European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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National and EU-Level Tissue and Cell Activity Data Collection and Reporting

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PROCEEDINGS OF THE TECHNICAL MEETING

22-23 March 2018

Strasbourg, France

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INTRODUCTION

Founded in 1949, the Council of Europe is the oldest and largest of all European institutions and now numbers 47 member States. One of its founding principles is that of increasing co-operation between member States to improve the quality of life for all Europeans. Transplantation activities at the Council of Europe are co-ordinated by the European Directorate for the Quality of Medicines & HealthCare (EDQM) through its European Committee on Organ Transplantation (CD-P-TO). The EDQM is a key European organisation involved in the harmonisation, co-ordination, standardisation, regulation and quality control of medicines, blood transfusion, organ transplantation, pharmaceuticals, pharmaceutical care, consumer health, cosmetics and food packaging.

Since 1987, the EDQM has, through a number of initiatives, programmes and legal instruments, actively contributed to the development and implementation of quality, safety and ethical standards in the field of organs, tissues and cells, facilitating the exchange of knowledge between countries and institutions, securing fundamental rights and ensuring respect for the human body.

Within this context of intergovernmental co-operation in the field of health, the EDQM regularly selects technical problems for study. Monitoring of practices in the member States has become an evident need for the sake of transparency and international benchmarking. Keeping this goal in mind, the EDQM elaborates since 1996 and on a yearly basis the Newsletter Transplant. This work, performed in close cooperation with the Spanish National Transplant Organisation (ONT) and under the aegis of the CD-P-TO, has evolved into a unique official source of information that continues to inspire policies and strategic plans globally. This publication summarises comprehensive data provided by national focal points designated by governments on donation and transplantation activities, management of waiting lists, organ donation refusals and authorised centres for transplantation activities. As of today, the Newsletter Transplant provides information from almost 70 countries worldwide, including Council of Europe member States, observer countries and observer networks. The Newsletter Transplant database is connected with other international data collection projects, e.g. the WHO Global Observatory on Organ Donation and Transplantation (GODT) and the EUROCET database, to avoid duplication of efforts.

In parallel, many other organisations and professional societies are also performing relevant data collection exercises. In the current context where countries, as well as organisations, have to optimise and improve the efficiency of their efforts, it is essential that all relevant parties sit around the same table to benefit from each other's expertise, competences and strengths, make better use of existing resources, and search for added value while avoiding duplication of work.

The EDQM also has a standing and fruitful cooperation with the European Union (EU) on a number of health related issues. Since 2007, when the Lisbon Treaty further developed the scope for the EU in the area of health and allowed the establishment of the EU Health Programme funding instrument used to implement the EU Health Strategy, the EDQM has

been awarded with 4 grant agreements related to the field of substances of human origin due to its long-standing experience on the subject matter. In addition, the EDQM has also been awarded two separate contracts (SANTE/2016/B4/050 and SANTE/2017/B4/047) to take over from the European Commission (EC) the tasks pertaining to the analysis of the serious adverse events and reactions (SARE) in Europe in the fields of blood, tissues and cells in the EU for the years 2015 and 2016 and the elaboration of the corresponding SARE summaries – one for each field and for each year. The activities resulting from all these cooperation agreements and contracts are widely recognised as important elements and tools for the implementation of high quality and safety standards in the field of health across Europe (in EU member States and non-EU member States) and even beyond Europe in a harmonised manner while also supporting the implementation/enforcement of the EU legislation. Furthermore, these activities and their results also provide an important source of information to support evidence-based policy-making in the field.

In the framework of a direct grant agreement between the EC and the EDQM signed in 2015 (Agreement 2014 54 01), a technical meeting on the topic "National and EU-level tissue and cell activity data collection and reporting" took place in Strasbourg (France) on 22-23 March 2018. The Grant Agreement did not specify the topic of the workshop, leaving this to the EC DG SANTE to decide in discussion with EDQM, on the basis of the issues that had emerged through the evaluation of the blood, tissues and cells legislation. The topic chosen was agreed as one that could not be adequately addressed only in the context of the evaluation and for a number of other specific reasons:

1. A commonly reported lack of clarity regarding the requirements for activity data reporting for different purposes in the existing legislation and the need to understand what was considered optimal and lacking.

2. An awareness that there were many different activity data collecting exercises ongoing, some by national Health Authorities and the EC, some by scientific and professional societies and some by standalone bodies such the EUROCET platform which was established through an EU-funded project (E-ten programme) and currently maintained by the Italian authority CNT.

3. A common perception that there was both duplication and inconsistency in the various reporting schemes.

4. Despite the many activities in place, there were uncertainties and a general lack of confidence in the data reported and published, either for transparency purposes or as denominators for vigilance.

The meeting was attended by representatives of the main professional societies or organisations actively involved in collecting data on donation and transplantation in Europe, i.e. the European Society for Human Reproduction and Embryology (ESHRE; that collected data

through the European IVF Monitoring programme), the European Society for Blood and Marrow Transplantation (EBMT), the European Eye Banking Association (EEBA), European Blood Alliance (EBA), the World Marrow Donor Association (WMDA), Newsletter Transplant (ONT) and EUROCET (CNT). For completeness, the European Association of Tissue Banks (EATB) was also invited to attend, even if they had no on-going data collection exercises, as well as the EU Vigilance Expert Subgroup (VES). Finally, EU member States that had an interest in the topic were also invited to send a representative.

The agenda was organised in separate discussion blocks in an attempt to assess:

- if there were overlaps, duplications or inconsistencies between the different data collection exercises in the processes/objectives/parameters/units/definitions;

- if the existing activity data collection processes could be streamlined/harmonised so that the burden on tissue establishments and Health Authorities was minimised and the data remained meaningful and useful;

- the role of Health Authorities/EDQM and professional societies in this kind of data reporting and publication and if there was room for collaborative work;

- if the legal requirements in the EU regarding data collection were clear and adequate; and

- if there was enough data available to evaluate self-sufficiency in Europe and dependence on third countries or supply from certain member States (concern about overreliance on few member States).

These proceedings summarise the discussions held during this meeting and the resulting conclusions and recommendations.

PROGRAMME OF THE TECHNICAL MEETING

Thursday 22 March 2018 9:00 – 18:00		
9:00 – 9:30	**WELCOME AND OPENING REMARKS**	
9:00 – 9:10	Welcome by the Director of the EDQM	**Susanne KEITEL**
9:10 – 9:20	Opening remarks	**Deirdre FEHILY** **Marta LÓPEZ FRAGA**
9:20 – 9:30	Tour de table	
9:30 – 12:40	**STATE-OF-THE-ART IN INTERNATIONAL DATA COLLECTION EXERCISES** *Please provide information on: governance, frequency, geographical coverage, source of the data (unique national focal point vs. centres), type of information collected, publication of raw vs. curated data, glossary of definitions available? dissemination/availability of data, other relevant information.*	
9:30 – 9:50	European Commission	**Deirdre FEHILY**
9:50 – 10:10	European Society for Blood and Marrow Transplantation (EBMT)	**Eoin MCGRATH**
10:10 – 10:30	European Society of Human Reproduction and Embryology (ESHRE)	**Christian De GEYTER**
10:30 – 10:50	European Blood Alliance (EBA)	**George GALEA**
10:50– 11:10	***Coffee break***	
11:10 – 11:40	World Marrow Donor Association (WMDA)	**Lydia FOEKEN**
11:40 – 12:00	European Eye Bank Association (EEBA)	**John ARMITAGE**
12:00 – 12:20	EUROCET	**Valentina CARAMIA**
12:20 – 12:40	Newsletter Transplant / WHO Global Observatory	**Mar CARMONA**
12:40 – 13:30	***Lunch***	
13:30 – 14:50	**NATIONAL DATA COLLECTION EXERCISES BY AUTHORITIES** *Please provide information on: data collection exercises to which your country provides information, who submits data to each, on-going additional national exercises, timing (case by case, monthly, annually…), interaction with professional societies for data reporting exercises, dissemination of data (public vs. restricted), is information on international distribution of tissues and cells and imports/exports collected, other relevant information.*	
13:30 – 13:40	Croatia	**Milena IVANKOVIC**
13:40 – 13:50	Cyprus	**Carolina STYLIANOU**
13:50 – 14:00	Estonia	**Siim SUUTRE**
14:00 – 14:10	Italy	**Eliana PORTA**
14:10 – 14:20	The Netherlands	**Robin VAN EECHOUD**
14:20 – 14:30	Poland	**Artur KAMINSKI**
14:30 – 14:40	Spain	**Mar CARMONA**
14:40 – 14:50	Sweden	**Mona HANSSON**

14:50 – 18:00	**ROUND TABLE DISCUSSION**	
14:50 – 16:00	Topics to be addressed: ➢ Is there overlap, duplication or inconsistency in processes/objectives/parameters/units/ definitions? ➢ Could the existing activity data collection processes be streamlined/harmonised so that the burden on tissue establishments and Competent Authorities was minimised and the data remained meaningful and useful?	*Facilitators*: **Deirdre FEHILY** **Marta LÓPEZ FRAGA**
16:00 – 16:20	***Coffee break***	
16:20 – 18:00	Topics to be addressed: ➢ What are/should be the roles of Competent Authorities/EDQM/professional associations in this kind of data reporting and publication and is there scope for collaborative work?	*Facilitators*: **Deirdre FEHILY** **Marta LÓPEZ FRAGA**
19:30	***Social dinner***	

Friday 23 March 2018 9:00 – 13:30		
9:00 – 9:40	**LEGAL FRAMEWORK FOR DATA COLLECTION ACTIVITIES**	
9:00 – 9:20	Denominators for the EU SARE exercise: are they fit for purpose? - Recommendations from the EU Vigilance Expert Subgroup.	**George GALEA**
9:20 – 9:40	Status update on the evaluation of the EU legislation on Tissues & Cells.	**Deirdre FEHILY**
9:40 – 12:40	**ROUND TABLE DISCUSSION**	
9:40 – 11:20	Topics to be addressed: ➢ Are the legal requirements clear and adequate and, if not, what should be recommended or mandated at a national/EU level?	Facilitators: **Deirdre FEHILY** **Marta LÓPEZ FRAGA**
11:20 – 11:40	***Coffee break***	
11:40 – 12:40	Topics to be addressed: ➢ Do we have enough data to evaluate self-sufficiency in Europe and dependence on third	Facilitators: **Deirdre FEHILY** **Marta LÓPEZ FRAGA**

	countries? ➢ Should the collection of data on international distribution and imports/exports be mandatory?	
12:40 – 13:20	**RECOMMENDATIONS AND NEXT STEPS**	
13:20 – 13:30	**FINAL REMARKS AND CONCLUSIONS**	

SUMMARY OF DISCUSSIONS

All major international activity data reporting schemes were invited to present their programmes with a common format during the session "State-of-the-art in international and national data collection exercises". They were asked to describe the governance of their exercises/platforms, frequency of the data collection and period covered, geographical coverage, source of the data (unique national focal point vs. individual centres or professionals), type of information collected, if data was public or access-restricted to certain groups, if they published raw data as submitted or if there was a revision and curation process, if they had a glossary of definitions available, and any other relevant information. **Table 1** summarises all the reported information.

During the session on "National Data Collection Exercises by Authorities", member State representatives were requested to report to which international data collection exercises they submitted data and if they performed other national exercises, who submitted data to each of the above mentioned exercises (national authorities vs. professionals/centres), the timing of submission of information (case by case, monthly, annually), if there was interaction with professional societies for data reporting exercises, dissemination of data (public vs. restricted), if they collected information on international distribution of tissues and cells and imports/exports, and any other relevant information. **Table 2** summarises all the reported information.

These exercises were evaluated based on their overall effectiveness, relevance, efficiency, coherence and value. As a means to assess the **effectiveness** of the ongoing exercises, their degree of completeness, accuracy and comparability was discussed. In general, the data collected by professional societies was the most complete. They had managed to collect some minimum data sets very consistently. However, fine data was still missing. They also reported they had not managed to capture the 100% of the data as their coverage was not complete (in some cases, only members or affiliated centres reported data to them). Reportedly, the problem was the voluntary nature of the reporting. Clear and binding rules for reporting, preferably at EU level, would greatly contribute to closing these gaps. The registries from professional societies were, in general, very accurate, as they invested a lot of resources and dedicated personnel to integrate internal triggers to control accuracy and internal consistency within the databases, to manually curate and verify the data and to establish sound governance systems. Their main interest in collecting this information was for research purposes. On the other hand, Health Authorities did not, in general, have so many resources to collect activity data, with this task sometimes circumscribed to regions or centres. Reportedly, the accuracy of data collected by them was heterogeneous and it relayed, on many instances, on the reporting bodies verifying their own data. Nonetheless, Authorities expressed that they had an interest in this information as a means to assess quality of their donation and transplantation systems and as a basis for future policy decisions.

When comparing the data gathered by professional societies and national authorities, it became evident that the source of the data was not always the same, which created

discrepancies. In addition, definitions and units being collected were interpreted in different manners for the various exercises. All this had an impact in the **coherence** of the data gathered.

When discussing the **relevance** of the different exercises, it was agreed that the type of information needed for citizens, regulators, end users, professionals, Health Technology Assessment (HTA) bodies and supranational/international organisations was not the same. Thus, the relevance of the on-going exercises for each one of them was variable.

In terms of **efficiency**, the group identified overlaps between the data collected by the different exercises, creating excessive burden for the reporting member States, tissue establishments and end users. To make things more complicated, the definitions and units used by the different exercises differed, creating misunderstanding and additional work for the reporting bodies to accommodate the needs of each exercise. It was felt that haematopoietic progenitor cell (HPC) collection centres were probably the ones suffering the greatest burden.

Finally, when analysing the **value** of these exercises, there was general agreement that there was room for improvement as many of them could be streamlined and harmonised to relieve the burden on member States, tissue establishments and end users while still collecting meaningful and useful data.

During the session on the "Legal Framework for Data Collection Activities", a representative from the EU VES provided their views on the extent to which the denominators currently collected by the EU during the annual SARE exercise were fit for purpose, i.e., if they were clear, sufficient, etc. It was made evident from this presentation and the subsequent discussions that it was no longer possible to approach biovigilance on its own and that this exercise should be better integrated with the collection of activity data done for other purposes (transparency towards citizens, quality assessment, policy guiding, research, etc.)

The representative from the EC also provided a comprehensive overview of the on-going evaluation of the legislation, which had put in evidence that some legal provision in the EU Directives were missing or no longer adequate, some of them including reporting obligations, donor safety, clinical outcomes, biovigilance and European self-sufficiency.

During the general discussions it was also highlighted that there was a remarkable lack of information on tissues and cells imports and exports within of the EU. Thus, it was very difficult to assess the dependency on third countries to ensure our supply of certain tissues and cells and reliable information was urgently needed. Furthermore, clinicians were in many cases ordering tissues from third countries without any involvement of tissue establishments within the EU. The panel agreed that mechanisms should be put in place to get information from end users (clinicians) about the tissues and cells they were using. If this was not possible through the direct inspection of end users, a partial solution to be explored could be the collection of

such information via the mandatory inspections of tissue establishments. However, this would still not address direct imports by clinicians from third countries.

Similarly, the on-going exercises reported it was impossible to assess overreliance on some EU countries for the supply of certain tissues and cells. Overall, obtaining a clearer picture on these matters could only be accomplished through legislative changes that made the collection of this type of data mandatory. In particular, Article 10(1) of Directive 2004/23/EC should provide clearer requirements on data reporting.

Table 1. Summary of the information reported by the attending international activity data reporting schemes.

Association/ Body	Governance of your exercises/platforms	Frequency of data collection	Period covered	Geographical coverage	Source of data	Type of information collected	Public/access restricted to certain groups	Raw data/ curated data	Glossary/ definitions available?	OTHER
EC	EU legislation – CA expert group	Annual publication	1 yr	28 EU MS (mandatory by EU Directive) + Iceland, Norway and Liechtenstein (voluntary)	CA of each country	Activity data (voluntary) and SARE (mandatory)	Summary report publically available at EC website	Curated data, verified with countries involved. In addition, VES revised reporting templates, Common Approach document and definitions, proposing changes as needed to improve accuracy of data	Common Approach document	EDQM performs data verification (contacting MS as needed) and analysis and drafts summary reports. It also provides feedback to the EC and VES in order to improve future exercises
European Society for Blood and Marrow Transplantation (EBMT)	EBMT (Head of Registry and the EBMT Executive Committee – report to the EBMT Board that in turn reports to the General assembly). There is also a Registry Committee	Annual publication. Frequency can be increased and decreased as needed	• Day 0 • Day 100 • Annual follow-up until death Data can be entered in real-time	Data from >500 centres/>50 countries Approx. 80% of European tx centres report their data to the registry (this covers 96% of EU tx)	Tx centres and National Registries. Each EBMT centre is represented in this database and given a Centre Identification Code. No fee for participation	HSCT, cell therapy, donor outcome	Access restricted to users (aggregated data) but data published annually in scientific journal	Database with internal quality controls. Over 4000 triggers control the accuracy and internal consistency of what is entered in the database. Statistical analyses allow to detect bias, data quality and unusual trends Data also curated manually	Statistical guidelines, glossary of definitions and manual	Data are pseudo-anonymised. To safeguard centre anonymity, all countries with less than 10 member centres appear under the label of "Other" In the process of reducing collected data set

Association/ Body	Governance of your exercises/platforms	Frequency of data collection	Period covered	Geographical coverage	Source of data	Type of information collected	Public/access restricted to certain groups	Raw data/ curated data	Glossary/ definitions available?	OTHER
European Society of Human Reproduction and Embryology (ESHRE)	ESHRE Board: European IVF Monitoring Programme	Annual	1 yr	38 countries (out of 51 Europe) in 2013. 85% EU countries send data to ESHRE. Completeness 89% In some countries, reporting is mandated by law No data from HR, or SK	Directly reported by centres in countries with no national registry. From national registries where they exist	IVF, ICSI, frozen/thawed embryo transfer/oocyte treatment, oocyte donation, in vitro maduration, PGT, gonadal tissue freezing	Publication in journal	Curated data (no additional data on how)	Yes	Estimated 85% completeness
European Blood Alliance (EBA)	EBA Board	Annual	1 yr	29 countries	Blood establishments with T&C activity (28 facilities, from those 14-15 are national organisations)	Activity data, units imported from another TE in the country, or other TE from outside the country (EU/non EU), tissues issued for export (outside the country), discarded by the bank prior to issue, in stock at the end of the year, infectious diseases markers, tests used Including umbilical cord blood	Restricted to EBA members. Countries are coded so only country knows their results	Curated data, 2 times verified by 3 people analysing it	Yes	Generally poor completeness of data

Association/ Body	Governance of your exercises/platforms	Frequency of data collection	Period covered	Geographical coverage	Source of data	Type of information collected	Public/access restricted to certain groups	Raw data/ curated data	Glossary/ definitions available?	OTHER
World Marrow Donor Association (WMDA)	WMDA Board	Daily/Annual	1 yr	52 countries (all donors and cord blood units are available for global search in centralised database).	National registries. Some EU (Estonia and Malta) do not have national registries.	Number of donors and number of cord blood units listed per organisation per country. Number of HPC products used for unrelated stem cell transplantation within a country specified (national, imported, exported). Serious adverse events and reactions occurring after unrelated stem cell donation.	Data are publicly available on: https://statistics.wmda.info/ and updated on a daily base. Import/export data collected once a year through an operational grant from the EU and shared with EU (not with CA) and WMDA members.	Curated data (crosschecked with EBMT). Data no cross-checked with CA	Yes	They also collect technical information from public CBB: address details, licenses, details how cord blood units are collected, processed, stored and shipped. Updated bi-annually. Will become publicly available in 2019
European Eye Bank Association (EEBA)	EEBA Board	Annual	1 yr (but collected 2 years after)	22 countries	Data from individual banks only if at least 1 member staff from that bank is a registered Ordinary Member at the EEBA.	Information per country (specific legislation, donation and cornea banking). Yearly activities and methods of eye banks in Europe. List of the contact details for all eye banks which have at least one EEBA	Published in the Annual Business Meeting (online and paper) for members in their Annual Directory. Available on request to regulatory/ CA.	Curated data (no additional data on how)	Yes (in questionnaire)	EU –funded ECCTR project (European Cornea and Cell Transplantation Registry) (EEBA is one of 8 consortium partners)

Association/ Body	Governance of your exercises/platforms	Frequency of data collection	Period covered	Geographical coverage	Source of data	Type of information collected	Public/access restricted to certain groups	Raw data/ curated data	Glossary/ definitions available?	OTHER
						ordinary member. Keeping track of new developments in eye banking. Also collect data on virology test results				
EUROCET	CNT	Annual	1 yr	33 countries	National Competent Authorities: In 2017: 27 T&C, 25 HPC, 22 ART CA provided data	Type of tissue/cell (including HPC and ART), activities collected, import/export outside EU	Public in EUROCET webpage and published in Newsletter Transplant.	Curated data: checked with CA	Yes, currently being revised and updated with other associations in a CD-P-TO project	10 years of experience
Newsletter Transplant/ WHO Global observatory **(Organs)**	ONT	Annual	1 yr	Worldwide: Newsletter Transplant : COE MS, observers RCIDT: Latin-American countries EC: EU countries WHO: Other WHO regions (AFR, EMR, SEAR, WPR and NIS/CAR MS).	National Health Authorities Population: UNFPA.	Data related donated and transplanted organs, including paediatrics, (per ages, living vs deceased).	Public (papier copies and pdf) also includes EUROCET information regarding T&C (but not ART).	Curated data verified with countries involved.	WHO global glossary.	This exercise feeds information to: • WHO-GODT • COE Newsletter Transplant • RCIDT - collaboration with Latin-American countries • EC indicators exercise- UE Action Plan

Table 2. Summary of the information reported by the attending Health Authorities.

