Scientific and Professional Societies, registries run by professionals or other non-governmental organisations for vigilance reporting, evaluation, investigation or outcome dissemination?	YES/NO (please delete as appropriate)
11.1	If Yes, please describe the collaboration:	<i>Insert your text here</i>
12.	Do you disseminate learning points arising from your vigilance system to the professional field or more widely?	YES/NO (please delete as appropriate)
12.1	If yes, please describe how this is done:	<i>Insert your text here</i>
13.	Do you publish the results of your vigilance system?	YES/NO (please delete as appropriate)
13.1	If yes: (Multiple choice - delete as appropriate)	a. In a consolidated report without centre identification b. As individual reports with centre identification c. In other ways (Describe):

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		<i>Insert your text here</i>
14.	Do you have a formal system for alerting professionals regarding new risks (e.g. emerging diseases, particularly serious incidents)?	YES/NO (please delete as appropriate)
14.1	If yes, please describe briefly:	<i>Insert your text here</i>
15.	Do you have a formal system for alerting professionals regarding RATC alerts from the European Commission?	YES/NO (please delete as appropriate)
15.1	If yes, please describe briefly:	<i>Insert your text here</i>
16.	When new disease transmission risks are identified (e.g. Q-fever, West Nile Virus) how are donor selection criteria modified to reduce risk? (Multiple choice - delete as appropriate)	a. New exclusion/testing criteria set nationally by the CA b. New exclusion/testing criteria set by other national organisation c. New exclusion/testing criteria set at Tissue Establishment level d. Other (describe): <i>Insert your text here</i>

Section 2: Investigation

17.	Does your CA participate actively in SARE investigations (site visits, participation in analysis of the cause, interviewing of those involved, review of TE findings, etc.)? (Multiple choice - delete as appropriate)	a. Always b. Sometimes c. Never
17.1	If sometimes, what are the criteria for deciding on your level of involvement?	<i>Insert your text here</i>
18.	Do you use experts in the field to assist in investigation and evaluation of SARE?	YES/NO (please delete as appropriate)
19.	Would your CA be interested in participating in an international team/pool of investigators which would be available to EU MS?	YES/NO (please delete as appropriate) Additional comments on this proposal (optional): <i>Insert your text here</i>

Section 3 : Responsible Individuals



20.	Do you have dedicated vigilance officer(s) in the CA?	YES/NO (please delete as appropriate)
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20.1	If yes, how many?	<i>Insert your text here</i>
20.2	If yes, what are their qualifications and training?	<i>Insert your text here</i>
20.3	If yes, do they also inspect TEs?	YES/NO (please delete as appropriate)
20.3.1	If no, do they interact with inspectors?	YES/NO (please delete as appropriate) If Yes, describe: <i>Insert your text here</i>
20.4	Would your CA be interested in sending your Vigilance Officers to an EU Training Course	YES/NO (please delete as appropriate)
20.4.1	If yes, which topics should be covered in the training course?	<i>Insert your text here</i>
21.	Do you provide specific vigilance training to individuals in the field (hospital staff, TE staff, Quality Managers, etc.)?	YES/NO (please delete as appropriate)
21.1	Do you consider it necessary?	YES/NO (please delete as appropriate)
21.2	If yes, how should this be delivered? (Multiple choice - delete as appropriate)	a. In European courses b. In national courses, delivered by trainers trained in a European course c. Other (describe) <i>Insert your text here</i>

Section 4: Vigilance (Safety) of the Living Donor

22.	Does your CA require reporting of SAR in donors even if the quality and safety of the donated tissues or cells has not been affected?	YES/NO (please delete as appropriate)
22.1	If yes, does this include? (Multiple choice - delete as appropriate)	a. Ovarian Hyperstimulation Syndrome (OHSS) in non-partner oocyte donors? b. OHSS in partner oocyte donors? c. Reactions to GCSF in autologous patients? d. Reactions to GCSF in allogeneic donors? e. Toxicity during PBSC collection in autologous donors?



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		f. Toxicity during of PBSC collection in allogeneic donors? g. Other: (Describe): <i>Insert your text here</i>
23.	Do you maintain a registry of living donors to follow their health in the long term?	YES/NO (<i>please delete as appropriate</i>)
23.1	If Yes, please describe:	<i>Insert your text here</i>
Section 5: Good Practice Recommendations		
24.	From your experience, do you have any recommendations of good practice principles that should be incorporated in the SOHO V&S guidance on vigilance and surveillance investigation for tissues and cells?	<i>Insert your text here</i>



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Annex a: Countries with or without a system in place for the reporting of serious adverse events and reactions. Information gathered by the European Commission *Questionnaire on the transposition and implementation of the European Tissues and Cells regulatory framework* in 2009

COUNTRY	SYSTEM IN PLACE FOR THE REPORTING
AUSTRIA	No
BELGIUM	Yes
BULGARIA	Yes
CROATIA	Yes
CYPRUS	No
CZECH REPUBLIC	No
DENMARK	Yes
ESTONIA	No
FINLAND	Yes
FRANCE	Yes
GERMANY	Yes
GREECE	No
HUNGARY	Yes
ICELAND	Yes
IRELAND	Yes
ITALY	Yes
LATVIA	No
LICHTENSTEIN	No
LITHUANIA	Yes
LUXEMBURG	-
MALTA	No
NORWAY	Yes
POLAND	Yes
PORTUGAL	No
ROMANIA	Yes
SLOVAKIA	Yes
SLOVENIA	Yes
SPAIN	Yes

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SWEDEN	No
THE NETHERLANDS	No
TURKEY	No
UNITED KINGDOM	Yes



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ANNEX II

RESULTS OF

NON-EU COUNTRIES

April, 2011

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RESULTS OF NON EU COUNTRIES

1.0: General

Four non-EU countries answered the questionnaire: Croatia, Iceland, Lichtenstein and Norway. They all described a common nationally organised system. Lichtenstein's system was put in place since the 2009 survey; the other countries already had a system at that time. Three of the four based their system on the EU Directives and only Croatia has additional legislation beyond the Directives (Medical Fertilisation Act 88/09, 137/09 which bans import and export of reproductive tissues and cells).

SARE reporting is via a common method for all tissue and cell types in Norway while the reporting is different for different tissue and cell types in the other countries. Norway's system does not overlap with other vigilance systems while in Croatia, Iceland and Lichtenstein, there is overlap with pharmacovigilance and in Lichtenstein also with haemovigilance. The four countries receive SARE reports on paper; only Lichtenstein has a software based reporting system. None of these countries has mandatory reporting times although Croatia requires reporting 'without any delay'. Croatia extends its reporting requirements to third parties. Croatia and Lichtenstein have incorporated some of the EUSTITE tools in their systems.

None of these countries publishes their vigilance programme results or involves professional societies in their programmes. One of them disseminates learning points to Responsible Persons working in the same field. Three of the four have a system for alerting the field regarding new risks three of them set new exclusion/testing criteria nationally. Two of them have systems for communicating the rapid alerts issued by the European Commission.

2.0: Investigation

With regard to investigation, the Competent Authority of one country always participates in investigations and in one other it sometimes does. Only one of these countries uses experts to help in investigations. Croatia would be interested in participating in a European investigation team.

3.0: Responsible Individuals

Three of these countries have at least one dedicated vigilance officer; these individuals do not also conduct inspections. Two of the countries would wish to send vigilance officers for EU training.

4.0: Vigilance of the Living Donor

Both Croatia and Lichtenstein require reporting of living donor reactions even when the quality or safety of the tissues or cells has not been affected but none of these countries has a registry of living donors.