Association	Who submits data	National exercises on-going	Timing	Interaction with professional societies	Disemination data (public/restricted)	Information imports/exports collected	Glossary/ definitions available?	OTHER
Croatia	TE (2) and ART centres (16) submit data to CA. Then, CA sends data to EUROCET and also publishes national data.	Also SARE reporting and EUROCET (extended)	Real time and annually. Data collection on number of cornea donors is monthly.	They provide data to ESHRE (ART)	Public (MoH webpage and EUROCET).	Yes – import/export data as requested by EUROCET. Number of donors, donation, received tissue, processed and discarded tissue, units distributed, stored tissues, imports/exports, transplants and recipients. Non- reproductive T&C, HPC, reproductive tissue and cells.	Yes	• TESE/ TESA, storage for delayed cycles • Cycles according to the age of women • Storage of reproductive cells and tissues for the purpose of later usage (oncological patients) • ART registry at the end of this year • Data is double checked
Cyprus	TE. Using EUROCET templates and also collection of information for SARE exercise.		Annually. Real time for SARE	HPC -> EBMT IVF-> ESHRE	Not publicly available	No real data of tissues used or distributed directly to centres in EU countries Bone distributed directly to dentists from other MS – CA gets no data on this	Yes	• No feedback provided to tx centres • No outcome data for ART
Estonia	TE	Also SARE reporting and EUROCET.	Annually (1 April).	No	Consolidated report is published by State Agency of Medicines on their website (aggregated data at the end of year) Also an annual roundtable meeting with ART community to discuss	Import/export activity data is reported case by case (if tissue moves from or to EEA or outside EEA). This information is included in the national report Licences are issued for 3td country exchanges	Yes, using EUROCET glossary	

Association	Who submits data	National exercises on-going	Timing	Interaction with professional societies	Disemination data (public/restricted)	Information imports/exports collected	Glossary/ definitions available?	OTHER
Italy	From 30 TE (tissue for transplant) and 2 pancreatic islets processing units. Hospitals, TE and end users provide data to regional CA. 87 HSC centres and 18 CB banks report data to GITMO and + 300 ART centres report to a national ART activity registry	3 exercises annually: 1. ART national registry. 2. GITMO, (registro italiano donator di midollo osseo) for HPCs 3. Tissue activity to CNT . Also SARE reporting and EUROCET	Data collection on quarterly basis for tissues for transplant to CNT	ESHRE -> ART	Public – on the CNT website	Tissue within the region, Italy, inside EU and import/export is annually collected.	Yes, using EUROCET glossary	
The Netherlands	1 multi tissue bank, 1 eye bank. Procurement centres also report their data	National data collection: TRIP, Dutch Transplant Foundation, Tissue banks, Associatio of ophtalmologists, clinical centres and patient associations. EUROCET and SARE collected by TRIP.	Monthly collection (depending tissue).	No	Public data: SARE, consent to donation, tissue donation, tissue transplantation and distribution and waiting lists (cornea and heart valves).	Import/export and distribution is collected by TRIP (corneas, heart valves, bones).	Yes	• This information only covers tissue donation from deceased donors)
Poland	TE, donor recruitment centres, HLA typing laboratories, qualification centres procurement and transplant centres. Use EUROCET form (extended)		Annually except waiting list cornea (collect daily and published monthly)	No	Public (webpage)	Import/export (international) is collected and disseminated – including cross-border within the EU. Close co-operation with Customs authorities.	Yes	• National waiting list (ocular, pancreatic, HSC)

Association	Who submits data	National exercises on-going	Timing	Interaction with professional societies	Disemination data (public/restricted)	Information imports/exports collected	Glossary/ definitions available?	OTHER
Spain	Individual TE, centres, HSC registry. Data is collected from centres to regional CA and then to ONT.	Also SARE reporting and EUROCET	Yearly basis	No (they only have a consultant role)	Public (webpage): tissues and HSCT, once they are approved by the regional CA	Collection of number of tissues imported/exported outside EU	Yes	• Centres also report to EBMT
Sweden	TE	Also SARE reporting and EUROCET	Annually (February). Real time for SARE	ART centres report to quality registry -> ESHRE. Eye bank -> Swedish registry eye bank HPC tx centres directly to EBMT	Public (webpage)	TE inside Sweden/EU/outside EU. How many for clinical use outside EU. Dentist no information but they believe that all comes in through TEs	Yes.	• Also collect non-serious SARE for national overview

CONCLUSIONS AND RECOMMENDATIONS

Activity data collection in the EU was being performed by a number of stakeholders. Having access to this data was considered necessary, with different objectives and purposes by the different bodies undertaking it. However, after this two day technical meeting, it became clear that there was clear room for improvement and, most of all, harmonisation and streamlining in order to decrease the burden on the reporting bodies and to have better, more coherent and accurate data in the level of detail necessary for each stakeholder. Focus should be on the quality, completeness and accuracy of the data collected, avoiding duplications. The common theme should be: "**Collect once and use often**".

In this sense, the group defined different levels of information that should be collected and made available for different groups of people. The amount of information and detail would increase according to the purpose of the data collection (see **Figure 1**).

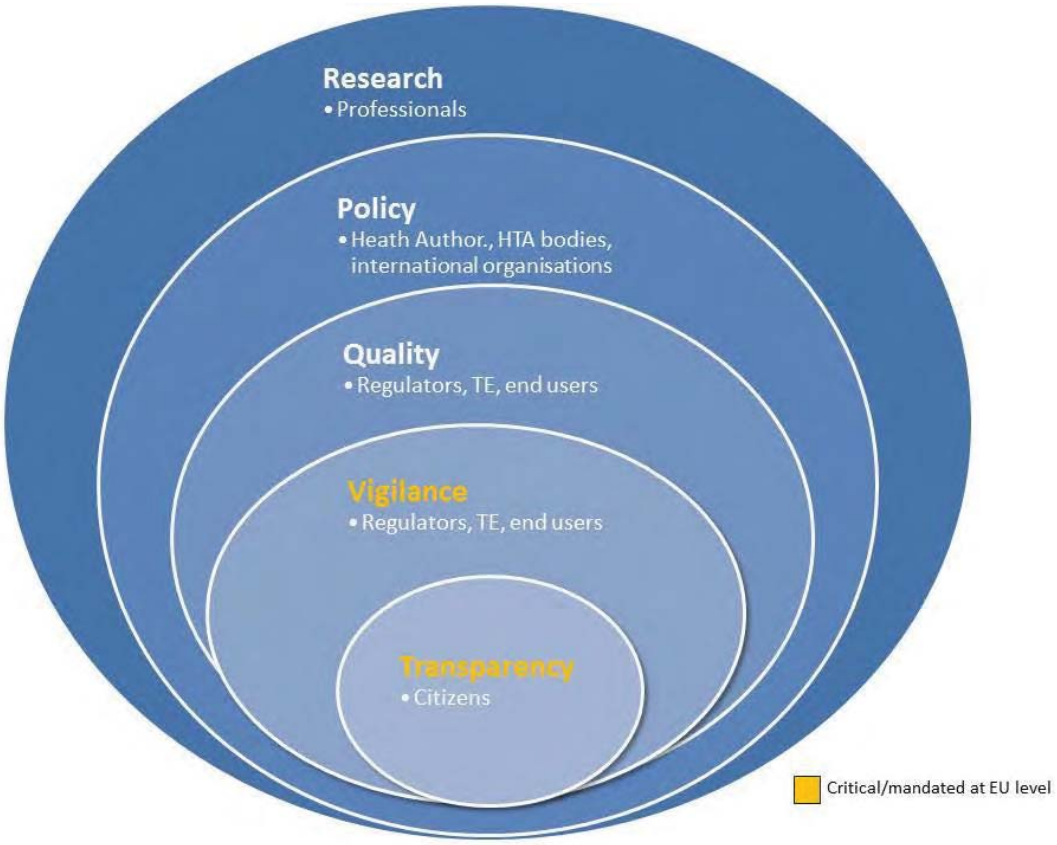


Figure 1. Levels of data that should be necessary for the different stakeholders in the EU. HTA: Health Technology Assessment; TE: Tissue Establishments.

The first level of data, the most basic but also essential, would be needed for transparency purposes and should be made available to all citizens. It would provide information about national/EU self-sufficiency and the availability of care for patients and it would include data such as number of donations per tissue/cell type; the number of recipients for each tissue/cell type; figures on distribution within the EU, imports and exports; risks for living donors; safety of recipients; efficacy data related to the use of different tissues/cells (in cooperation with HTA bodies); etc.

The second level of data would be essential for regulators, tissue establishments and end users for biovigilance purposes. It would provide detailed information about the safety of tissues and cells of human origin and include data such as serious adverse events and serious adverse reactions in donors and recipients, as well as the children born as a result of medically assisted reproduction. It should also include appropriate denominators to put all the above figures into context, and these denominators should be disaggregated into national figures, tissues/cells distributed from other EU member States or imported from third countries.

Due to their special value and relevance, these two first levels of data should be of mandatory collection in the EU. However, in order to enforce this collection, legislative changes would be necessary.

Going one level of detail up, we would find data to be collected in order to assess the quality of donation and transplantation programmes. This information would be necessary for regulators, tissue establishments and end users. Above this, we would have information necessary to guide policy making decisions (i.e. to understand trends and needs), and thus relevant for national Health Authorities, HTA bodies and supranational/international organisations. Finally, professionals and professional societies would also need to collect more detailed and specific data to support their research efforts.

In summary, the collection of a basic data set, harmonised and common to all parties and including information that would serve the purpose of transparency for citizens and as denominators for vigilance exercises, should be mandatory. Additional data should also be collected, although not enforced at EU level, in order to support the different stakeholders meet their needs and objectives (see **Figure 2**).

It remained to be defined who should coordinate or perform these data collections exercises, at least the basis data set. Several options were discussed, including one body collecting all the information and distributing it to the rest of interested parties, or multiple bodies collecting the same harmonised and validated data. The general feeling was that the collection of the basic data set should be the responsibility of Health Authorities, whereas professional societies would be better fitted to collect the expanded data set. However, this debate should be the subject of future discussions.

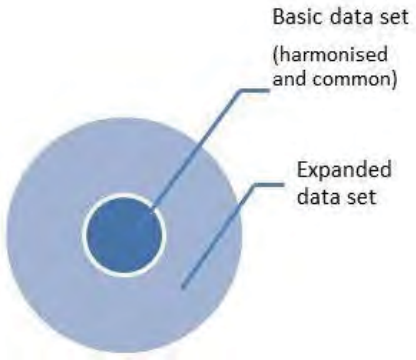


Figure 2. Scheme of the levels of data intended for collection in the EU, defining a mandatory data set and an expanded set of variables.

All these discussions were summarised in the following recommendations elaborated by the group:

1. The collection of a basic data set should be mandated at EU level (this would require legislative changes). This data set would serve the purpose of transparency for citizens and as denominators for vigilance exercises.
2. The basic data set should be common for Health Authorities and professional societies.
3. The Health Authorities should be responsible for the collection of the basic data set and for reporting it to the EC.
4. There should be interaction between the EU (Health Authorities) and data-collecting professional societies and registries (e.g. ESHRE, EBMT, WMDA, EUROCET) for the definition of the common data set. This interaction could be facilitated by the EDQM based on existing experience (e.g. elaboration of technical guides, EU serious adverse events and reactions exercise analysis).
5. There should be interaction between the Health Authorities and the data-collecting professional societies and registries for the validation of the collected data (health insurance companies could also contribute to the validation of data).
6. The EC should annually publish separate activity and vigilance reports (this would require legislative changes). This could be delegated to other bodies (e.g. EDQM, EUROCET).

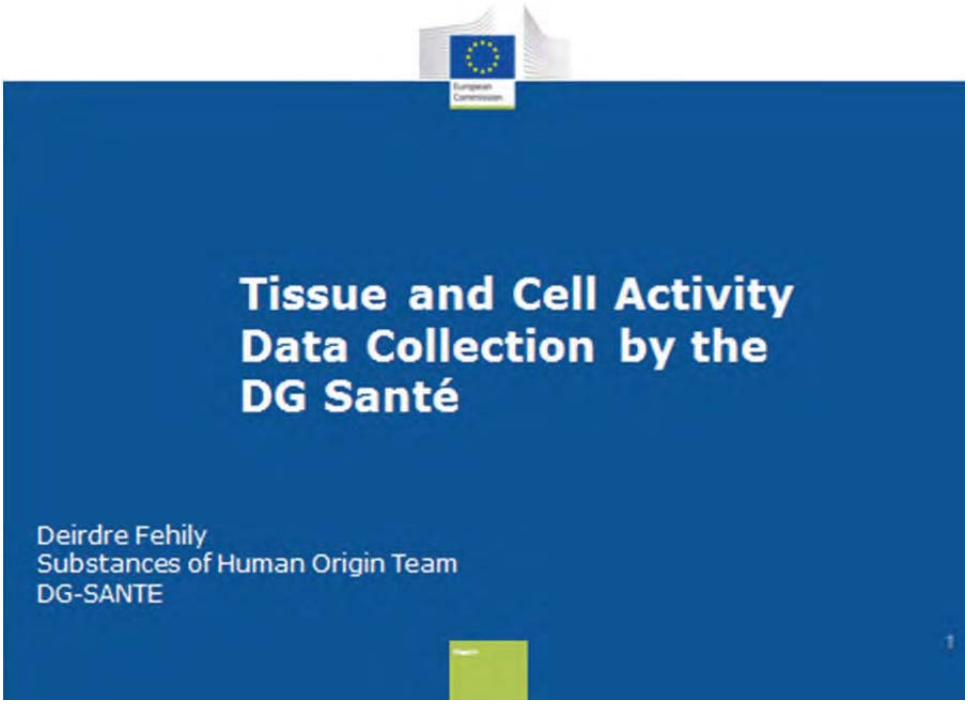
The participants at the meeting agreed that further meetings involving professional societies and a larger number of member States should be organised to continue with the discussions and ensure the appropriate implementation of these recommendations. These meetings could be organised by the EDQM in the same manner as the current technical meeting in the framework of future cooperation agreements between the EU and the EDQM. Ultimately, what would be important would be to ensure appropriate communication and involvement of Health Authorities, professional societies and supranational/international organisations in order to guarantee common understanding and agreement on the objectives, methods and

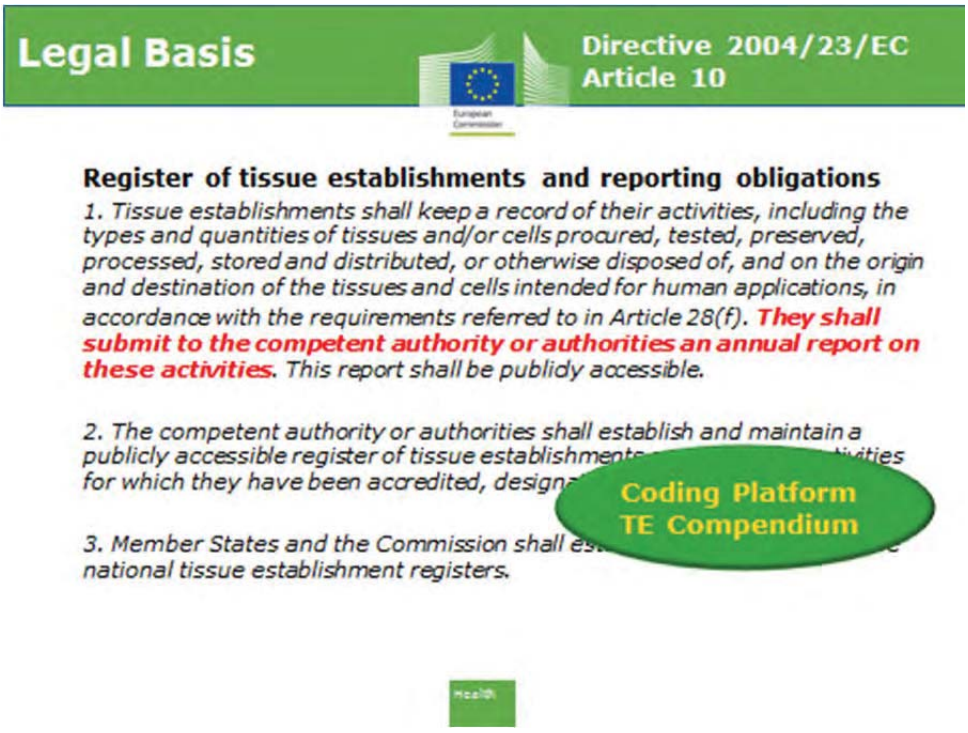
resources that would be necessary to ensure effective, relevant, efficient, coherent and valuable results.

Finally, the representative from the European Commission informed the participants that the conclusions and recommendations from the technical meeting would be used during the evaluation of the EU tissues and cells legislation and in any potential future revisions.

PRESENTATIONS

- **Tissue and cell activity data collection by the DG-SANTE - Deirdre Fehily (European Commission)**





Legal Basis

Directive 2006/86/EC
Article 7

Annual reports

1. Member States shall submit to the Commission an annual report, by 30 June of the following year, on the notification of serious adverse reactions and events received by the competent authority. The Commission shall submit to the competent authorities of Member States a summary of the reports received. The competent authority shall make this report available to tissue establishments.

2. Data transmission shall comply with the data exchange format specifications as set out in Annex V, part A and B, and shall provide all the information necessary to identify the sender and maintain its reference data.

No mention of denominator data reporting

Legal Basis

Directive 2006/86/EC
Annex V Part A

ANNUAL NOTIFICATION FORMAT - SAR

Reporting country			
Reporting date 1 January-31 December (year)			
Number of serious adverse reaction(s) per type of tissue and cell (or product in contact with the tissues and cells)			
	Type of tissue/cell (or product in contact with the tissues and cells)	Number of serious adverse reaction(s)	Total number of tissues/cells of this type distributed (if available)
1			
2			
3			
4			
...			
Total			
Total number of tissues and cells distributed (including type of tissue and cell for which no serious adverse reactions were reported):			
Number of recipients affected (total number of recipients):			

Legal Basis

Directive 2006/86/EC
Annex V – Part B

ANNUAL NOTIFICATION FORMAT - SAE

Reporting country				
Reporting date 1 January-31 December (year)				
Total number of tissues and cells processed				
Total number of serious adverse events, which may have affected quality and safety of tissues and cells due to a deviation in:	Specification			
	Tissues and cells defect (specify)	Equipment failure (specify)	Human error (specify)	Other (specify)
Procurement				
Testing				
Transport				

Common Approach – Non-reproductive

SAR denominators

3.3. Number of tissues and cells of this type distributed (if available)

Article 3 (k) of Directive 2004/23/EC defines "distribution" (see Glossary).

In the annual report, the number of tissues and cells of this type distributed should be understood as 'the total number transported or delivered to a clinical unit, even if the clinical unit is in the same building or the same floor'.

If tissues and cells are returned to the Tissue Establishment (TE) without use and for subsequent redistribution, they should be counted only when subsequently redistributed.

Where tissues or cells pass from one TE to another TE before distribution, they should not be included in this total until finally distributed for clinical application.

The quantity of tissues and cells distributed by a TE could be extracted from the annual activity report that TEs submit to the CA in accordance with Article 10 of Directive 2004/23/EC. This is the national distribution activity that provides a denominator for the frequency of reactions for this type of tissue or cells.

Common Approach – non-reproductive — SAR denominators

T&C	One (1) unit equals to:
Skeletal Tissues	One individually packaged graft (e.g. one femoral head, one unit of demineralised bone, one container of bone chips, one femoral strut, one osteochondral allograft, one individually packaged tendon or part of a tendon)
Haematopoietic Stem Cells	One single bag or container of cells
Ocular Tissues	One individually packaged or contained graft (e.g. one cornea, one piece of sclera)
Cardiovascular Tissues	One individually packaged or contained graft (e.g. one valve, one package containing one or more lengths of vessel)
Skin	One container of skin, regardless of the area of skin it contains[2].
Amniotic Membrane	One container of tissue, regardless of the area of tissue it contains.

2 *If this data is recorded by cm2 in your MS, you should divide the total by the average number of cm2 included in a single package. Although this will be an estimate, it will be adequate for the purposes of providing a denominator for SAR monitoring. If you don't have data on the average number of cm2 included in a single package, please provide the total area of distributed skin in the comments box only.*

3.4. Total number of recipients for this type tissues and cells (number of recipients affected)

In the annual report, this should be understood to mean the total number of patients who had at least one unit of tissues or cells applied during the year concerned in a given country, **regardless of whether they had a reaction or not**. This is the national activity that provides a denominator for the frequency of reactions for this type of tissue or cells.

It is acknowledged that not all Member States currently collect data on the total number of patients treated with each type of tissue or cells. If this information is not available, it should be noted in the comments space provided.

Health

Common Approach – Reproductive — SAR denominators

4.3. Number of tissues and cells of this type distributed (if available)

Article 3 (k) of Directive 2004/23/EC defines "distribution" (see Glossary).

*In the annual report, **the number of tissues and cells of this type distributed** should be understood as 'the total number transported or delivered to a clinical unit, even if the clinical unit is in the same building or on the same floor'. In the ART context, it should be understood to mean the number of sperm units that have been delivered to a clinic for insemination or to a laboratory for IVF; the number of oocytes delivered to a laboratory for IVF or the number of embryos delivered to a clinic for transfer to patients.*

If gametes or embryos are returned to the Tissue Establishment (TE) without use and for subsequent redistribution, they should be counted only when subsequently redistributed.

Where tissues or cells pass from one TE to another TE before distribution for clinical use, they should not be included in this total until finally distributed for clinical application.

Health

Common Approach - Reproductive contd. SAR denominators

The quantity of gametes or embryos distributed by a TE could be extracted from the annual activity report that TEs submit to the CA in accordance with Article 10 of Directive 2004/23/EC. The following is a proposed common approach to counting units distributed:

- *one unit of **sperm** is one individual straw, the contents of which will be applied at once or*
- *one individual **embryo** or*
- *one individual **oocyte**.*

If you don't have the number of units distributed for oocytes/sperm, please provide the number of cycles only in the comments box, otherwise your data will distort the total.

This is the national distribution activity that provides a denominator for the frequency of reactions for this type of tissue or cells.

Common Approach – reproductive contd. SAR denominators

4.4. Total number of recipients for this type tissues and cells (number of recipients affected)

In the annual report, this should be understood to mean the total number of patients who had at least one unit of tissues or cells applied during the year concerned in a given country, regardless of whether they had a reaction or not. In the context of ART, this means the number of patients who have been inseminated with sperm or have had an embryo transfer. This is the national activity that provides a denominator for the frequency of reactions for this type of tissue or cells.

It is acknowledged that not all Member States currently collect data on the total number of patients treated with each type of tissue or cells. If this information is not available, it should be noted in the comments space provided.

Common Approach — SAE denominators

5.1. Total number of tissues and cells processed

Article 3(g) of Directive 2004/23/EC defines processing as 'all operations involved in the preparation, manipulation, preservation and packaging of tissues or cells intended for human applications'. In the annual report, this term refers to tissues and cells processed in TEs but not necessarily distributed. These data will allow the calculation of SAE rates in relation to numbers of tissues or cells processed in the European Union.

The total number of tissues and cells processed should be reported for non-reproductive and reproductive tissues and cells.

Extract from most recent SARE report

As in previous years, many countries acknowledged that accurate activity data for certain types of tissues and cells were difficult to collect and some of them provided incomplete numbers for SAR denominators. A few countries could not provide data as the measurement units collected at national level are not harmonised among countries and do not always correspond to those requested during the EU exercise (e.g. assisted reproduction cycles vs. 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, EL ES, FI, FR, HR, HU, IE, IT, LT, LV, MT, NL, NO, PT, SI, SE and UK) and 20 (AT, BG, CZ, DK, EE, ES, FI, FR, EL, HR, HU, IE, IT, LT, MT, NL, NO, PT, RO and SE) on recipients. For reproductive tissues and cells, 14 (AT, BE, DE, DK, EE, ES, HR, HU, IE, LV, MT, NL, SI and SE) and 10 countries (AT, BG, DK, ES, HR, IE, MT, NL, PT and SE) reported data on units distributed and number of recipients, respectively.

Extract from most recent SARE report

The overall number of *distributed* tissues and cells in 2015, as submitted by the reporting countries, amounted to 2,102,332 units (322,389 non-reproductive and 1,086,888 oocytes delivered for IVF, 455,248 sperm delivered for insemination or IVF and 235,781 embryos delivered for transfer. Additionally, 85 ovarian tissues and 1941 testicular tissue were distributed). This number had increased considerably compared to previous years – one of the reasons being that two countries reported reproductive numbers for the first time in the 2016 exercise.

The main types of non-reproductive tissues and cells distributed were skeletal tissues (192,037 units), followed by haematopoietic progenitor cells (HPC; 57,841 units) and ocular tissues (35,515 units).

From EDQM presentation to CAs – February 2017

Countries reporting

≥0

Total number of countries reporting = 30

		Non- reproductive	Reproductive
Denominators for SAR	Number of T&C distributed	24	14
	Number of recipients	20	10
	SAR	12	12
Denominator for SAE	Number of T&C processed	20	15
	SAE	18	18
	SAR in donors	8	15

CY, LI, LU and SK reported "0" tissues distributed and "0" recipients.
LI and LU also reported "0" tissues processed.

14

- **The EBMT Registry - Eoin McGrath (European Society for Blood and Marrow Transplantation; EBMT)**

EBMT European Society for Blood and Marrow Transplantation

The EBMT Registry

Mr. Eoin McGrath
on behalf of the EBMT

EU COMMISSION/EDQM TECHNICAL MEETING
NATIONAL AND EU-LEVEL TISSUE AND CELL ACTIVITY DATA COLLECTION AND REPORTING

22 -23 MARCH 2018
STRASBOURG

EBMT European Society for Blood and Marrow Transplantation

Interests

- EBMT Employee
- EBMT funded through membership fees and corporate sponsorship

EBMT
European Society for Blood and Marrow Transplantation

EBMT - non-profit organisation

Top ten countries in terms of number of centres participating in the EBMT

Our 558 centre members are located in 57 different countries

Physician 2,697
Nurse 747
Data Manager 636
Laboratory Technician 124
Quality Manager 201
Other 240

Total: 4,645

Structure based on Working Parties

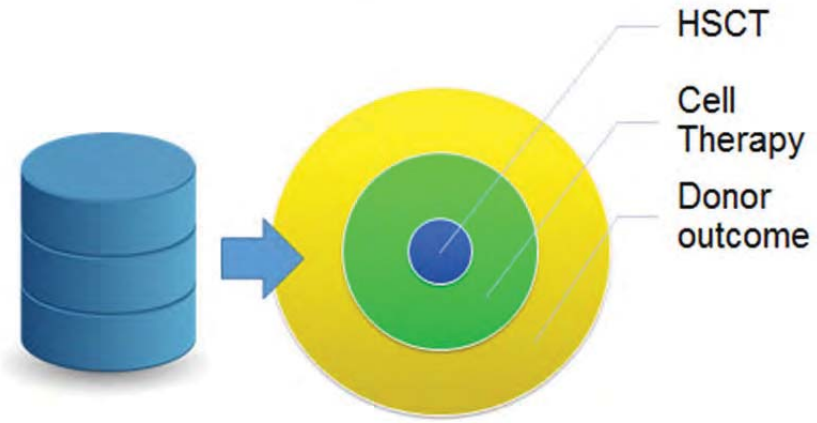
EBMT
European Society for Blood and Marrow Transplantation

The EBMT Registry

- Started early 1970's
- The single biggest data source of its kind in Europe.
- Data from >500 centres / >50 countries.
- Currently contains data on more than > 530.000 HSCT.
- Accrues >30,000 new HSCT registrations last year.

EBMT European Society for Blood and Marrow Transplantation

Registry content



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What are the interests of registry users?

Quality Control of Clinical Care	Science & Education	Market Surveillance
• Contributing centres • Donor registries • National registries • Accreditation • Benchmarking	• EBMT (Working parties, Clinical Trials) • International and national study groups	• Health authorities • Corporate sponsors

EBMT European Society for Blood and Marrow Transplantation

Governance

- The purpose of the Registry is to provide a pool of data to EBMT members to perform studies, assess epidemiological trends, and ultimately improve patients' lives.
- Registry is governed by the Head of Registry and the EBMT Executive Committee (accountable to EBMT Board and General Assembly)
- There is also a Registry Committee dedicated to Registry matters.

EBMT European Society for Blood and Marrow Transplantation

Governance

- Each EBMT centre is represented in this database and given a Centre Identification Code (CIC)
- Uers from a centre can enter, view, modify, obtain reports and download their own data once the necessary permissions have been granted by the Principal Investigator of the centre.
- All EBMT member centres can obtain

Frequency of collection and period covered

- Day 0
- Day 100
- Annual follow-up until death

- Data can be entered in real-time

- Data collection is labour intensive and requires knowledge of transplantation

Frequency

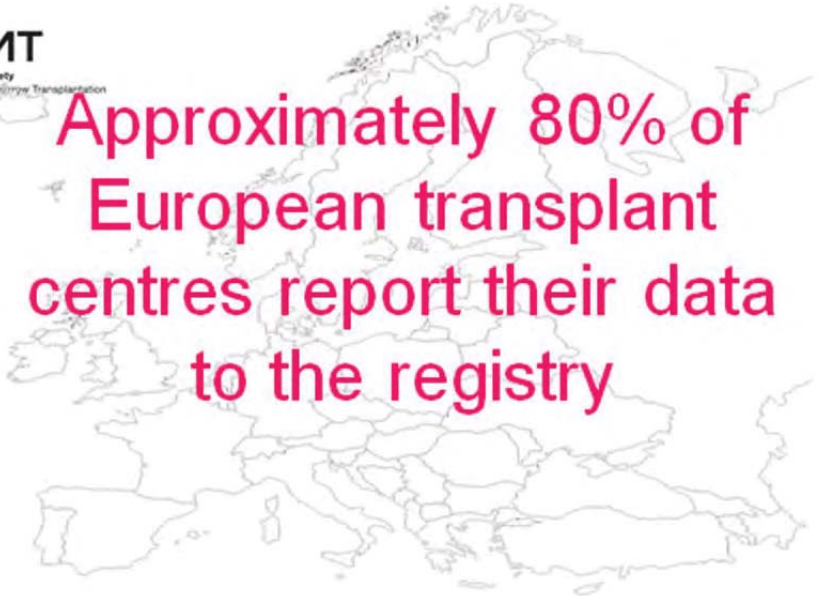
- In **technical** terms, the frequency of data collection is entirely open to discussion.
  - Frequency can be increased or decreased as need.
- In **practical** terms, frequency must take into account the real capacity of centres to report – high frequency may be very challenging to centres unless they had very strong support.
  - Increased frequency of reporting should be clearly justified and resourced as necessary

EBMT European Society for Blood and Marrow Transplantation

Data sources

- Transplant centres
- National Registries
- Data provided for **FREE** to EBMT
  - Centre can continue to access data and use for own purposes
  - Strong collaborative spirit
  - Common need to achieve critical mass of data to be meaningful

EBMT European Society for Blood and Marrow Transplantation



EBMT European Society for Blood and Marrow Transplantation

Geographical coverage

- Based on 2016 activity survey, 4% (20) of EU centres not reporting to the EBMT registry = approximately 1% (460) of the total transplants reported to that survey.
- Of these centres, the average total autologous transplants reported to the survey were 18 (min 0-max 43) compared to 34 (min 0-max 178) in centres reporting to the Registry.

EBMT European Society for Blood and Marrow Transplantation

Quality control

- Database with internal quality controls
- Over 4000 triggers control the accuracy and internal consistency of what is entered in the database at the point of entry
- Data quality **reports** can be run by users at any point to check for missing or unusual data
- Regular follow-up requests issued by the Registry and Study Offices
- Periodic queries on missing / incorrect data and follow-up requests
- Missing data is queried in the context of studies from the Registry and Study Offices to the centres
- Statistical analyses allow to detect bias, data quality and unusual trends
- Statistical guidelines

EBMT European Society for Blood and Marrow Transplantation

Privacy, confidentiality, data protection

- Secure central server based in The Netherlands (Leiden Univ.)
- Subjects consent to their data being sent to the EBMT
- Data are pseudo-anonymised (full anonymity would preclude Registry)
- Centres can control the data at all times, restricting access should they wish
  - By subject
  - By specific characteristics
  - For a specific length of time
- Specific items can be hidden for specific users

EBMT European Society for Blood and Marrow Transplantation

Consent

- Patients own their data
- With regard to the CONTROL of the data, EBMT has full freedom to operate with regard to the data in the registry, only restricted by applicable legislative and ethical rules.
  - Based on legal advice
- Regarding access policies, EBMT refers to its 'Registry Function' policy, v. 5.1, especially chapter 4.2.
  - www.ebmt.org/Contents/Data-Management/Documents/EBMTRegistryFunction.pdf

Consent

- It is the responsibility of the individual centres or donor registries submitting data to the EBMT to make certain that the respective national laws are followed before submitting the data.
- It is the responsibility of the EBMT to ensure that centres and donor registries are aware of this.
- The EBMT requests that all centres outside the EU sign an EU Regulations Statement declaring they will follow EU regulations regarding data safety.
  - If a centre fails to provide the EBMT with this declaration, the data can be kept, but that centre cannot be allowed access to the Registry through ProMISe, not even for its own data.
- It is the EBMT's legal responsibility to ensure that no access is given to centres which have failed to provide this declaration.
- EBMT is actively adapting to the GDPR requirements

Consent

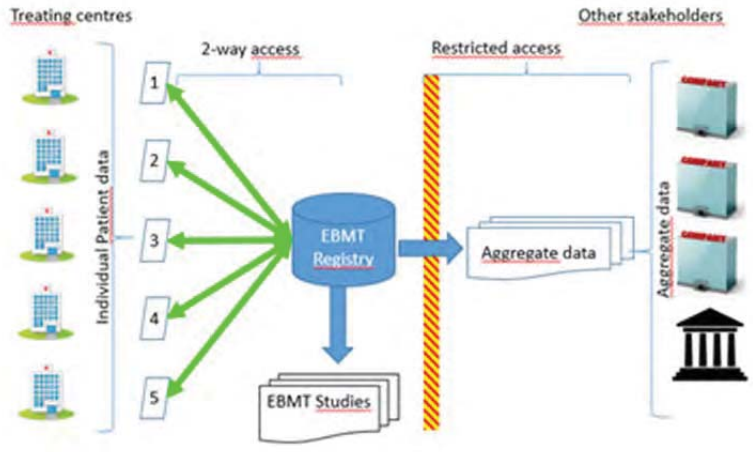
- EBMT members commit to reporting their data to the EBMT as part of their membership obligations.
- EBMT monitors centres' reporting annually.
  - If a member is found to have not reported for more than two years, they are demoted from full to associate members with the consequent loss of voting rights in the society and blocked from participation in studies.
- If a centre is reporting data as part of a funded study, they will not receive payment(s) per patient reported.
  - Note – sponsors do not report data, centres do.

EBMT European Society for Blood and Marrow Transplantation

Consent

- All centres inside and outside the EU must obtain informed consent from their patients and/or donors before the data can be submitted to the EBMT.
- This informed consent must explicitly state that the data is to be kept in an "international" database and can be exported to a non-EU/EEA country.
  - This is to avoid misunderstandings pertaining to the data being kept in a national database or even in an EU database.
- It is the legal responsibility of the member institution to ensure this is the case for all data submitted to the EBMT.

EBMT European Society for Blood and Marrow Transplantation



Data sharing

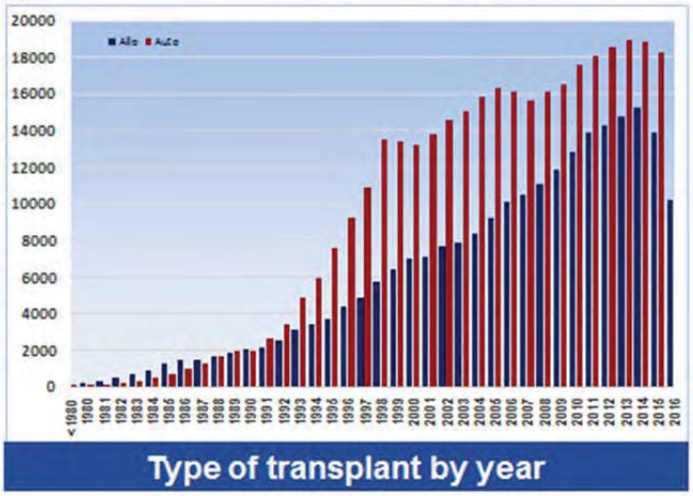
- EBMT members including corporates can obtain aggregate anonymised data where neither the patient nor the centre are identifiable as part of their contract.
- Corporates cannot obtain outcome data.
- To safeguard centre anonymity, all countries with less than ten member centres appear under the label of "Other".
- Regulators can be given access on request by the centre(s) providing the data
  - National registries could supply regulators with data extracted from the Registry

Requesting new elements/fields

- Technically speaking, there is no limit on the number of elements that can be included.
- Constraints are the complexity of the element itself and its impact on the rest of the form(s) which can affect the time required in order to implement additional elements.
- Consideration should also be given to the capacity of centres to provide the additional data.

EBMT European Society for Blood and Marrow Transplantation

Number of HSCT: Allografts and autografts by year



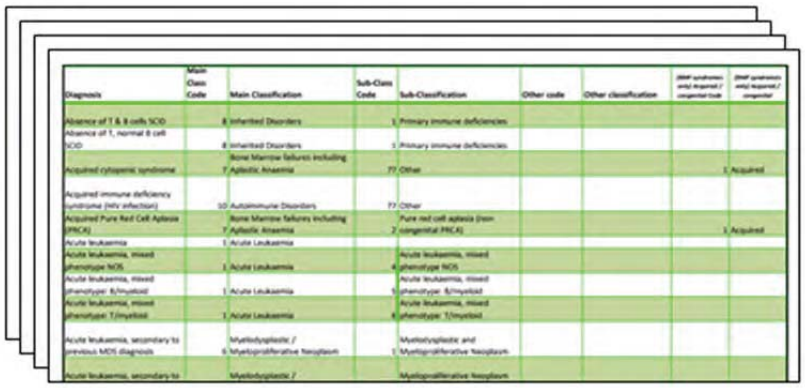
EBMT European Society for Blood and Marrow Transplantation

Diseases

Disease	Patients	Transplants
Acute leukaemias: AML	79,683	87,517
Acute leukaemias: ALL	45,504	49,071
Acute leukaemias: other/unknown	2,859	3,177
Chronic leukaemias: CML	21,488	23,138
Chronic leukaemias: CLL	6,655	7,324
Chronic leukaemias: other/unknown	903	999
Lymphomas: NHL	97,347	108,174
Lymphomas: Hodgkins	33,003	38,226
Lymphomas: other/unknown	1,573	1,786
Multiple myeloma/Plasma cell disorders	113,345	153,070
Solid tumours	41,504	56,221
Myelodysplastic/Myeloproliferative	29,626	33,194
Bone marrow failure	12,238	13,500
Primary immune deficiency	5,338	6,031
Inborn errors: other / unspecified	2,298	2,593
Histiocytic	1,354	1,485
Autoimmune diseases	2,261	2,316
Haemoglobinopathies	5,990	6,303
Other/unknown	240	276
Total:	503,309	594,401

EBMT European Society for Blood and Marrow Transplantation

Disease synonyms and sub classifications

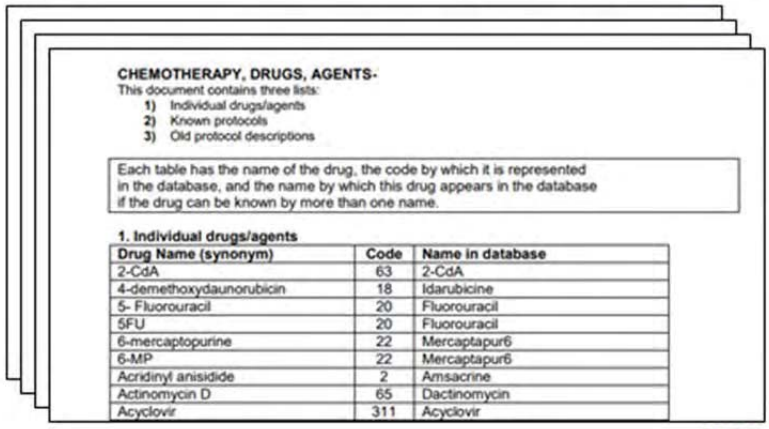


Diagnosis	Main Class Code	Main Classification	Sub-Class Code	Sub-Classification	Other code	Other classification		
Absence of T & B cells SCID	8	Inherited Disorders	1	Primary immune deficiencies				
Absence of T, normal B cell SCID	8	Inherited Disorders	1	Primary immune deficiencies				
Acquired cytopenic syndrome	7	Bone Marrow failures including Aplastic Anaemia	77	Other				1 Acquired
Acquired immune deficiency syndrome (HIV infection)	10	Autoimmune Disorders	77	Other				
Acquired Pure Red Cell Aplasia (PRCA)	7	Bone Marrow failures including Aplastic Anaemia	2	Pure red cell aplasia (non congenital PRCA)				1 Acquired
Acute leukaemia	1	Acute Leukaemia						
Acute leukaemia, mixed phenotype NOS	1	Acute Leukaemia	4	Acute leukaemia, mixed phenotype NOS				
Acute leukaemia, mixed phenotype: B/myeloid	1	Acute Leukaemia	5	Acute leukaemia, mixed phenotype: B/myeloid				
Acute leukaemia, mixed phenotype: T/myeloid	1	Acute Leukaemia	6	Acute leukaemia, mixed phenotype: T/myeloid				
Acute leukaemia, secondary to previous MDS diagnosis	9	Myelodysplastic / Myeloproliferative Neoplasm	1	Myelodysplastic and Myeloproliferative Neoplasm				
Acute leukaemia, secondary to		Myelodysplastic /		Myeloproliferative Neoplasm				

21 pages

EBMT European Society for Blood and Marrow Transplantation

Chemotherapy, Drugs, Agents



CHEMOTHERAPY, DRUGS, AGENTS-

This document contains three lists:

1) Individual drugs/agents
2) Known protocols
3) Old protocol descriptions

Each table has the name of the drug, the code by which it is represented in the database, and the name by which this drug appears in the database if the drug can be known by more than one name.

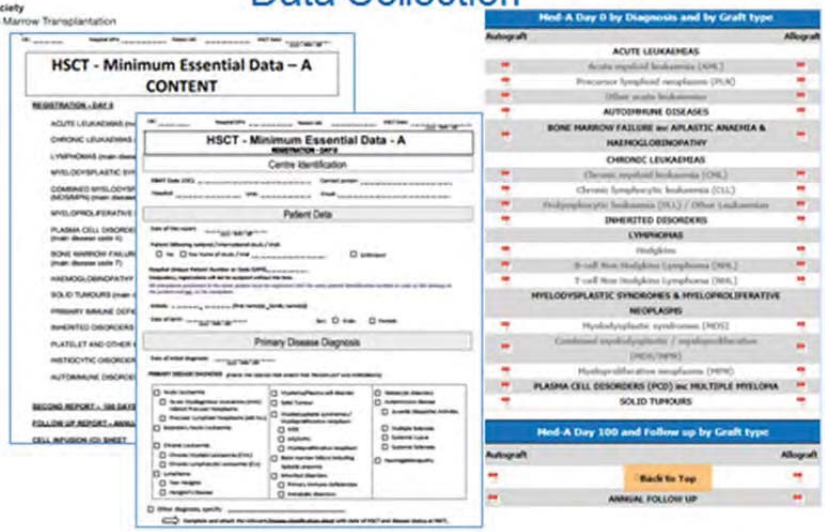
1. Individual drugs/agents

Drug Name (synonym)	Code	Name in database
2-CdA	63	2-CdA
4-demethoxydaunorubicin	18	Idarubicine
5- Fluorouracil	20	Fluorouracil
5FU	20	Fluorouracil
6-mercaptopurine	22	Mercaptapur6
6-MP	22	Mercaptapur6
Acridinyl anisidide	2	Amsacrine
Actinomycin D	65	Dactinomycin
Acyclovir	311	Acyclovir

19 pages

EBMT European Society for Blood and Marrow Transplantation

Data Collection



EBMT European Society for Blood and Marrow Transplantation

Minimum Essential Data Day 0

- 10 pages of common information
- Dedicated forms for diseases

EBMT European Society for Blood and Marrow Transplantation

Minimum Essential Data Day 0

- Centre identification
- Patient data
- Primary disease diagnosis
- Comorbidity index
- Type of transplant (autologous/allogeneic)
- Donor data
- Donor product data
- HLA typing
- Preparative regime
- Survival status

EBMT European Society for Blood and Marrow Transplantation

Minimum Essential Data Day 100

- 5 pages of common information


HSCT - Minimum Essential Data - A
SECOND REPORT - 100 DAYS AFTER HSCT
Disease
Centre Identification
Patient Data
Recovery

EBMT European Society for Blood and Marr

Minimum Essential Data Day 100

- Centre identification
- Patient data
- Recovery
- Acute GvHD
- Additional cell infusions
- Additional disease treatment
- Best response
- Last contact data for 100-d assessment
- Chronic GvHD
- Relapse/Progression
- Relapse of Leukaemias
- Disease assessment
- Survival status

EBMT European Society for Blood and Marrow Transplantation

Minimum Essential Data Annual Follow-up

- 5 pages of common information


HSCT - Minimum Essential Data - A
FOLLOW UP REPORT - ANNUAL
Disease
Centre Identification
Patient Data
Date of Last Contact
Best response after HSCT (CLL & Myeloma only)

EBMT European Society for Blood and Marrow Transplantation

Minimum Essential Data Annual Follow-up

Disease	Centre identification	Patient data	Date last contact
Best response after transplant	Complications	Secondary malignacy	Additional Disease Treament including Cell Therapy
Relapse/Progression	Last disease status	Pregnancy after transplant	Survival status

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Minimum Essential Data - Annual Follow-up – Cell Infusion Sheet

- 1 page of common information
  - Revised Jan 2018


HSCT - Minimum Essential Data - A
FOLLOW UP REPORT - ANNUAL

EBMT European Society for Blood and Marrow Transplantation

MED-B forms –Allo / Auto

- More detailed reporting
- Research-grade
- Submitted spontaneously by minority of centres - used for studies


FOR ALL DISEASES

MED-B ALLOGRAFT REGISTRATION – DAY 0

PATIENT

EBMT European Society for Blood and Marrow Transplantation

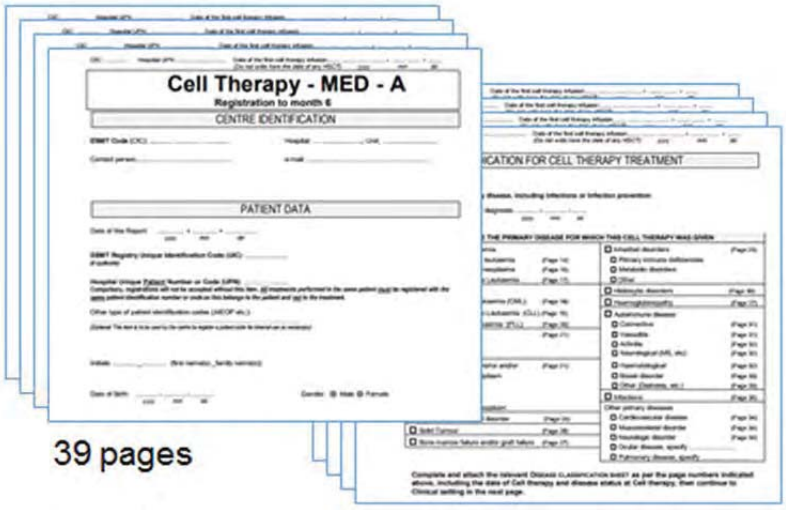
Cellular Therapy & Immunobiology Working Party and Cell Therapy Registry

- The Cell Therapy Registry (CTR) aims to collect data on stem cells, progenitors or mature cells, such as T-lymphocytes, unmanipulated, such as DLI, or sorted and/or cultured and/or genetically manipulated, such as CAR-T cells, used for treatment in combination with hematopoietic stem cell transplantation or alone, and including advanced therapeutic medicinal products (ATMP), as well as data on the clinical characteristics and outcome of the patients.

- The new form also collects details of laboratory manipulation for all types of cells before they are infused into the patient. They include: selection, modification, genetic engineering and others.

EBMT European Society for Blood and Marrow Transplantation

Cell Therapy data collection form



EBMT European Society for Blood and Marrow Transplantation

Cell Therapy Minimum Essential Data – to month 6

Centre identification	Patient data	Indication for Cell Therapy	Therapy
Donor	Cell Therapy Infusion Unit •Description & collection •Manipulation	Therapy and infusion(s)	Response
Last contact date	Toxicity in first 6 m	Secondary malignancy	Graft assessment
First replase/progression	Last disease status	Survival status	Persistence of cells

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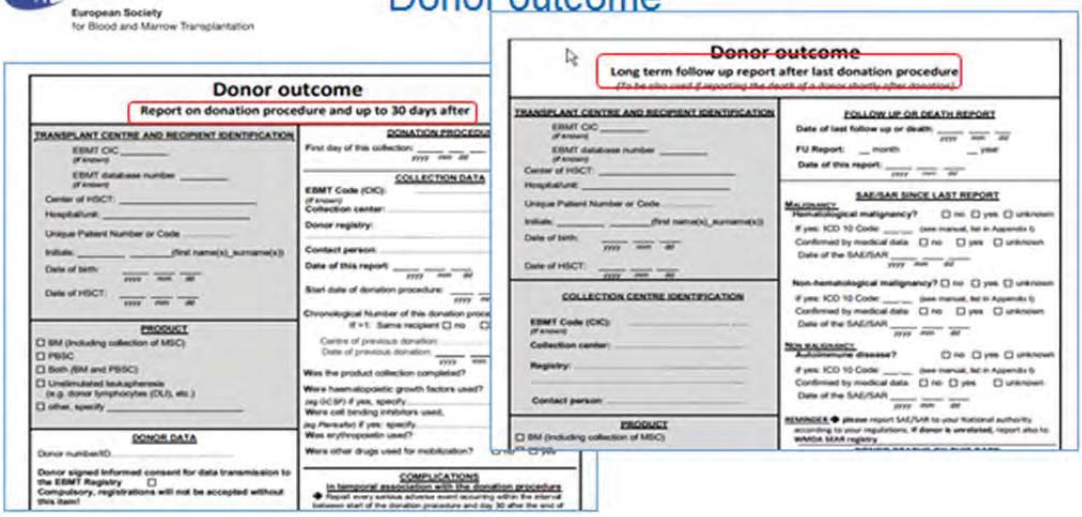
Donor outcome



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Donor outcome form content

Examples:

- SAE at donation
- Length of follow up
- Status on date last seen
- SAE during follow up
  - haematological malignancy
  - non-haematological malignancy
  - autoimmune disease
- Intention to donate again

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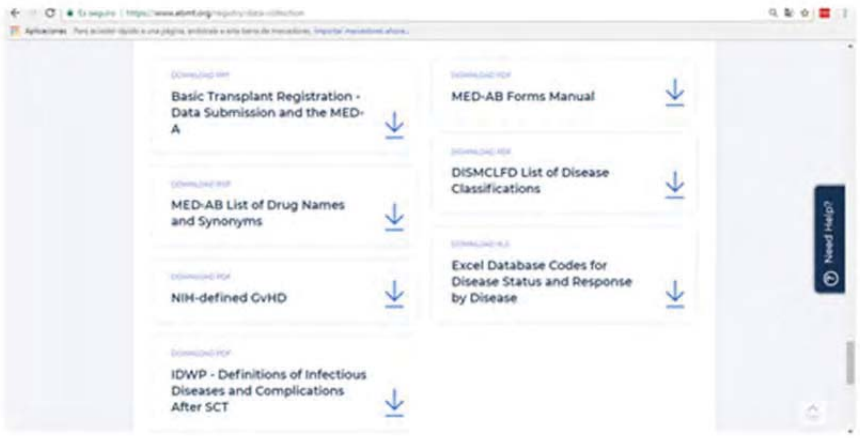
Glossary of definitions



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Data quality is maintained by

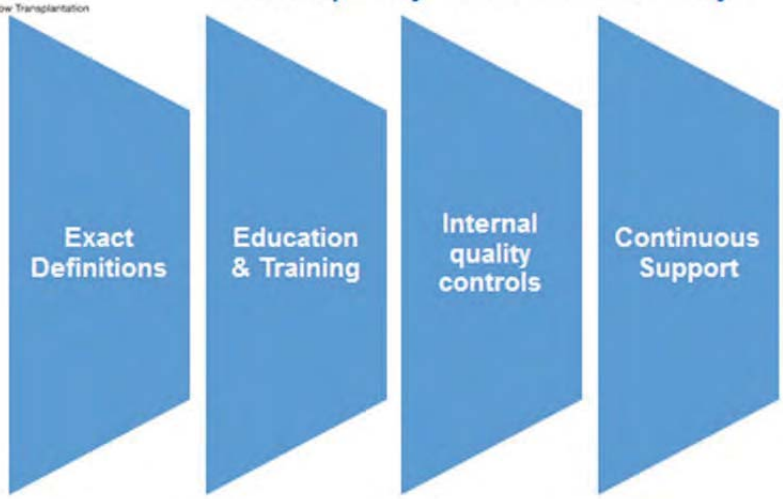

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Table 1 Examples of system triggers

Data entry user action	Message	Action
On attempting to enter a diagnosis that already exists in the patient	A similar diagnosis has already been registered for this patient with another date	Block data entry
On changing the type of transplant from allogeneic to autologous in the presence of donor information	There is a donor record in the Donor table. Please, remove it if the transplant is autologous.	Block data entry
On attempting to say that the patient is in complete remission or relapse from complete remission when a previous entry indicates that the patient had never achieved complete remission	Complete remission achieved in the past has been answered as No, therefore patient cannot be either in CR or in relapse	Block data entry
On attempting to say that the patient is in complete remission at transplant when the responses to previous treatments have not been answered or are not CR	You have not indicated a CR as a previous status after treatment	Warning only, as it is possible that a last treatment with its response has not been entered.
On attempting to enter an episode of cGvHD before 100 days have elapsed since the allograft.	This date is within 100 days from last allograft	Warning only, since it is possible to have cGvHD within a 100 days even if it would be very rare.
On attempting to enter a syngeneic donor with a different sex to the patient	Identical twin and yet patient and donor sex are different	Block data entry
On attempting to enter a date of chimerism testing that precedes the transplant	Chimerism test cannot be before the HSCT	Block data entry

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Patient consent & EU regulations

EBMT MEMBERSHIP APPLICATION FORM
Full Membership

COMMITMENT:

I confirm that I will comply with the Data Directive 95/46/EC in all aspects relating to the transfer of data to the EBMT. In particular, I confirm that all patients whose registrations are being forwarded to the EBMT have given consent for the data to be sent to the EBMT by signing a Patient Consent Form for Data Registration.

In case the patient does not consent for his/her data to be transmitted to the EBMT,
please provide –for auditing and accreditation purposes-:
- Diagnosis
- Date of HSCT
- Type of HSCT
- Chronological number of HSCT

Consent to transfer data outside the European Economic Area must be explicitly obtained if the centre requests the EBMT to transfer data to institutions not located in this area.

44

Other Registry-related aspects

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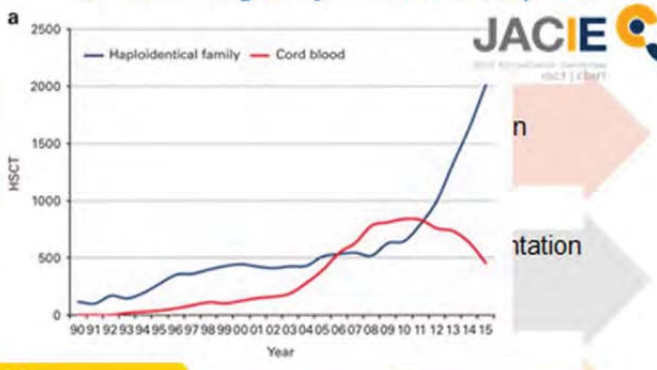
JACIE



Non-Interventional Studies

- Investigator or Pharma-initiated
- No interference in treatment
- Post-marketing follow-up

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Donor outcome form content

Examples:

- SAE at donation
- Length of follow up
- Status on date last seen
- SAE during follow up
  - haematological malignancy
  - non-haematological malignancy
  - autoimmune disease
- Intention to donate again

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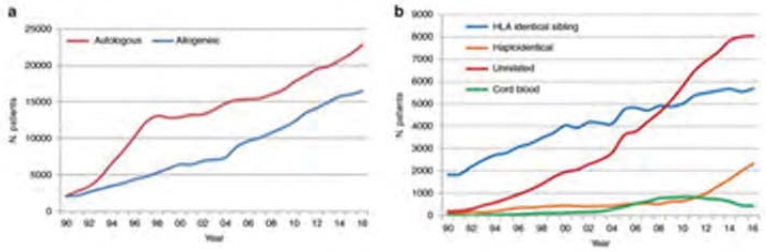
Activity survey

Bone Marrow Transplantation
https://doi.org/10.1038/s41409-018-0153-1

ARTICLE

Is the use of unrelated donor transplantation leveling off in Europe? The 2016 European Society for Blood and Marrow Transplant activity survey report

Jakob R Passweg[1] · Helen Baldomero[1] · Peter Bader[2] · Grzegorz W. Basak[3] · Chiara Bonini[4] · Rafael Duarte[5] · Carlo Dufour[6] · Nicolaus Kröger[7] · Jürgen Kuball[8] · Arjan Lankester[9] · Silvia Montoto[10] · Arnon Nagler[11] · John A. Snowden[12] · Jan Styczynski[13] · Mohamad Mohty[14] for the Eurpoean Societv for Blood and Marrow



Bone Marrow Transplantation (2017) 52, 811 – 816

www.nature.com/bmt

EB European for Blood a

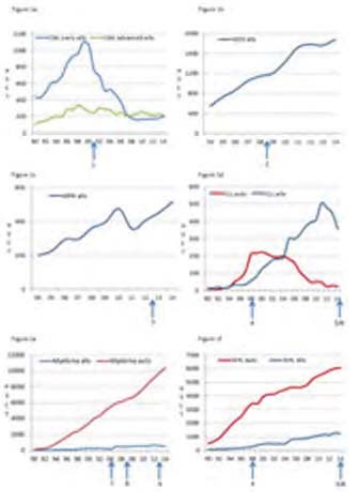
SPECIAL REPORT

Impact of drug development on the use of stem cell transplantation: a report by the European Society for Blood and Marrow Transplantation (EBMT)

(R Passweg, H Baldomero, P Bader, C Bonini, S Cesaro, P Dreger, MF Duarte, C Dufour, J Kuball, D Farge-Bancel, N Kröger, F Lanza, A Nagler and M Mohty for the European Society for Blood and Marrow Trans (EBMT)

Data base offers a neutral ecosystem for monitoring the impact of novel drugs on treatment choices

Drugs:
1 imatinib, 2 azacitidine, 3 ruxolitinib,
4 rituximab, 5 ibrutinib, 6 idelalisib,
7 bortezomib, 8 lenalidomide,
9 pomalidomide



EBMT European Society for Blood and Marrow Transplantation

PROJECT 2020: CONTINOUS STRUCTURAL IMPROVEMENT of the Registry

1. DATA QUALITY
2. EFFICIENCY
3. BENCHMARKING SURVIVAL OUTCOMES
4. ENHANCE COLLABORATION
5. LAWS AND REGULATION
6. DATA ENRICHMENT

€1.5 million Budget approx.
(¡CHALLENGING!)

ELSEVIER

MACRO
Advanced data collection for clinical research

EBMT European Society for Blood and Marrow Transplantation

More information
www.ebmt.org

eoin.mcgrath@ebmt.org

EBMT European Society for Blood and Marrow Transplantation

Closing remarks

- Data as integral part of therapy
- Mantra: Collect data once, use it often
- EBMT open to sharing
- Registries cost money €€€

EBMT European Society for Blood and Marrow Transplantation

- **European IVF-Monitoring (EIM) of the European Society of Human Reproduction and Embryology - Christian De Geyter (European Society of Human Reproduction and Embryology; ESHRE)**

eshre
SCIENCE MOVING PEOPLE MOVING SCIENCE

European IVF-Monitoring (EIM) of the European Society of Human Reproduction and Embryology (ESHRE)

Ch. De Geyter

Current chair of the EIM-Steering Committee

eshre
SCIENCE MOVING PEOPLE MOVING SCIENCE

- ESHRE is a multidisciplinary society dealing with reproductive medicine and embryology.
- It was initiated in 1985 by Robert Edwards (UK) and Jean Cohen (F).
- Since 1985 ESHRE organizes annually an international scientific meeting, but also dedicated seminars and workshops.
- Topics: reproductive endocrinology, medical ethics, andrology, psychology, endometriosis, early pregnancy, reproductive surgery, quality management in assisted reproductive medicine, reproductive genetics and stem cells.

EIM

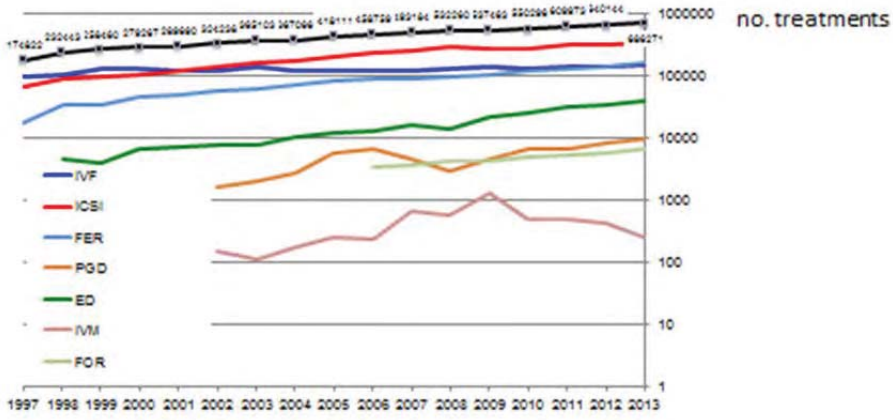
- The European IVF Monitoring Programme was established in 1999 to collect, process and publish European data on clinical results and side-effects of assisted reproductive technology (ART), follow-up of children's well-being but also the availability and structure of services in the various European countries.
- The EIM is a „bottom up"-type of data collection assembling the representatives of the national registries of almost all European countries.
- The data collection is not exhaustive, as the standards of data reporting are very different in the different participating countries: in some countries data reporting on assited reproduction is mandatory, in others voluntary.
- Notwithstanding these hurdles, the number of participating countries has risen from 18 in 1997 to 38 in 2013 (out of 51 European countries).

EIM ESHRE 2013

Which are the treatments in ART being recorded?

- In vitro fertilisation (IVF)
- Intracytoplasmic sperm injection (ICSI)
- Frozen/Thawed embryo transfer (FER)
- Frozen/Thawed oocyte treatment (FOR)
- Oocyte donation (ED)
- In vitro maturation (IVM)
- Preimplantation genetic testing (PGT)
- Gonadal tissue freezing, postpubartal
- Gonadal tissue freezing, prepubertal

Surveillance



IVF: in vitro Fertilisation
ICSI: intracytoplasmic sperm injection
FER: frozen thawed embryo replacement
PGD: preimplantation genetic diagnosis
ED: oocyte donation
IVM: in vitro maturation
FOR: social freezing

since 1999: 17 reports

Human Reproduction, Vol.29, No.10 pp. 2099–2113, 2014
Advanced Access publication on July 27, 2014 doi:10.1093/humrep/deu175
human reproduction ESHRE PAGES

Assisted reproductive technology in Europe, 2010: results generated from European registers by ESHRE†

Human Reproduction, Vol.31, No.2 pp. 233–248, 2016
Advanced Access publication on January 5, 2016 doi:10.1093/humrep/dev319
human reproduction ESHRE PAGES

Assisted reproductive technology in Europe, 2011: results generated from European registers by ESHRE†

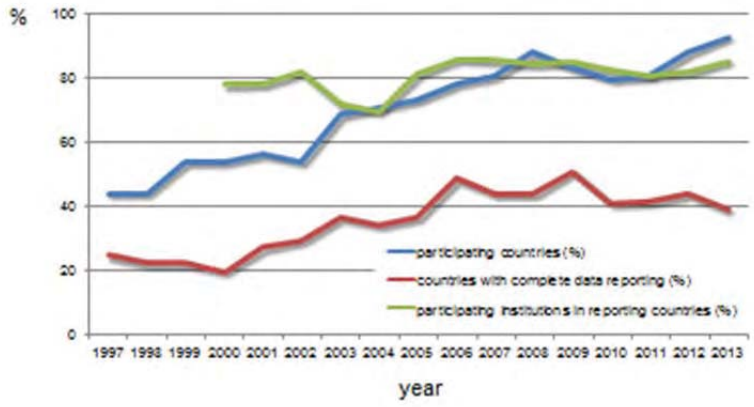
Human Reproduction, Vol.31, No.8 pp. 1638–1652, 2016
Advanced Access publication on June 19, 2016 doi:10.1093/humrep/dew151
human reproduction ESHRE PAGES

Assisted reproductive technology in Europe, 2012: results generated from European registers by ESHRE‡

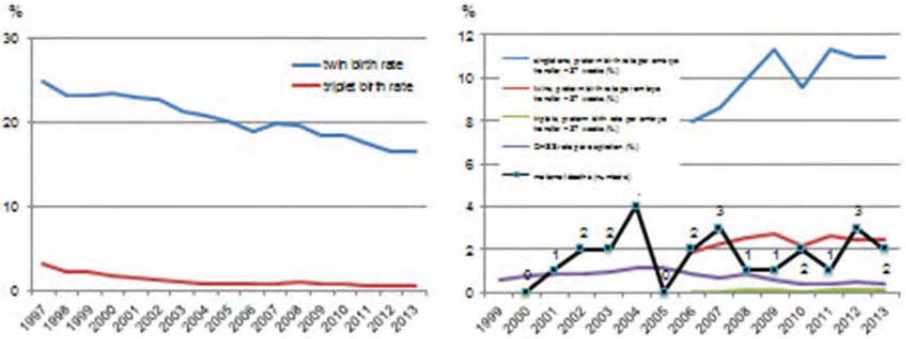
The European IVF-Monitoring Consortium (EIM)‡ for the European Society of Human Reproduction and Embryology (ESHRE)

C. Calhaz-Jorge*, C. de Geyter, M.S. Kupka, J. de Mouzon, K. Erb, E. Mocanu, T. Motrenko, G. Scaravelli, C. Wyns, and V. Goossens

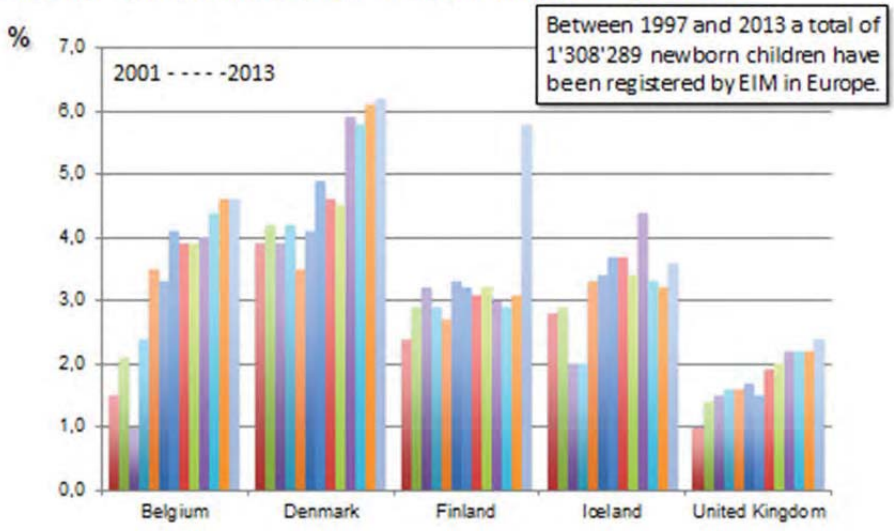
The rising degree of completeness of collected data sets



Vigilance



Number of newborns born after ART with respect to overall number of newborns born in five European countries



Data extracted from the EIM reports 2001 to 2013

Human Reproduction, Vol.31, No.10 pp. 2160–2163, 2016
Advanced Access publication on September 2, 2016 doi:10.1093/humrep/dew199

human reproduction OPINION

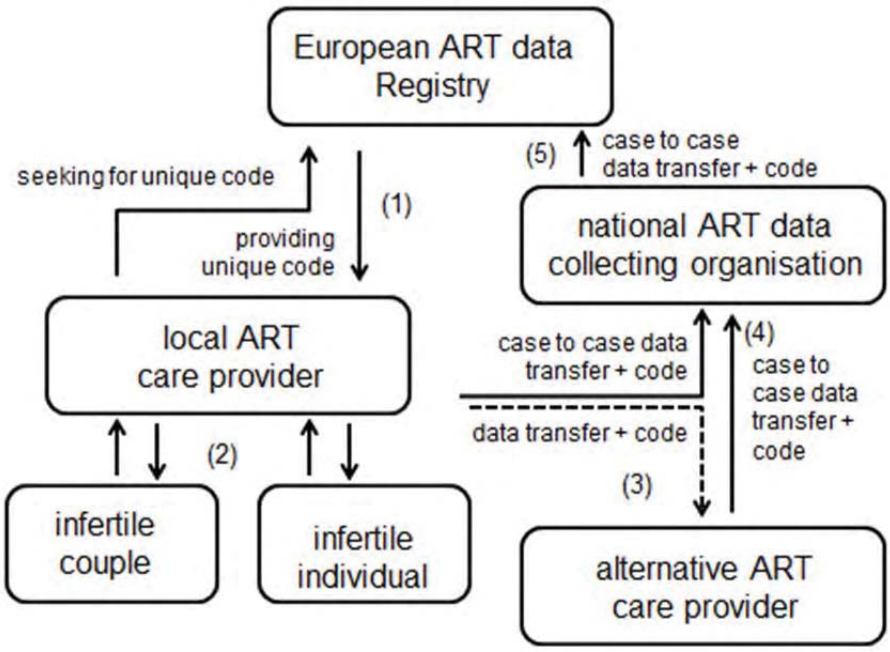
Data collection systems in ART must follow the pace of change in clinical practice

Ch. De Geyter[1,*], C. Wyns[2], E. Mocanu[3], J. de Mouzon[4], and C. Calhaz-Jorge[5]

[1]Clinic of Gynecological Endocrinology and Reproductive Medicine, University Hospital, University of Basel, Basel, Switzerland [2]Clinique universitaire Saint-Luc, UCL, Brussels, Belgium [3]ACCI Unit, Rotunda Hospital, Dublin, Ireland [4]INSERM, Paris, France [5]Departamento de Obstetrícia, Ginecologia e Medicina da Reprodução, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal

- The role of cryostorage of gametes, embryos and gonadal tissues is rising.
- The duration of storage of that material is increasing.
- Due to population mobility there is an rising trend for transport of this material.
- Cross-sectional data collection and analysis (once every year) does not reflect medical reality any more.
- We should start to collect data on collected, used and stored material prospectively, aiming at analyzing the data sets in a cumulative fashion.

Hum. Reprod. (2016) 31: 2160-2163



ANNEX VII

THE STRUCTURE OF THE SINGLE EUROPEAN CODE SEC

DONATION IDENTIFICATION SEQUENCE			PRODUCT IDENTIFICATION SEQUENCE			
EU TISSUE ESTABLISHMENT CODE		UNIQUE DONATION NUMBER	PRODUCT CODE		SPLIT NUMBER	EXPIRY DATE (YYYYMMDD)
ISO country code	Tissue establishment number		Product Coding System identifier	Product number		
2 alphabetic characters	6 alpha-numeric characters	13 alpha-numeric characters	1 alphabetic character	7 alpha-numeric characters	3 alpha-numeric characters	8 numeric characters

The SEC Code may provide a mean to install a „top down" data collection including a prospective data collection continued over time and with well defined outcome parameters.

Our vision

- The EU and ESHRE should collaborate to set the stage for a prospective cycle by cycle prospective data collection in reproductive medicine for Europe.
- This system should be developed towards true surveillance and vigilance in assisted reproductive medicine.
- We should also think about how to include paediatric medicine for the follow-up of the children.

Benchmarking and Audit by EBA - George Galea (European Blood Alliance; EBA)

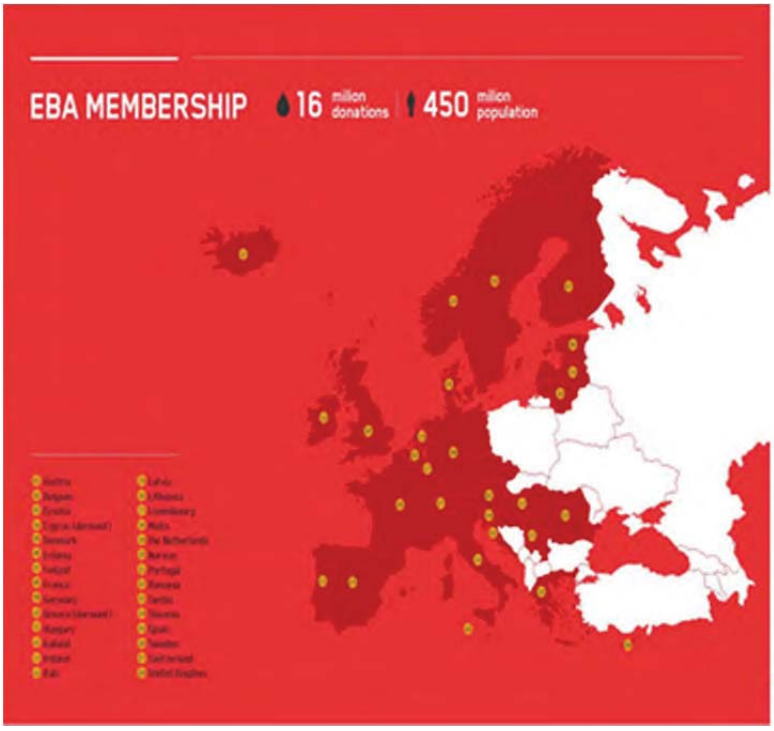
EUROPEAN BLOOD ALLIANCE

Benchmarking and Audit by EBA

A journey

Dr George Galea
Chair EBA Tissue and cells Working group ***Strasbourg 2018***

Safe blood for Europe



Safe blood for Europe

Mission of EBA

"To contribute to the safety, security and cost effectiveness of the blood and tissue and cell supply for the citizens of Europe by developing and maintaining an efficient and strong collaboration amongst European blood and tissue and cell services".

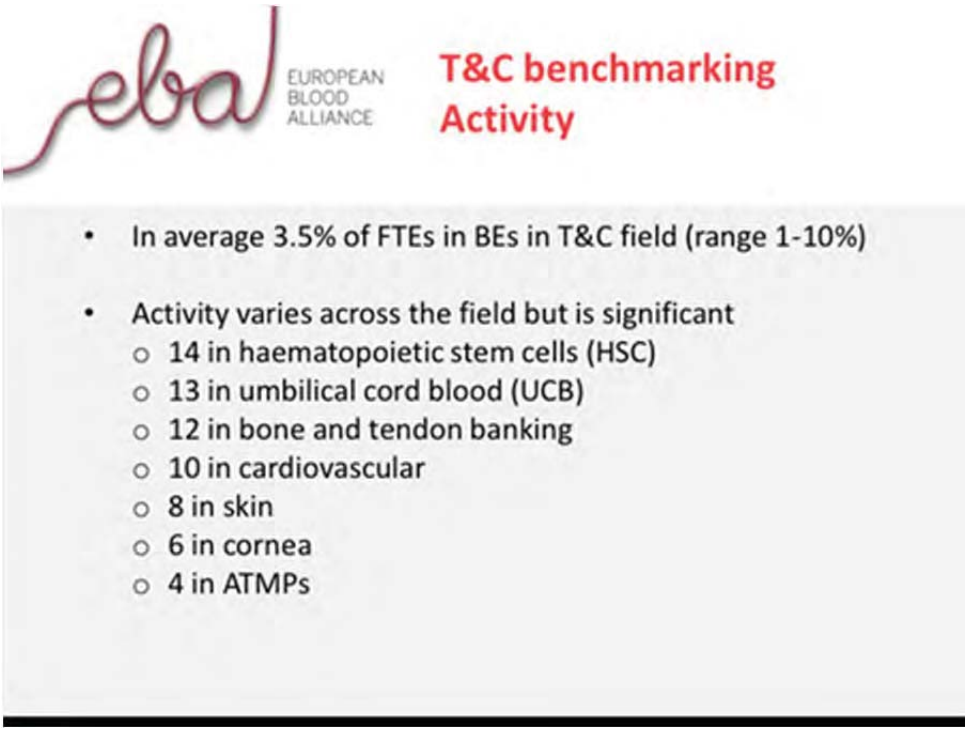
Audits started 10 years ago

Establish tissue and cell activity within EBA Blood services

Initial Top level Questionnaire

Annual questionnaire for the past 7 years

Safe blood for Europe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ALLIANCE
T&C benchmarking
Activity
In average 3.5% of FTEs in BEs in T&C field (range 1-10%)
Activity varies across the field but is significant
14 in haematopoietic stem cells (HSC)
13 in umbilical cord blood (UCB)
12 in bone and tendon banking
10 in cardiovascular
8 in skin
6 in cornea
4 in ATMPs


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BLOOD
ALLIANCE
Questions asked:
FTE
Infectious disease markers and Tests used
Activity:
Number of donors (deceased/live)
Number of units received for processing and storage
Number of units imported from another TE in your country
Number of units imported from another TE from outside your country EU/non EU
Safe blood for Europe

Number of tissues stored

Number of tissues issued or grafting from your bank in your own country

Number of tissues issued for export (outside your country)

Number of tissues discarded by the bank prior to issue

Number of tissues in stock at the end of the year

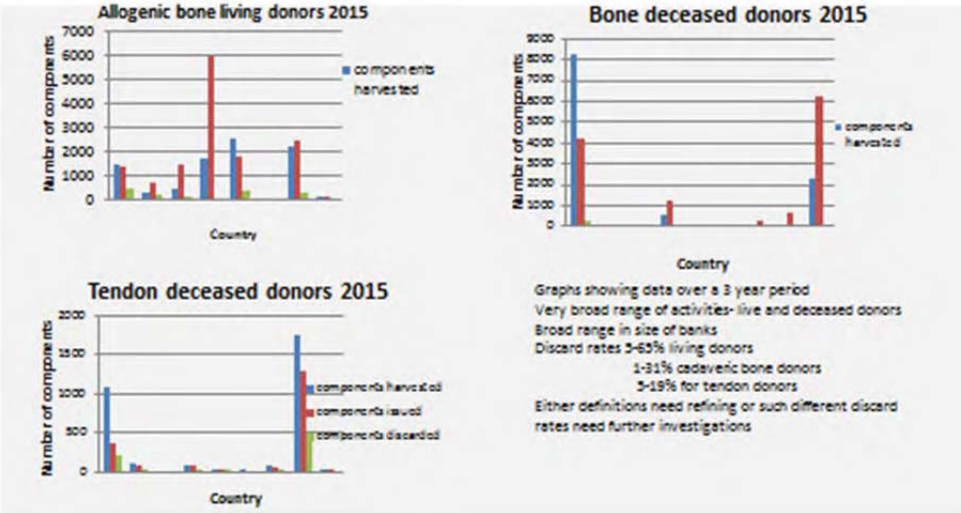
Safe blood for Europe

Analysis of data received

COUNTRY	Inf disease	ATMPs	Bones and tendons	CVS	HSC	UCB	Corneas	Skin	Others	FTEs
	NR	NR	NR	NR	x	NR	NR	NR	NR	x
	NR	NR	NR	NR	NR	x	NR	NR	NR	x
	x	NA	X (incomplete)	x	NA	NA	X (incomplete)	NA	x	X
	NR	NR	X (queries)	x	X(incomplete)	X(incomplete)	X(incomplete)	x	X(?incomplete)	x
	x	X(CPH)	x	NR	x	NR	NR	NR	x	x
	NR	NR	X	x	X(incomplete)	x	x	NR	NR	NR
	X	x	X	x	x	x	X(incomplete)	X(inc)	x	x
	X	NR	X(incomplete	X (inc)	x	NA	X(incomplete)	x	NR	X(queries)
	X	NR	NA	NR	x	NA	NR	NR	NR	x
	NR	x	x	NR	x	x	NR	NR	NR	x
	x	NA(queries)	x	x	x	NA	NR(queries)	x	x	x
	X	NA(queries)	X(queries)	x	x	x	X(queries)	x	x	X(queries)
	NR	NR	x	x	x	x	x	x	x	x
	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

EUROPEAN BLOOD ALLIANCE

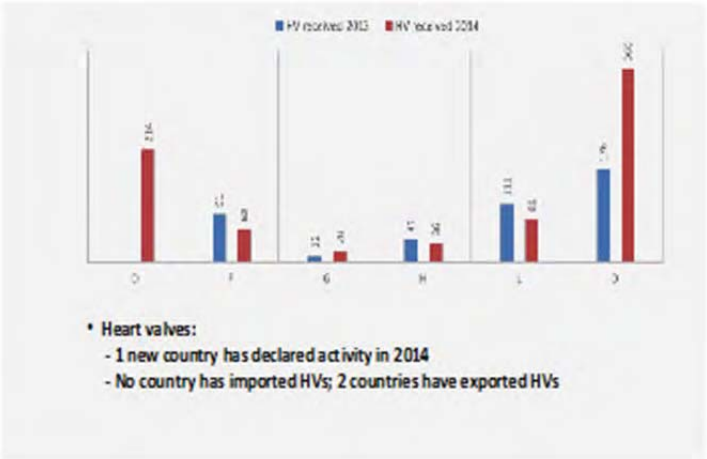
Musculoskeletal activity



Graphs showing data over a 3 year period
Very broad range of activities- live and deceased donors
Broad range in size of banks
Discard rates 5-65% living donors
1-31% cadaveric bone donors
5-19% for tendon donors
Either definitions need refining or such different discard rates need further investigations

EUROPEAN BLOOD ALLIANCE

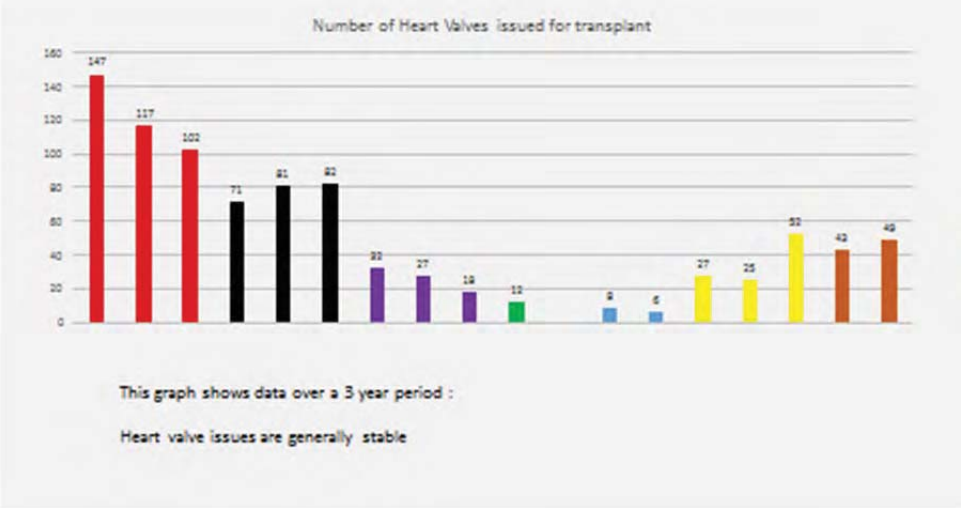
T&C benchmarking
Heart valves



- Heart valves:
  - 1 new country has declared activity in 2014
  - No country has imported HVs; 2 countries have exported HVs

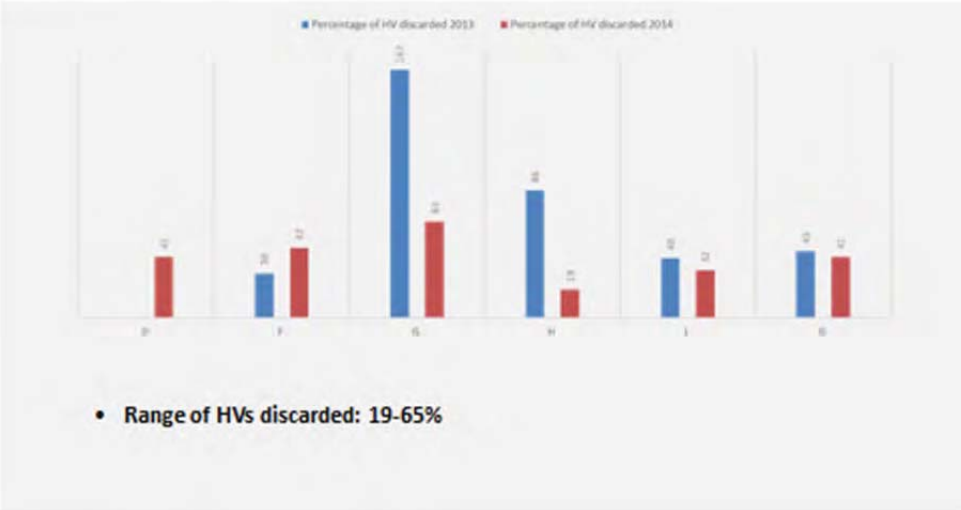
EUROPEAN BLOOD ALLIANCE

T&C benchmarking
Heart valves



EUROPEAN BLOOD ALLIANCE

- T&C benchmarking
- Heart valves



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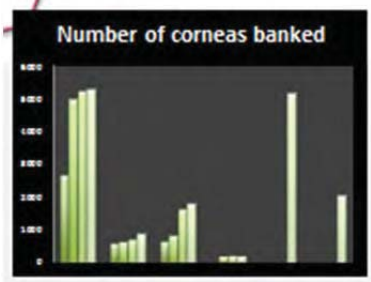
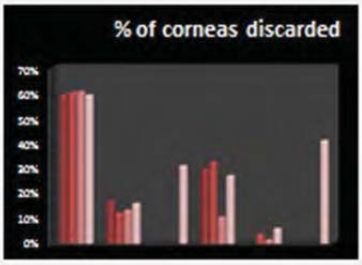
T and C Benchmarking
Corneas





These graphs show data over a 4 year period:
Broad range of sizes of banks
Significant differences in discard rates 11-65%

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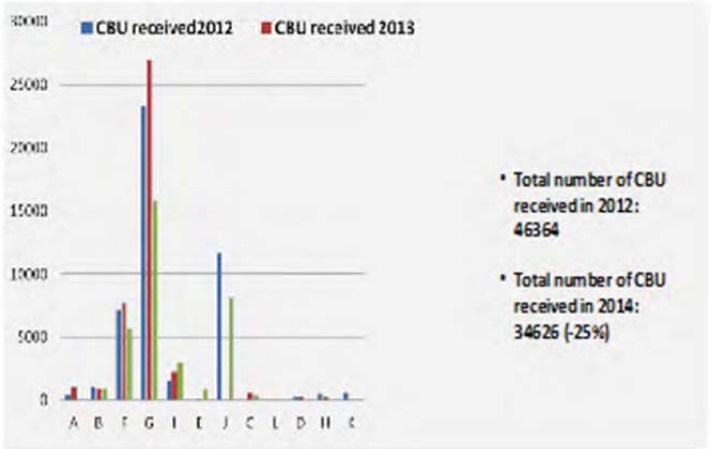
T&C benchmarking
Umbilical cord blood (UCB)



- Total number of CBU received in 2012: 46364
- Total number of CBU received in 2014: 34626 (-25%)

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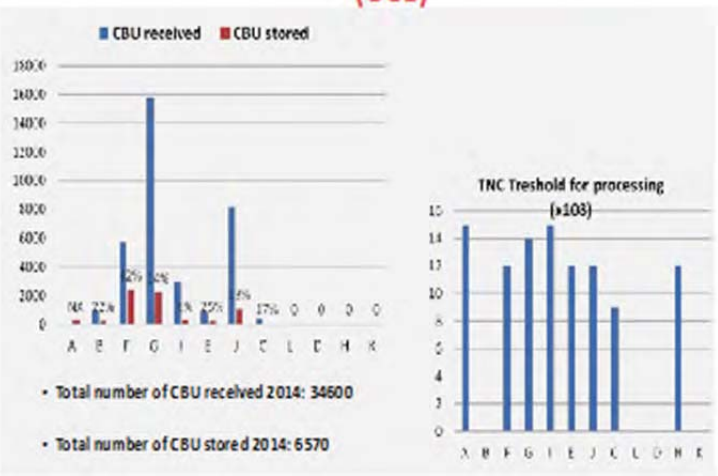
T&C benchmarking Umbilical cord blood (UCB)



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Main Findings

Significant differences in sizes of banks

Significant differences in discard rates

Are we comparing apples to apples?

Some qualitative differences

Safe blood for Europe

In depth Analysis Heart Valves

- Decision to carry out a detailed benchmarking exercise on heart valve banking
- Heart valves:
  - Precious resource
  - May be life-saving
  - Unmet clinical demand

HV Workshop Questionnaire

- Collaboration between European Blood Alliance and the Foundation of European Tissue Banks.
- 2016: questionnaire sent out to 15 countries in Europe and 11 countries world-wide.

EUROPEAN BLOOD ALLIANCE

FOUNDATION OF EUROPEAN TISSUE BANKS

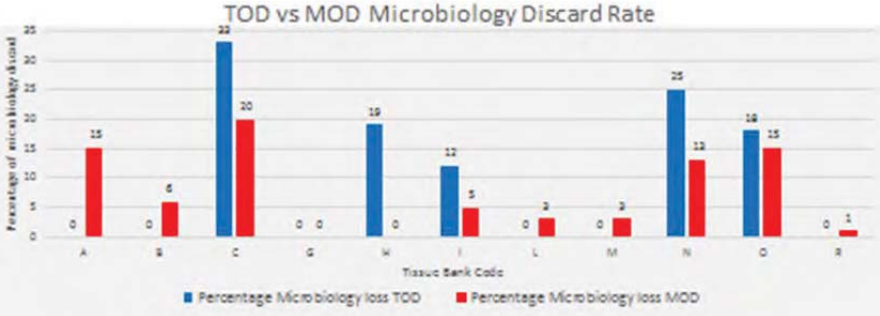
Donor Suitability Assessment

Tissue Bank Code	Donor Assessment pre donation	Post-donation Medical Notes	Post-donation Family Doctor	Post-donation PM	Overall Discard rate TOD+MOD+LD
A	Yes	Yes	Yes	Yes	38%
B	Yes	n/a	n/a	n/a	16%
C	Yes	Yes	Yes	Yes	33%
D	No	No	No	Yes	25%
E	Yes	Yes	Yes	Yes	34%
F	n/a	n/a	n/a	n/a	0
G	Yes	Yes	Yes	Yes	16%
H	Yes	Yes	No	n/a	48%
I	Yes	Yes	Yes	Yes	45%
J	Yes	Yes	No	Yes	50%
K	n/a	n/a	n/a	n/a	56%
L	Yes	No	No	No	56%
M	Yes	No	Yes	Yes	33%
N	Yes	Yes	Yes	Yes	52%
O	n/a	n/a	n/a	n/a	63%
P	n/a	n/a	n/a	n/a	78%
S	Yes	No	No	Yes	47%

EUROPEAN BLOOD ALLIANCE

FOUNDATION OF EUROPEAN TISSUE BANKS

TOD vs MOD Microbiology Discard Rate



- Of TBs retrieving both TOD & MOD – 10/12 report microbiology losses from MOD but only 5/12 report microbiology losses from TOD
- "A" has dedicated mortuary for tissue retrieval: no microbiology losses from TOD but 15% microbiology loss from MOD.
- Does the donor type (ITU) or the order of retrieval affect microbiology losses particularly for MOD?

EUROPEAN BLOOD ALLIANCE

FOUNDATION OF EUROPEAN TISSUE BANKS

Heart Valve Processing

Tissue Bank Code	Critical timings for Heart Processing	Percentage HV Microbiology loss TOD+MOD+LD
D	Immediate	0
G	Immediate	0
R	Immediate	1%
M	Immediate	3%
H	Immediate	11%
C	Immediate	25%
F	24 hours	0
L	24 hours	3%
B	24 hours	5%
I	24 hours	8%
A	24 hours	9%
O	24 hours	13%
J	24 hours	20%
E	32 hours	3%
P	36 hours	5%
K	46 hours	11%
N	48 hours	23%
S	72 hours	2%

EUROPEAN BLOOD ALLIANCE

- Is questionnaire too complex?
- Are we following the responses effectively enough?
- Is the questionnaire achieving its aim?

Conclusions

KISS

Not too many questionnaires sent to same people

Try and ensure uniformity from year to year

Provide feedback to respondents

Useful information but needs some rationalisation

Safe blood for Europe

Thank you

Safe blood for Europe

Registry of the WMDA - Lydia Foeken (World Marrow Donor Association; WMDA)

WMDA
matching donors • serving patients

Technical Meeting on National and EU-level Tissue and Cell Activity Data Collection and Reporting

World Marrow Donor Association

A changing world

A changing world

Information is shared through social media

And would it be possible to share between Professional Societies and Competent Authorities?

Pillar 1: Optimising 'Search, Match & Connect'

A global search platform that facilitates the best possible match between stem cell donors and transplant patients.

User friendly with automation to improve & simplify searches and improved training to support users.

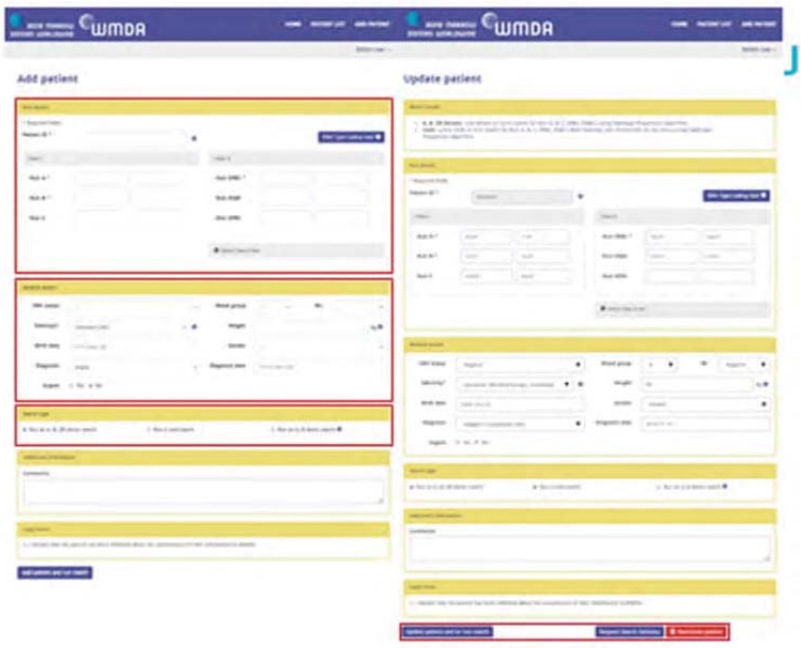
Privacy & data security are safeguarded through the implementation of GRID & data agreements

WMDA hosts the global database: Search & Match

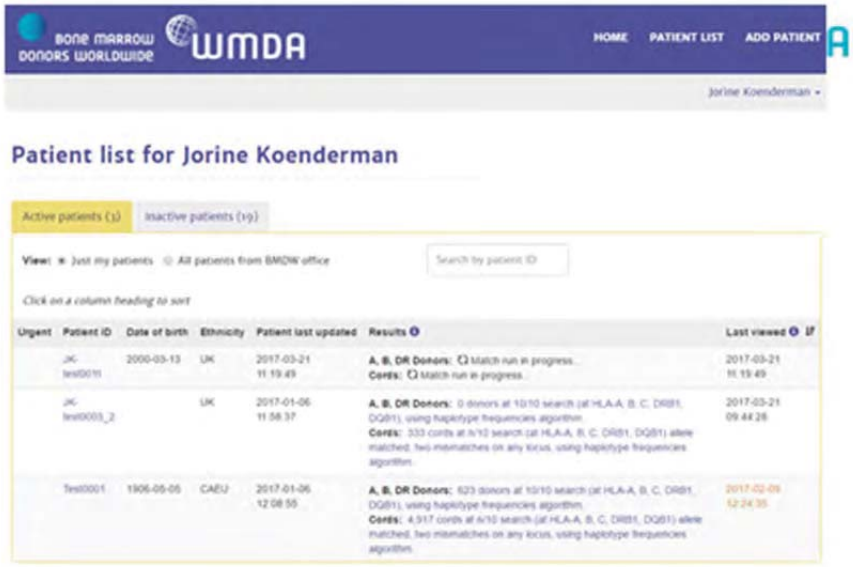
- All donors and cord blood units are available for global search in a centralized database
- At the moment:
  - 52 countries
  - > 32 million donors worldwide

7

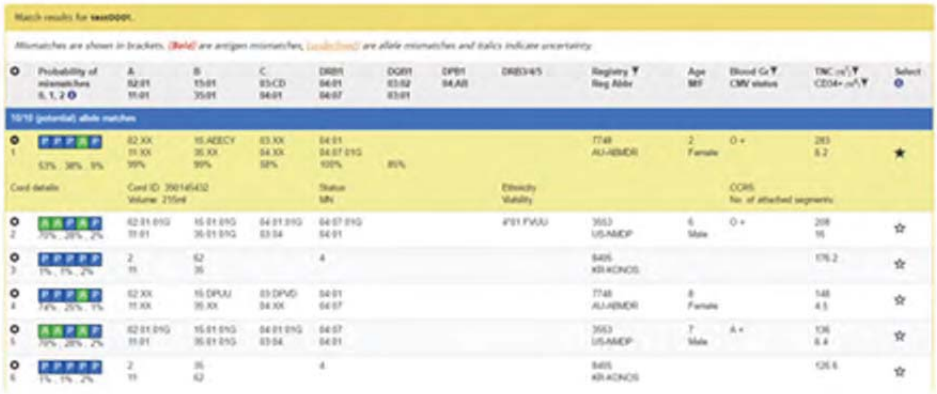
WMDA



JMDA


BONE MARROW DONORS WORLDWIDE
WMDA
HOME
PATIENT LIST
ADD PATIENT
Jorine Koenderman
Patient list for Jorine Koenderman
Active patients (3)
Inactive patients (19)
View: Just my patients
All patients from BMDW office
Search by patient ID
Click on a column heading to sort
Urgent
Patient ID
Date of birth
Ethnicity
Patient last updated
Results
Last viewed
A, B, DR Donors:
Cords:
Match run in progress...


WMDA

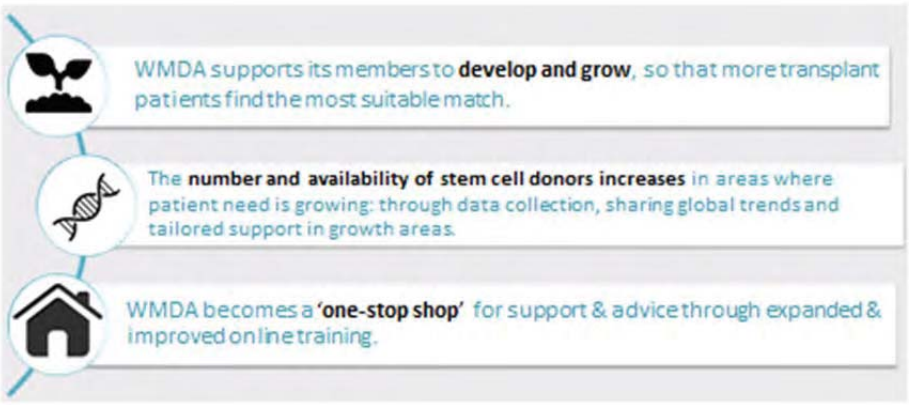

Probability of mismatches
A
B
C
DRB1
DQB1
DPB1
DRB3/4/5
Registry
Reg Abbr
Age
Blood Gr
CMV status
Select
10/10 (potential) allele matches

WMDA

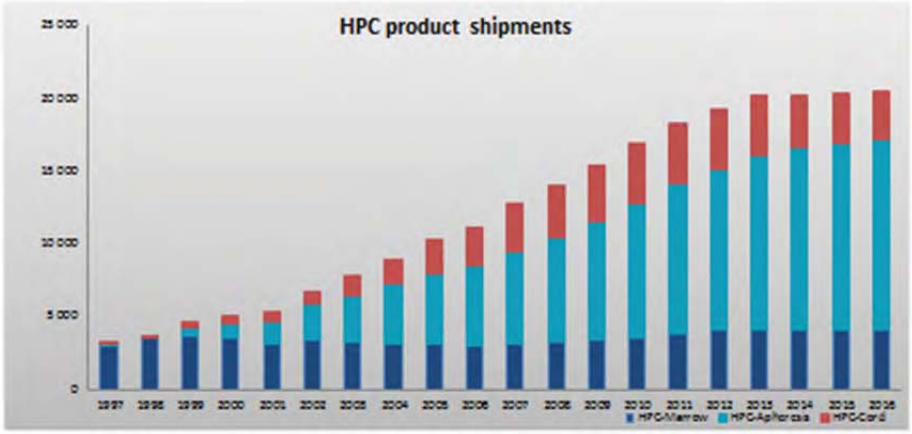
What might be valuable information for regulators?

- Number of donors, specified per EU Member State
- Number of cord blood units, specified per EU Member State
- Growth of the donor file over the past year
- Growth of the cord blood file over the past year
- Quality of the HLA typing
- Number of patients registered for search

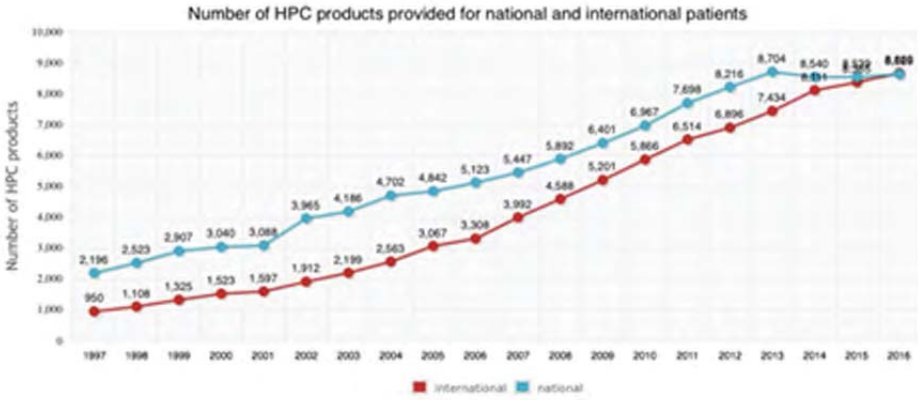
Pillar 2: Supporting Global Development



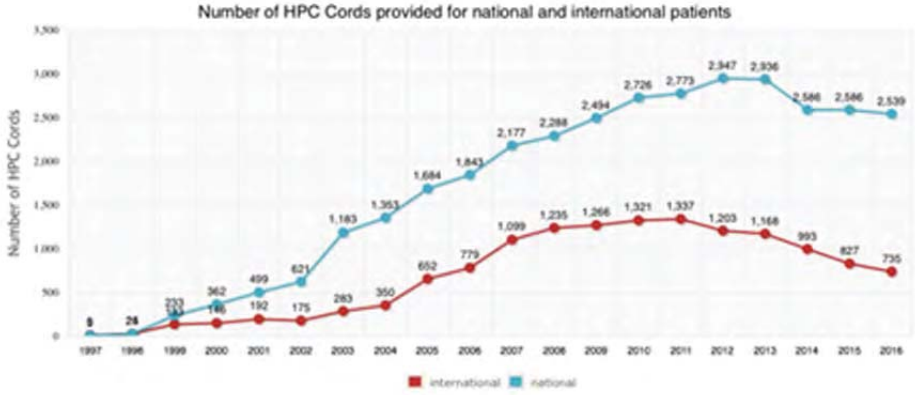
Number of unrelated transplants worldwide



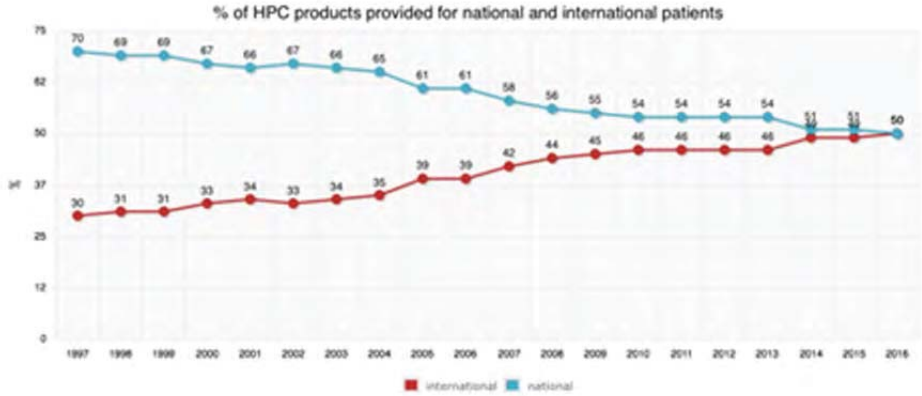
WMDA

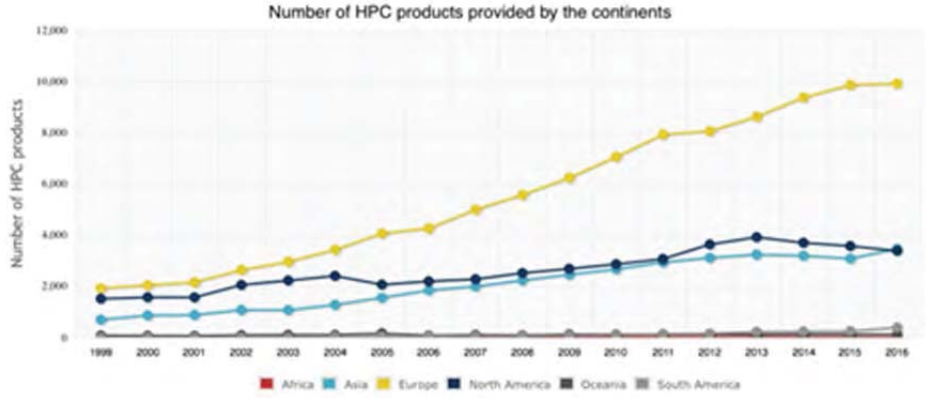


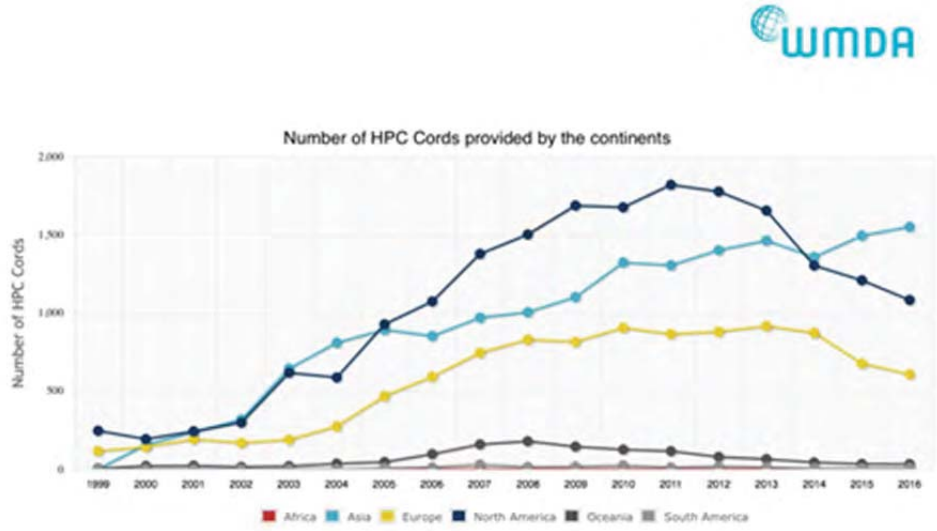
WMDA


Number of HPC Cords provided for national and international patients
Number of HPC Cords
international
national

WMDA


% of HPC products provided for national and international patients
international
national


WMDA
Number of HPC products provided by the continents
Number of HPC products
12,000
10,000
8,000
6,000
4,000
2,000
0
1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016
Africa Asia Europe North America Oceania South America


WMDA
Number of HPC Cords provided by the continents
Number of HPC Cords
2,000
1,500
1,000
500
0
1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016
Africa Asia Europe North America Oceania South America

How WMDA data are collected

Two way validation

Each country reports how much they have provided

Bone Marrow	Austria
Austria	10*
USA	10*
TOTAL NUMBER OF PRODUCTS	20*

Each country reports how many patient have received a product

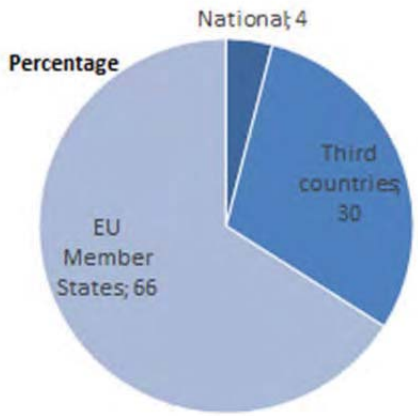
Austrina patients receiving marrow from	
Nationaldonor	10*
International donor	10*
TOTAL NUMBER OF PATIENTS	20*

* Example data

19

WMDA

What might be valuable information for regulators?



Country	Bone Marrow	PBSC	Cord
USA	2	10	3
Vietnam	0	0	1

WMDA

Pillar 3: Promoting Donor Care

- Ensure rights and safety of donors are **promoted and protected.**
- Inform donor care standards & practices through new and improved online **SEAR/SPEAR reporting system** for related & unrelated donors.
- Introduce **professional training programme** for those working with donors.

Serious Adverse Events and Reactions Reporting

WMDA

SEAR
Donor event occurs during work-up or stem cell collection (collection centre)

SEAR
Event reported by donor at follow-up (donor centre)

SPEAR/SEAR
Event reported when product is received or infused (transplant centre)

Registry responsible for providing the donor/cord blood unit is informed

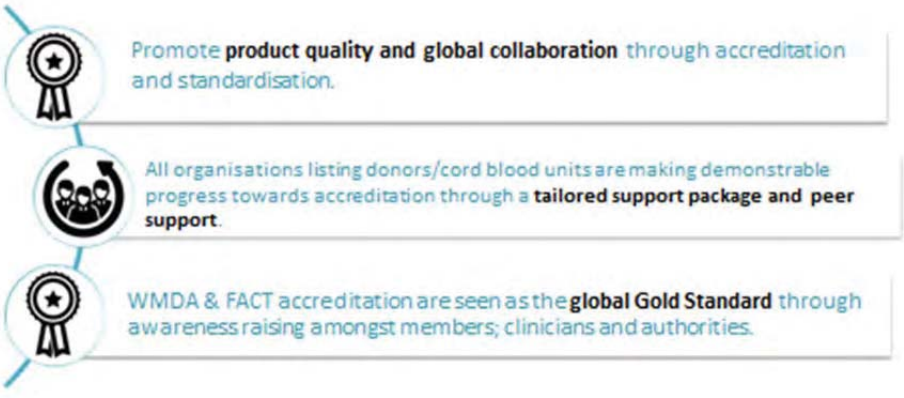
Registry reports to WMDA S(P)EAR Committee

What might be valuable for regulators?

WMDA

- One central point for reporting where professional expertise and regulatory experience are combined
- Rapid alert system

Pillar 4: Ensuring Quality



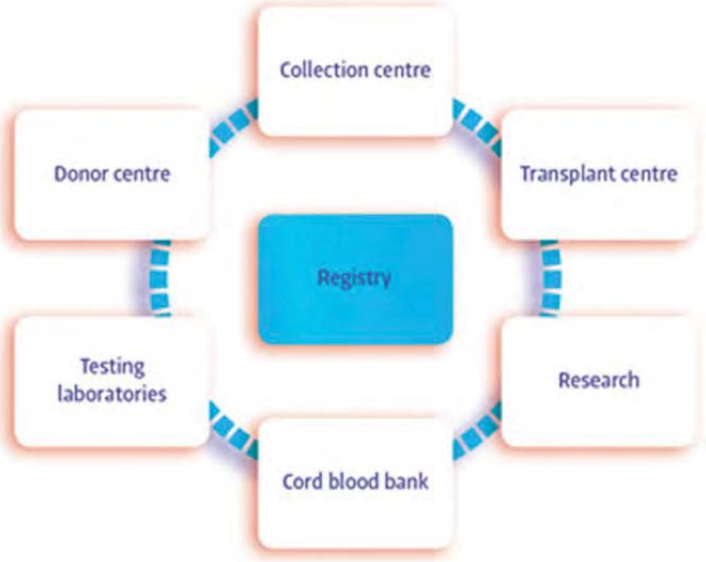
WMDA Accreditation

WMDA

EUROPEAN DIRECTIVE 2004/23/EC; article 9

Import/export of human tissues and cells

Member States and tissue establishments that receive such imports from third countries shall ensure that they meet standards of quality and safety.



What might be valuable for regulators?

WMDA

- Shared resources on import/export knowledge
- List of accredited organisations

- **State-of-the-art in international data collection exercises for eye banks - Philip Maier (European Eye Bank Association; EEBA)**

EUROPEAN EYE BANK ASSOCIATION

European Eye Bank Association (EEBA)

Prof. Dr. Philip Maier (Lions Cornea BW)

STATE-OF-THE-ART IN INTERNATIONAL DATA COLLECTION EXERCISES FOR EYE BANKS

Technical Meeting on National and EU-level Tissue and Cell Activity Data Collection and Reporting

Thursday 22 March 2018 / Friday 23 March 2018

Venue: EDQM premises, 7 Allée Kastner, Strasbourg

EUROPEAN EYE BANK ASSOCIATION

EEBA Directory - Governance

- The EEBA Directory is
  - produced on an annual basis
  - published in time for the Annual Business Meeting.
- Data collection
  - Data from individual banks published only if at least one member of staff from that bank is a registered Ordinary Member at the EEBA
  - One Member of the Association from each Eye Bank is identified as the "Corresponding Member" for that Eye Bank.
  - Corresponding Members are responsible to annually return data on request using the forms provided in order to compile a Directory of the Association.
- Directory Supervisor
  - oversees the collection and processing of data for the Directory
  - Coordinates the publication of the Directory.
  - Additional support and editing staff may be appointed by the Directory Supervisor with approval of the President.

EUROPEAN EYE BANK ASSOCIATION

EEBA Directory Aims

- Chronicling the yearly activities and methods of eye banks in Europe
  => Valued resource for eye bankers and ophthalmologists
- Key information on transplant legislation concerning donation and eye banking
- List of the contact details for all eye banks which have at least one EEBA Ordinary Member
- Keeping track of new developments in eye banking
  - e.g. increasing propensity for posterior lamellar grafts to be prepared in the eye bank laboratory versus the operating theatre
- Directory is only made available to EEBA Members (+ on request to regulatory/competent authorities)

EUROPEAN EYE BANK ASSOCIATION

EEBA Annual Directory – Data for 2016 (but published in 2018!)

EUROPEAN EYE BANK ASSOCIATION

EEBA Annual Directory – Summary Statistics for the past 5 years

Table 1 - Numbers

	2012	2013	2014	2015	2016
Number of banks providing data	63	66	65	68	66
Number of countries	21	21	22	22	22
Number of corneas processed	33302	34121	37541	39467	40894
% of corneas issued for grafting	63	63	64	66	67

Table 2 - Number of differently sized banks

Corneas used per year	2012	2013	2014	2015	2016
< 50	4	6	3	3	5
50 - 100	6	7	10	9	8
100 - 500	31	27	24	29	26
500 - 1000	11	14	17	15	15
> 1000	11	10	11	12	12

Table 3 - Donor information

		2012	2013	2014	2015	2016
Age	Organ culture	62.9	62.7	63.3	63.9	64.6
(yrs)	Hypothermic storage	54.3	55.2	62.6	54.6	62.7
Death to enucleation	Organ culture	17:20	18:36	18:14	18:19	17:58
(hrs)	Hypothermic storage	8:00	8:59	06:22	08:04	08:46
Death to excision in the lab	Organ culture	21:32	22:55	22:24	22:35	22:14
(hrs)	Hypothermic storage	12:21	10:59	08:09	11:12	12:00
Death to in situ excision	Organ culture	14:02	13:16	13:54	14:12	15:03
(hrs)	Hypothermic storage	8:00	7:24	08:36	09:35	07:57

Table 4 - Storage methods in the EEBA

		2012		2013		2014		2015		2016	
		nr	%	nr	%	nr	%	nr	%	nr	%
Received (after pre-selection)		39459		38441		43822		40056		40497	
Not futher processed for grafting (incl pre-evaluation / pre-selection)		13299	34	12827	33	14553	33	13178	39	16284	35
Preserved in bank	Organ culture	26788	68	25699	67	30859	70	32549	71	34270	74
	Hypothermic storage	6290	16	7942	21	6222	14	6505	14	6167	13
	Moist chamber	224	0.6	270	0.7	460	1.0	471	1.0	451	1.0

EUROPEAN EYE BANK ASSOCIATION

EEBA Annual Directory – Summary Statistics for the past 5 years

Table 5 - Corneas not transplanted in 2016

not transplanted because of:		percentage of received corneas
medical history		3.2%
blood tests		5.4%
microbiology	bacteria	5.1%
	multi-resistant bacteria	0.0%
	fungi	0.5%
	multi-resistant fungi	0.0%
	combination bacteria and fungi	0.1%
	not specified	0.4%
	negative	0.1%
	total microbiology	2.6%
morphology		17.7%
other or unknown reasons (e.g. organizational reasons)		8.4%

Table 5a - Selection and transplantation in 2016

	selected	transplanted	selected not transplanted	percentage not transplanted
emergency	1767	1169	498	28%
anterior lamellar	212	205	32	15%
deep anterior lamellar	675	655	17	3%
posterior lamellar	4536	4450	194	4%
DMEK	4548	4430	190	4%
PKP	12646	11717	749	6%
unknown	267	302	16	6%
total	24449	23218	1654	7%

Table 6 – Serology testing of all received corneas 2016

	percentage tested		percentage tested
HIV 1/2 antigen	99.7%	HTLV	40.0%
HIV 1/2 antibody	96.8%	syphilis	99.0%
Hepatitis B antigen	98.0%	mycoplasma	0.0%
Hepatitis B antibody	92.6%	toxoplasmosis	0.3%
Hepatitis C antigen	28.9%	EBV	0.0%
Hepatitis C antibody	80.0%	CMV	0.0%
		Hepatitis A	0.3%

Table 6a - Mean frequency of positive serology (%).

	2012	2013	2014	2015	2016
HIV 1/2	0.4	0.4	0.3	0.3	0.2
Hepatitis B	1.8	1.8	1.8	1.8	1.7
Hepatitis C	1.1	0.8	0.8	0.9	1.1
Syphilis	0.7	0.5	0.6	0.6	0.4
Additional serology / not specified	0.5	2.6	0.3	0.3	0.5
Total positive serology (incl. Hep A and others)	6.5	7.5	5.6	5.2	5.5
Serology tests inconclusive or impossible	2.0	1.4	2.1	1.2	1.1

EEBA Annual Directory – Summary Statistics for the past 5 years

Table 9 - Other tissue used for ocular surgery

		2012	2013	2014	2015	2016
Sclera	banks	28	32	33	35	34
	tissues	1379	1410	1557	1641	2989
Limbal grafts	banks	2	2	2	1	2
	tissues	4	3	3	1	4
Stem cells	banks	5	5	4	1	4
	tissues	196	221	87	10	32
Amniotic membrane	banks	41	41	37	41	41
	tissues	4999	3533	5310	5947	5927

Table 10 - Quality Management

EU Directive related items:	2012	2013	2014	2015	2016
Standard Operating Procedures present	55	59	61	63	64
Standard Operating Procedures in preparation	0	0	0	0	0
Quality Manual present	51	57	60	61	60
Quality Manual in preparation	1	1	1	0	1
ISO 9001-2000 certification	18	19	15	19	15
other certification	14	12	17	14	51
certification in preparation	4	4	2	4	4
Quality and technical summary present	48	52	52	54	53
Quality and technical summary in preparation	1	1	0	0	1

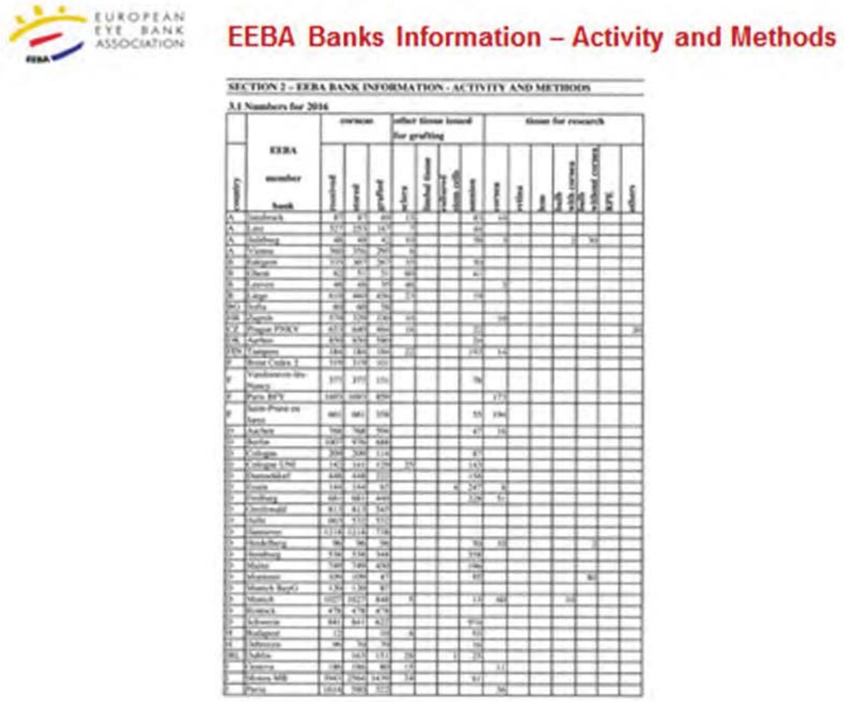
Table 11 – Working circumstances in the laboratory

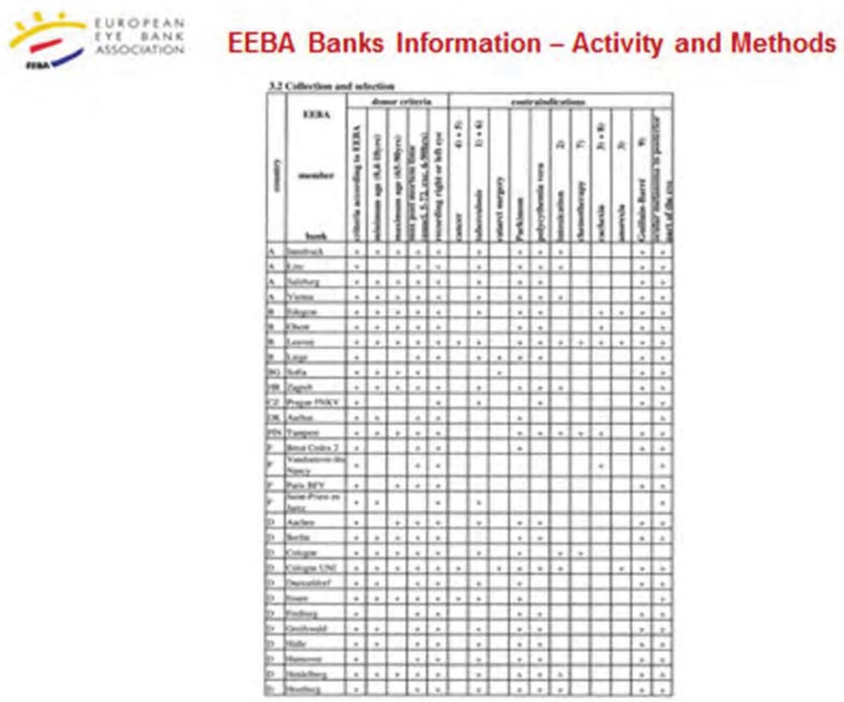
		nr of banks
Tissue received as	whole eyes	48
	corneoscleral buttons	34
	both	20
Decontamination before eyes come into the laboratory		17
Laminar flow bench used		58
Room environment	normal room with free access	0
	normal room with limited access	9
	room with limited access via changing room	11
	clean room grade B	18
	clean room grade C	17

EEBA Banks Information – Activity and Methods

Section 2: EEBA banks information – Activity and methods

15 Numbers
17 Collection and selection
22 Decontamination
24 Organ culture, preservation medium
32 Organ culture, preservation method
34 Hypothermic storage
36 Endothelium evaluation
40 Cell counting
45 Microbiology testing
47 Sclera
49 Amnion
51 Stem cells
53 Quality assurance


EUROPEAN EYE BANK ASSOCIATION
EEBA Banks Information – Activity and Methods
SECTION 2 - EEBA BANK INFORMATION - ACTIVITY AND METHODS
3.1 Numbers for 2016


EUROPEAN EYE BANK ASSOCIATION
EEBA Banks Information – Activity and Methods
3.2 Collection and selection

EUROPEAN EYE BANK ASSOCIATION

EEBA Banks Information – Activity and Methods

EUROPEAN EYE BANK ASSOCIATION

EEBA Banks Information – Activity and Methods

EUROPEAN EYE BANK ASSOCIATION

EEBA Banks – Information per Country

Specific legislation for each country
- Donation
- Cornea Banking

AUSTRIA

Legislation Austria
Donation:
- No distinction is made between the eye and the cornea: both are considered as tissues.
- Removal of the eye is allowed.
- Organ donation is an opting out system (presumed consent): objections are registered in the 'Widerspruchregister' or made known personally.

Cornea banking:
- In 2008 the Austrian Tissue Safety Act (Gewebesicherheitsgesetz) based on the EC-directives on tissues and cells was implemented.
- An accreditation by a competent authority according to the Gewebesicherheitsgesetz is executed biannually, including inspection of eye banks.

Gewebebank Innsbruck
Department of Ophthalmology and Optometrie
Medical University Innsbruck
Anichstrasse 35
A-6020 Innsbruck
Telephone +43 512 504 235 84
Fax +43 512 504 237 68
E-mail [redacted]

Correspondent: Werner Wohlfarter

Staff: Werner Wohlfarter, Mag. Christof Seifarth
Date established: 19-10-1995

Red Cross Blood Transfusion Service of Upper Austria
Multi-Tissue and Blood Bank
Krankenhausstrasse 7
A-4020 Linz
AUSTRIA
Telephone: +43 732 777 000 206
Fax: +43 732 777 000 290
E-mail: [redacted]

Correspondent / Responsible Person: Mag. Dr. Simone Hennerbichler-Lagscheider

Staff: Claudia Leitmayr, Eva Schachermayer, Daniela Muellegger, Daniela Hager, Doris Prener, Ursula Franz
Date established: 2007

EUROPEAN EYE BANK ASSOCIATION

EEBA Banks – Summary Information per Country

General

For extended information see data per country.

			Donation legislation					Cornea banking legislation					
country	responding banks	National follow-up system	Legislation concerning organ donation	Eye considered as tissue (t), or organ (o)	Cornea considered as tissue (t), or organ (o)	Removal eye allowed, bb = only heart beating donors	Donation system o = opting out, i = opting in,	Accreditation required	Inspection by competent authority required	National Eye Bank Organisation	National Tissue Bank Organisation	Legal requirements for storage solutions	EU directives implemented
Austria	4	no	yes	o	o	yes	o	yes	yes	no	no	no	yes
Belgium	6	yes	yes	t	t	yes	o	yes	yes	no	yes	no	yes
Bulgaria	1	yes	yes	o	t	yes	both	yes	yes	no	no	yes	yes
Croatia	1	no	yes	o	t	yes	o	yes	yes	no	no	no	yes
Czech Republic	1	yes	yes	o	t	yes	o	yes	yes	no	no	no	yes
Denmark	1	no	yes	o	t	yes	i	yes	yes	no	no	no	yes
Finland	1	no	yes	t	t	yes	o	yes	yes	no	no	no	yes
France	4	no	yes	o	t	bb	i	yes	yes	yes	yes	no	yes
Germany	18	yes	yes	o	t	yes	i	yes	yes	yes	no	no	yes
Hungary	2	yes	yes	o	t	yes	o	yes	yes	yes	yes	no	yes
Italy	5	no	yes	o	t	yes	i	yes	yes	yes	no	no	yes
Ireland	1	no	yes	o	t	o	i	yes	o	o	o	o	yes
The Netherlands	2	yes	yes	o	o	yes	i	yes	yes	no	yes	no	yes
Norway	2	no	yes	o	t	yes	i	yes	yes	no	no	no	yes
Poland	2	yes	yes	o	t	yes	o	yes	yes	no	yes	no	yes
Portugal	3	yes	yes	t	t	yes	o	no	yes	p	yes	no	yes
Russia **)	1	no	yes	o	t	yes	o	yes	yes	no	no	yes	no
Slovenia	1	no	yes	o	o	yes	i	yes	yes	no	no	no	yes
Spain	3	no	yes	both	t	yes	both	yes	yes	no	yes	yes	yes
Sweden	6	yes	yes	o	o	bb	i	no	no	yes	no	no	yes
Switzerland **)	4	no	yes	o	t	yes	i	yes	yes	no	no	yes	yes
United Kingdom	1	yes	yes	t	t	yes	i	yes	yes	yes	yes	no	yes

Other data collection activities

- European Cornea and Cell Transplantation Registry (ECCTR)
  - EEBA is one of 8 consortium partners in the (**http://www.ecctr.org/**)
- Aims
  - Build a common outcome assessment methodology for corneal transplantation
    - Clinical outcome measures
    - Patient reported outcome measures
  - Establish an EU web-based registry and network for academics, health professionals and authorities
  - Assess and verify activity data and the safety, quality and efficacy of corneal transplants

EEBA Secretariat

Via Paccagnella n. 11 - Padiglione Rama
30174 Zelarino – Venice (Italy)
Tel: +39 041 9656422
Fax:+39 041 9656421
Fiscal code: 90111850278

E-mail: admin@europeaneyebanks.org

www.europeaneyebanks.org

- **Past and present of the European collection of tissue, cells and ART data of activity - Eliana Porta, Valentina Caramia (Italian National Transplant Centre; CNT)**

EUROCET

European Registry Of Competent Authorities For Tissues And Cells

Past and present of the European collection of Tissue, Cells and ART data of activity.

Eliana Porta, Valentina Caramia, Maura Mareri, Francesca Vespasiano, Paola Di Ciaccio and Alessandro Nanni Costa
Istituto Superiore di Sanità, Italian National Transplant Centre, Rome, ITALY

EUROCET

SOME INFO ON THE HISTORY OF EUROCET

From a European Project to The European Network of Competent Authorities for Tissues and Cells

EUROCET

2005

EUROCET (European Registry for Organs, Tissues and Cells) was a project funded under the e-TEN program of the European Commission, DG INFSO.
Its aim was to set up a registry on organ, tissue and cell donation and transplantation activity shared by old and new Member States.

Directive 23/2004/EC:

art. 10.3: MS are required to establish a publicly accessible register of national TEs and these registers should be linked through an EU network

art. 10.1: TEs must submit to their national Competent Authority an annual report on donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells

May 2009 Competent Authorities Annual meeting, Brussels

EU Commission encouraged the use of Eurocet portal as

"A way to fulfil the obligations of the tissues and cells Directive to provide information on an EU-networked basis regarding tissue and cell donation and transplantation activities"

From 2009...

- a tool aiming at collecting annually updated data on tissues, hematopoietic and reproductive cells donation and transplantation activities;
- the European Registry of the Competent Authorities for tissues and cells;
- the registry of tissue establishments coming from all Competent Authorities;

eTEN:March 2007 Project of the Month: EUROCET

SOME INFO ON THE HISTORY OF EUROCET(II)

From a European Project to The European Network of Competent Authorities for Tissues and Cells

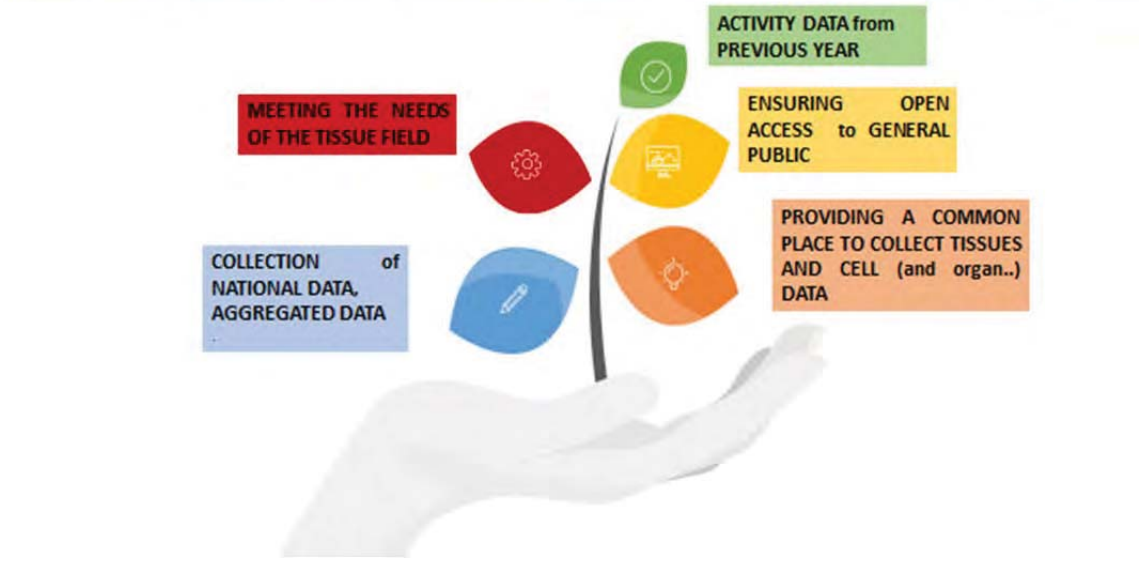
2011-2014

- the European Registry of the Competent Authorities for tissues and cells;
- the registry of tissue establishments coming from all Competent Authorities;

ARTMAN Technologies · ISBT 128 · EUROCET · ICCBA

SERVICE CONTRACT 2011 61 02

THE PHYLOSOPHY OF EUROCET DATA COLLECTION



TISSUE DATA COLLECTION FORM

Type of tissue:

- ocular tissue,
- skin,
- heart valves,
- blood vessels,
- musculoskeletal,
- Placenta
- other tissue.

Activities collected:

- donation,
- donation per type of tissue,
- procurement,
- banking,
- import and export of products,
- transplantation for human application.

HPC DATA COLLECTION FORM

Activities collected:

- Potential donation,
- Searching in the national registries,
- Import-export,
- donation,
- Banking of cord blood,
- Transplantation per HPC's origin,
- Transplantation per pathology,
- Other procedures associated with HPC transplantation.

ART DATA COLLECTION FORM

Types of treatment:

- IUI, IVF, ICSI, FET, Other

Activitiescollected:

- ART – with partner donation,
- Non partner donation activities,
- ART with non partner sperm donation,
- donation,
- ART with non partner oocyte donation,
- ART with non partner oocytes and sperm donation,
- ART with embryo donation.

DATA PROVIDED BY NATIONAL COMPETENT AUTHORITIES

Austria
AGES - Österreichische Agentur für Gesundheit und Ernährungssicherheit - Austrian Agency for Health and Food Safety

Belgium

Bulgaria
BEAT – Bulgarian Executive Agency

Cyprus
Ministry of Health of the Republic of Cyprus

Czech Republic
Ministry of Health of the Czech Republic

Germany
Paul Ehrlich Institut

Denmark

Estonia
Ravimiamet

Spain
ONT - Organización Nacional de Transplantes
Ministry of Health, Social Services and Equity

Finland
FIMEA – Finnish Medicines Agency

France
ABM – Agence de la biomedicine

Greece

Croatia
Ministry of Health of the Republic of Croatia

Hungary
Ministry of Human Capacities

Ireland

Italy
CNT – Italian National Transplant Centre

Lithuania
NTB - National Transplant Bureau

Luxembourg
Ministry of Health

Latvia
State Agency of Medicines of the Republic of Latvia

The Republic of Moldova
Transplant Agency

Macedonia

Malta
Ministry of Health of the Republic of Malta

Netherlands
Ministry of Health, Welfare and Sport

Norway
Helsedirektoratet

Poland
NCTCB - National Centre of Tissue and Cell Banking

Portugal
IPST - Institute for Blood and Transplantation Services

Romania
ANT – National Transplant Agency

Sweden
IVO - Health and Social Care Inspectorate

Switzerland
Federal Office for Public Health – Sub-Division Transplantation and Reproductive Medicine

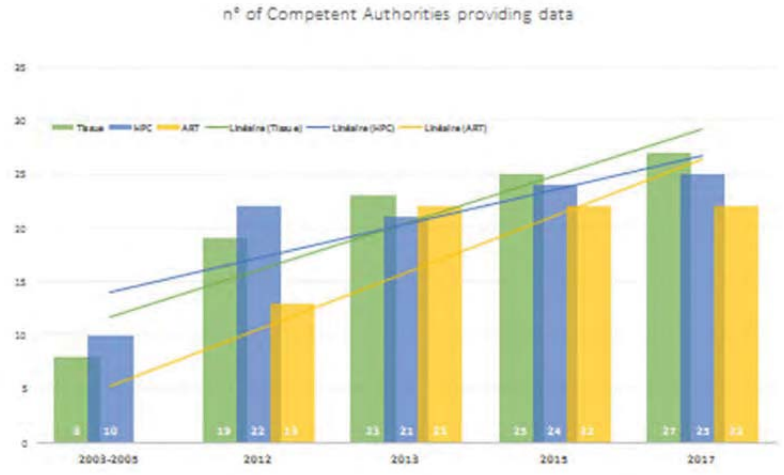
Slovenia
Institute for transplantation of Organs and Tissues of the Republic of Slovenia

Slovakia
Ministry of Health

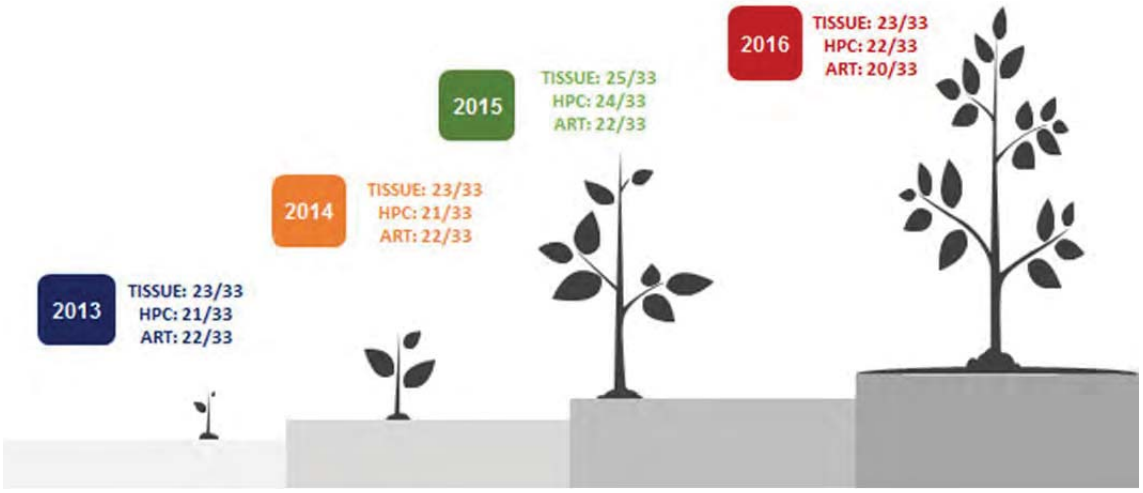
Turkey

United Kingdom
HTA – Human Tissue Authority
HFEA - Human Fertilisation and Embryology Authority

Eurocet's growth from 2003 to 2017

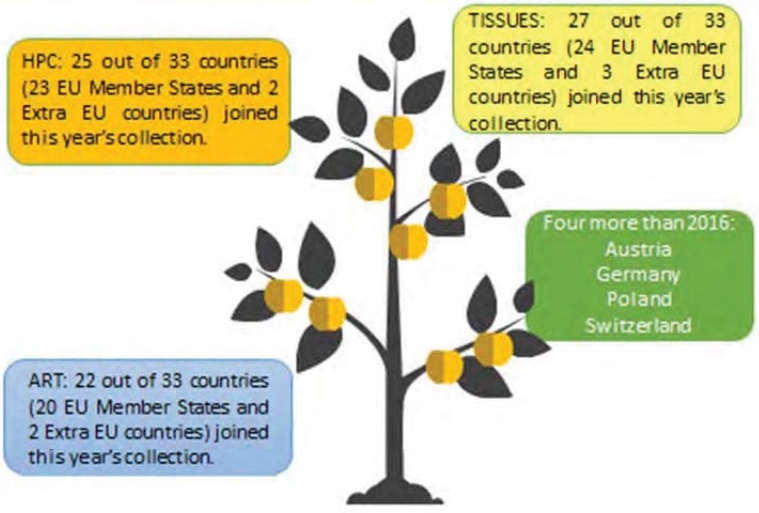


FOCUS: Number of countries which contributed from 2013 to 2016



FOCUS: Countries which contributed to the 2017 Collection

Countries	TISSUES	HPC	ART
Austria			
Belgium			
Bulgaria			
Croatia			
Cyprus			
Czech Republic			
Germany			
Denmark			
Estonia			
Spain			
Finland			
France			
Greece			
Hungary			
Ireland			
Italy			
Lithuania			
Luxembourg			
Latvia			
Moldova			
Macedonia			
Malta			
Netherlands			
Norway			
Poland			
Portugal			
Romania			
Sweden			
Slovenia			
Slovakia			
Switzerland			
Turkey			
United Kingdom			
Total	27	25	22



Where can people find the data?

Eurocet data are publicly available through the eurocet website (eurocet.org)

Since 2008, the data are annually published in the Newsletter Transplant.

THE PRESENT DISCUSSION ON EUROPEAN DATA COLLECTION

Since last year the issue of harmonizing data in the tissue and cell field was put on the table of the EDQM-CDTPO expert group. Italy's Competent Authority volunteered to lead the group that is discussing a way of **streamlining** and **updating** the common data collection forms and revising definitions.

Group members:

Eliana Porta - Italian National Transplant Centre, Italy (lead)

Jacinto Sanchez Ibanez, Simone Hennerbichler - European Association of Tissue Banks

Carlos Calhaz Jorge, Kersti Lundin - European Society of Human Reproduction and Embryology

Artur Kaminski - iKCBTiK/NCTCB, Poland

Ana Franca - IPST, Portugal

Aurora Dragomiristeanu - RNDVCSH, Romania

Mar Carmona - ONT, Spain

Eurocet intends to adopt the results of these agreed work for the collection of 2017 data.

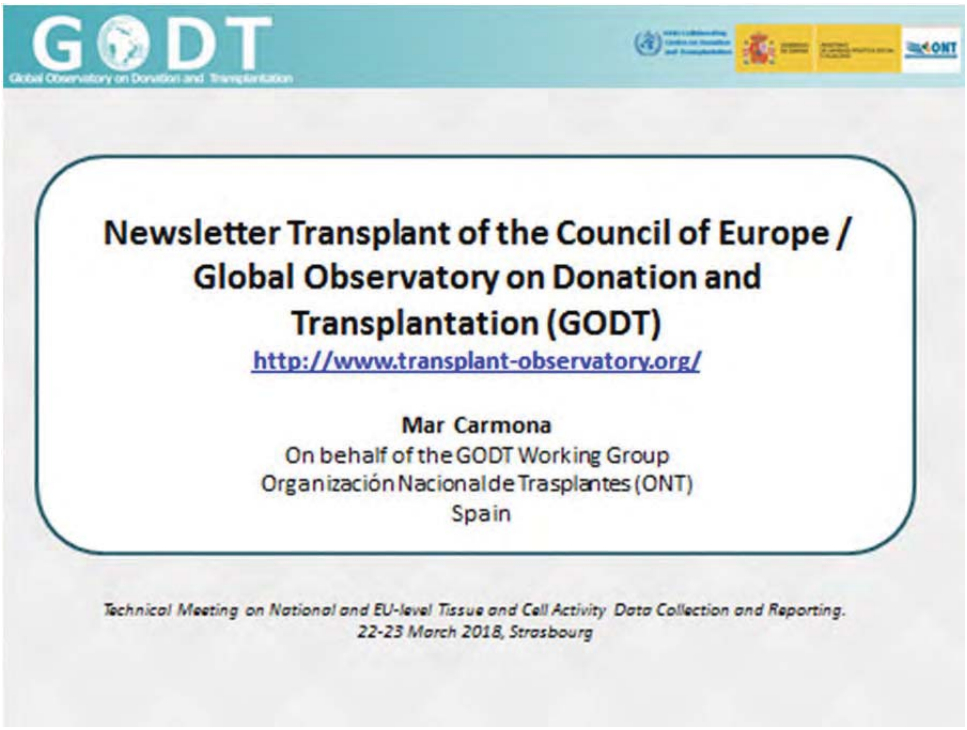
THE PHYLOSOPHY BEHIND THE CHANGES

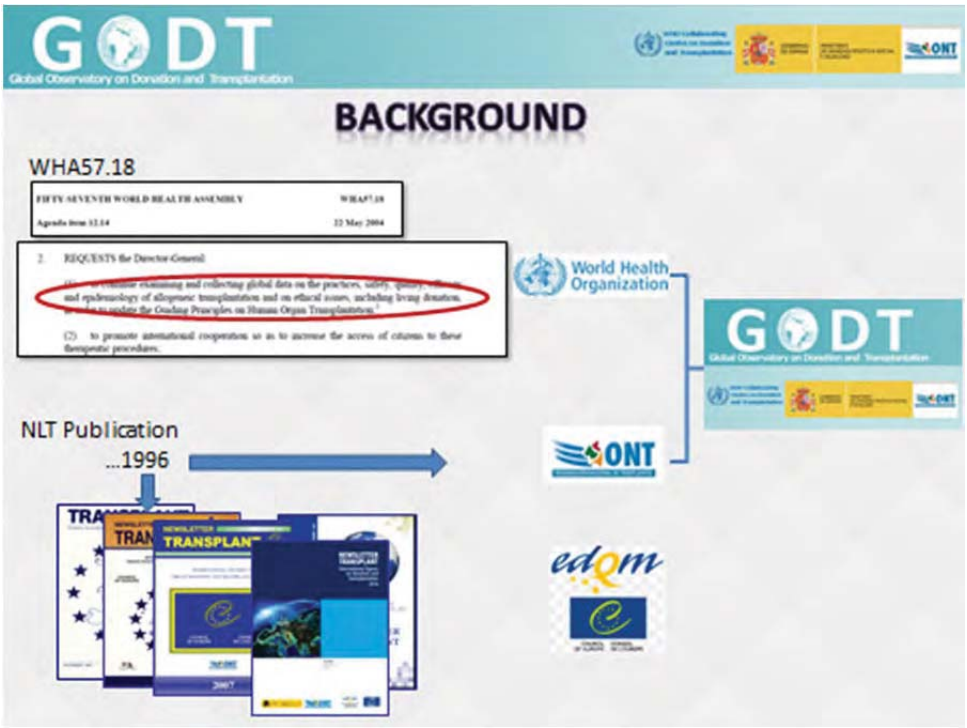
EUROCET

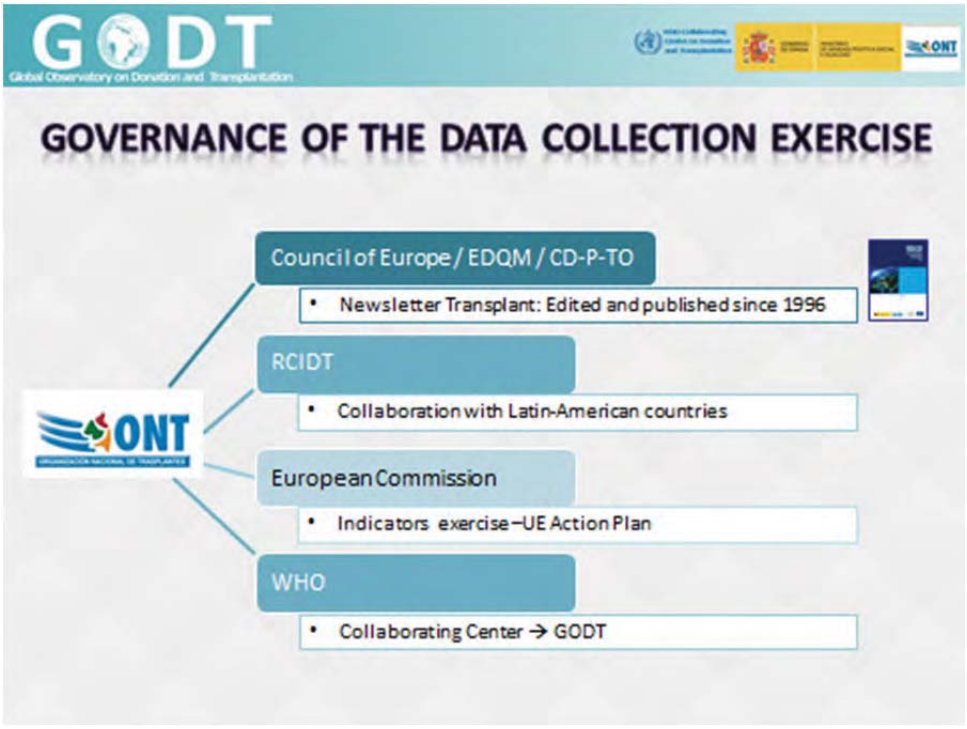
European Registry Of Competent Authorities For Tissues And Cells

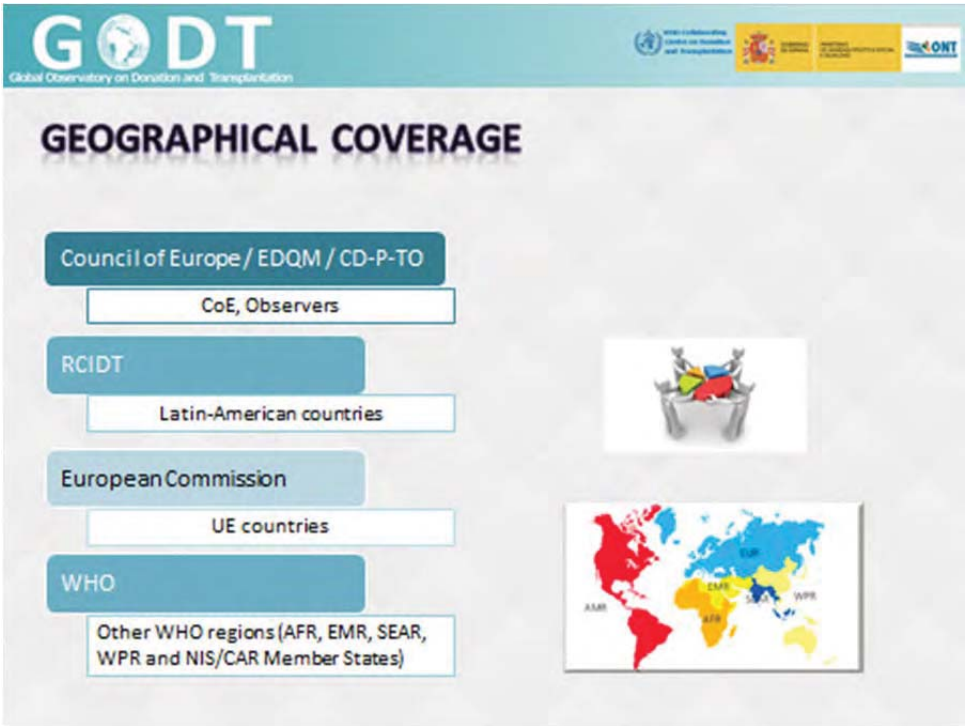
Thank you for your attention!

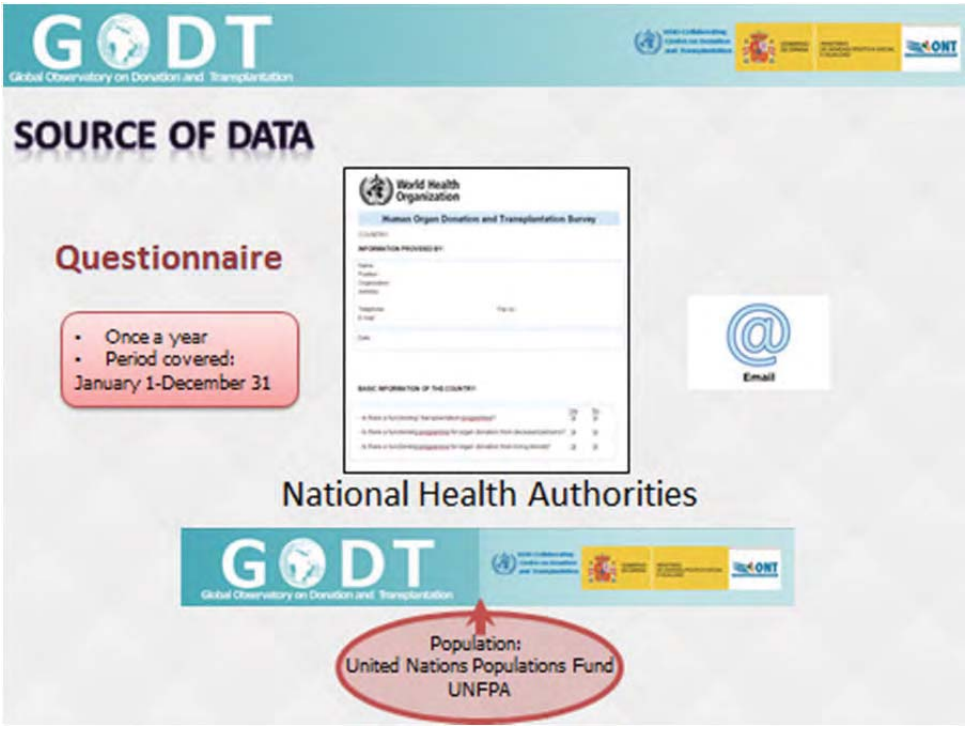
- **Newsletter Transplant of the Council of Europe/Global Observatory on Donation and Transplantation (GODT) - Mar Carmona (Spanish National Transplant Organisation; ONT)**

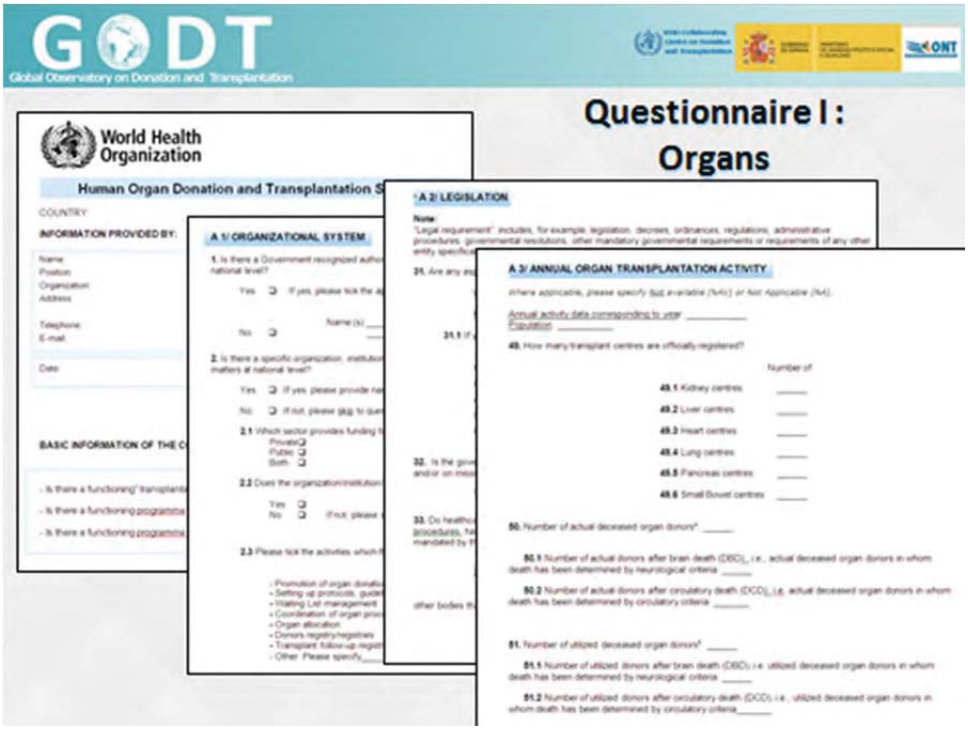


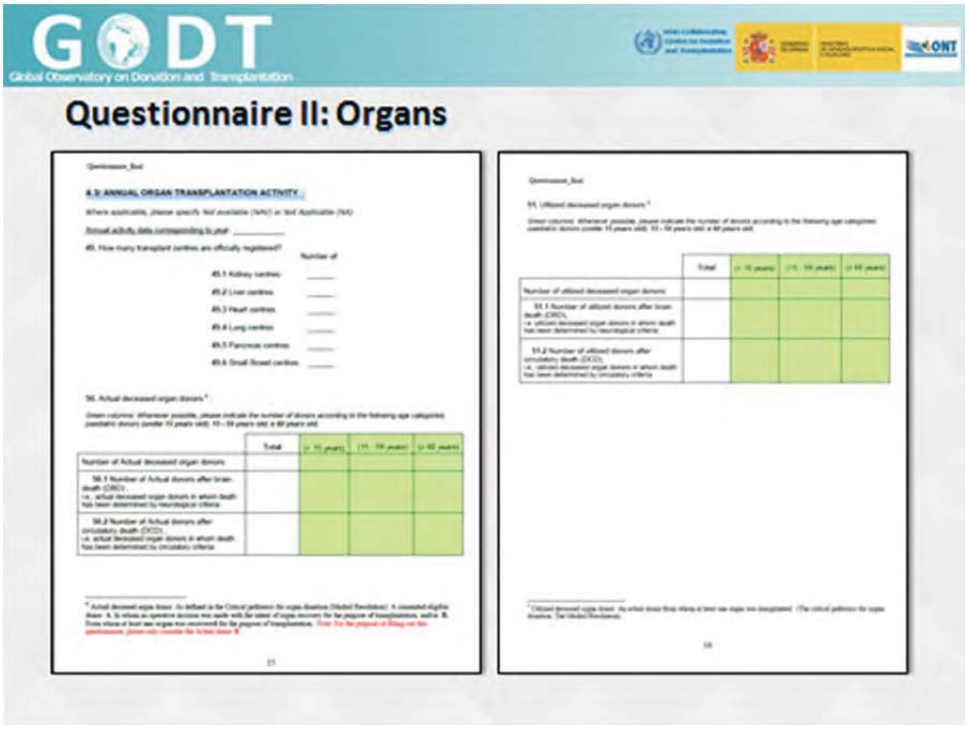


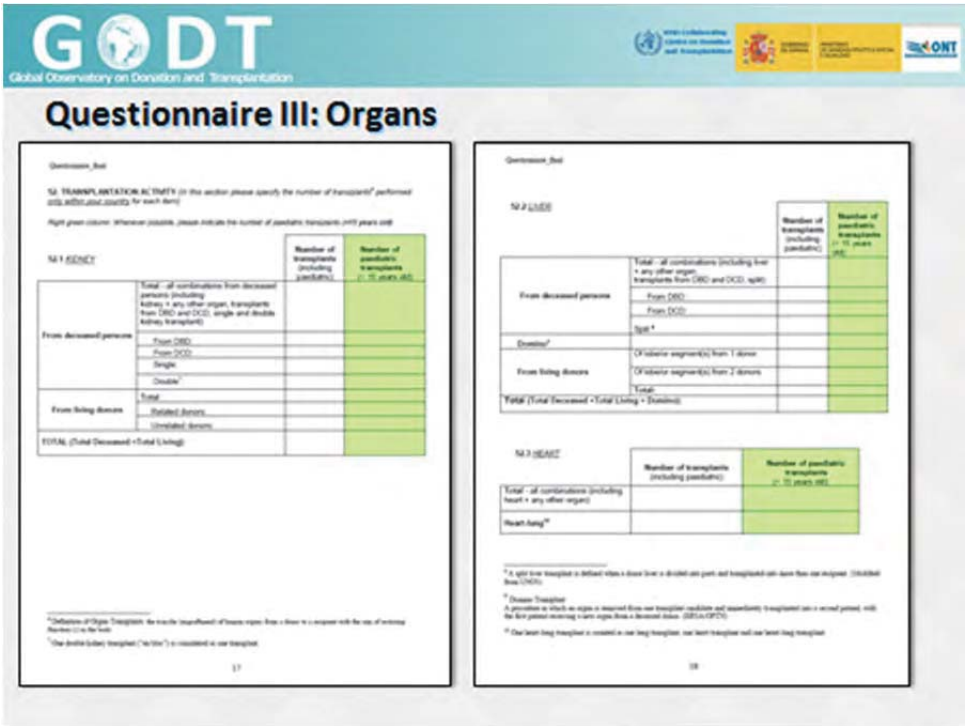

GODT
Global Observatory on Donation and Transplantation
GOVERNANCE OF THE DATA COLLECTION EXERCISE
ONT
Council of Europe / EDQM / CD-P-TO
• Newsletter Transplant: Edited and published since 1996
RCIDT
• Collaboration with Latin-American countries
European Commission
• Indicators exercise –UE Action Plan
WHO
• Collaborating Center → GODT

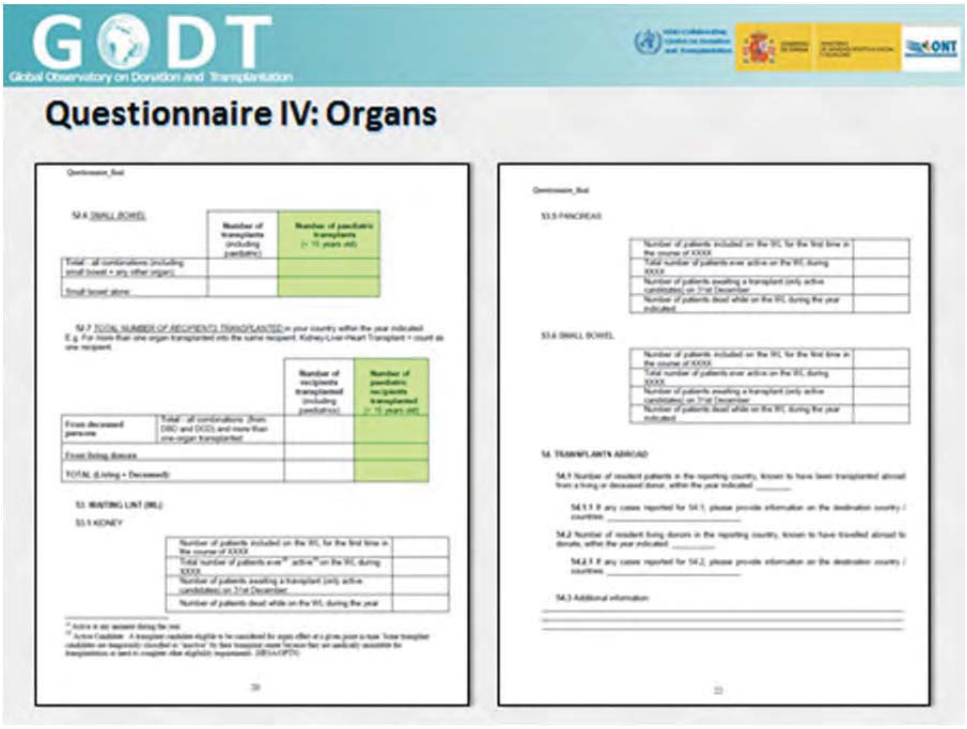

GODT
Global Observatory on Donation and Transplantation
GEOGRAPHICAL COVERAGE
Council of Europe / EDQM / CD-P-TO
CoE, Observers
RCIDT
Latin-American countries
European Commission
UE countries
WHO
Other WHO regions (AFR, EMR, SEAR, WPR and NIS/CAR Member States)

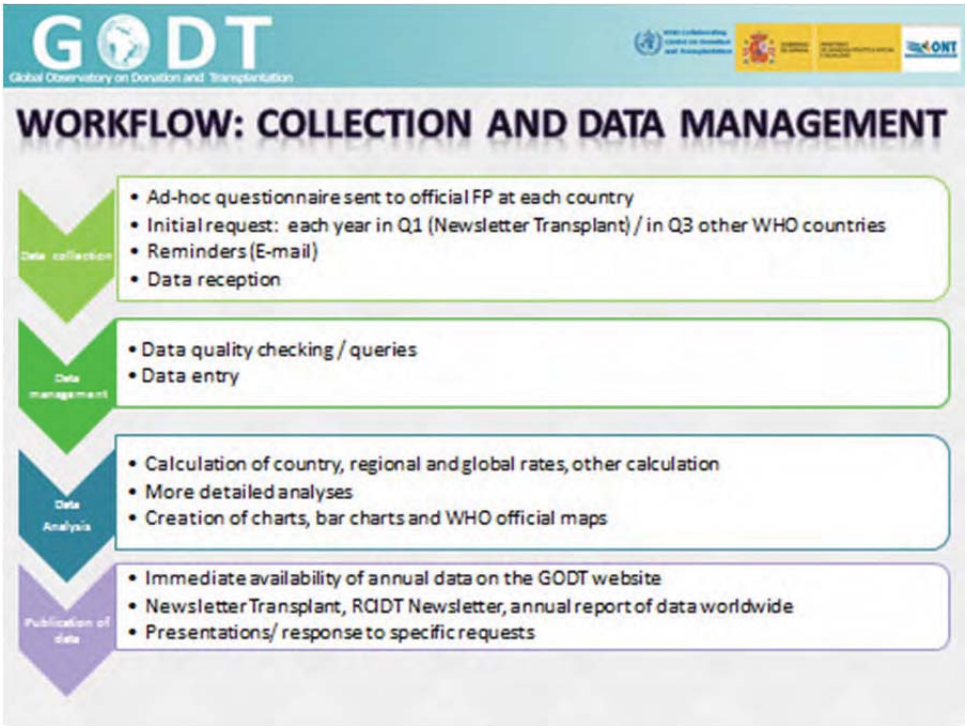

GODT
Global Observatory on Donation and Transplantation
SOURCE OF DATA
Questionnaire
Once a year
Period covered:
January 1-December 31
World Health Organization
Human Organ Donation and Transplantation Survey
Email
National Health Authorities
GODT
Global Observatory on Donation and Transplantation
Population:
United Nations Populations Fund
UNFPA

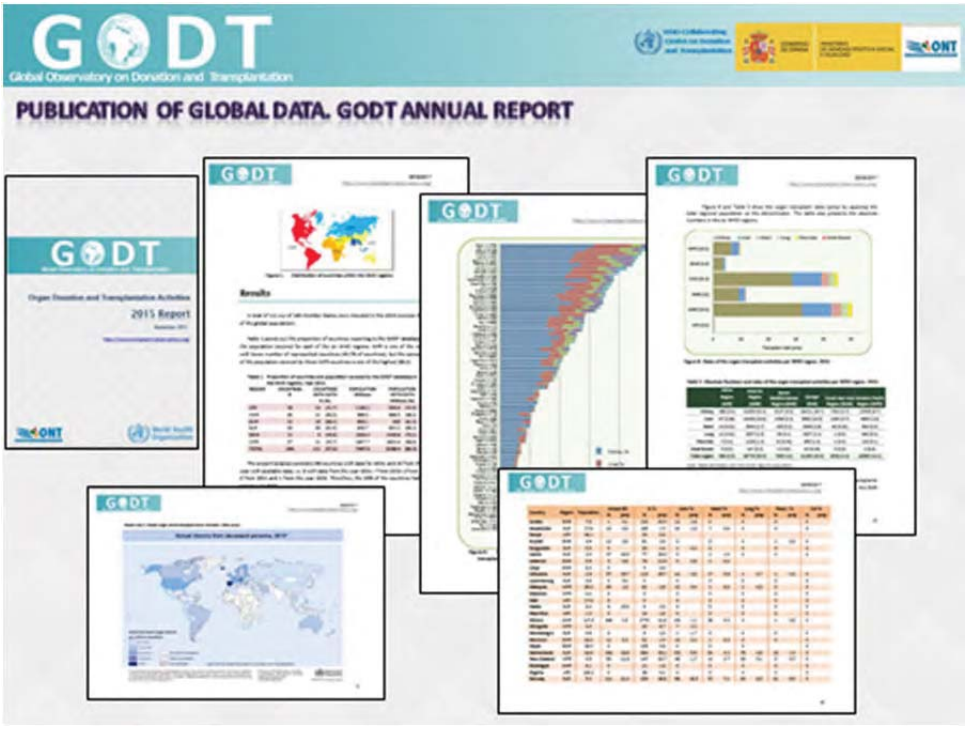

GODT
Global Observatory on Donation and Transplantation
Questionnaire I :
Organs
World Health Organization
Human Organ Donation and Transplantation
A 1/ ORGANIZATIONAL SYSTEM
A 2/ LEGISLATION
A 3/ ANNUAL ORGAN TRANSPLANTATION ACTIVITY

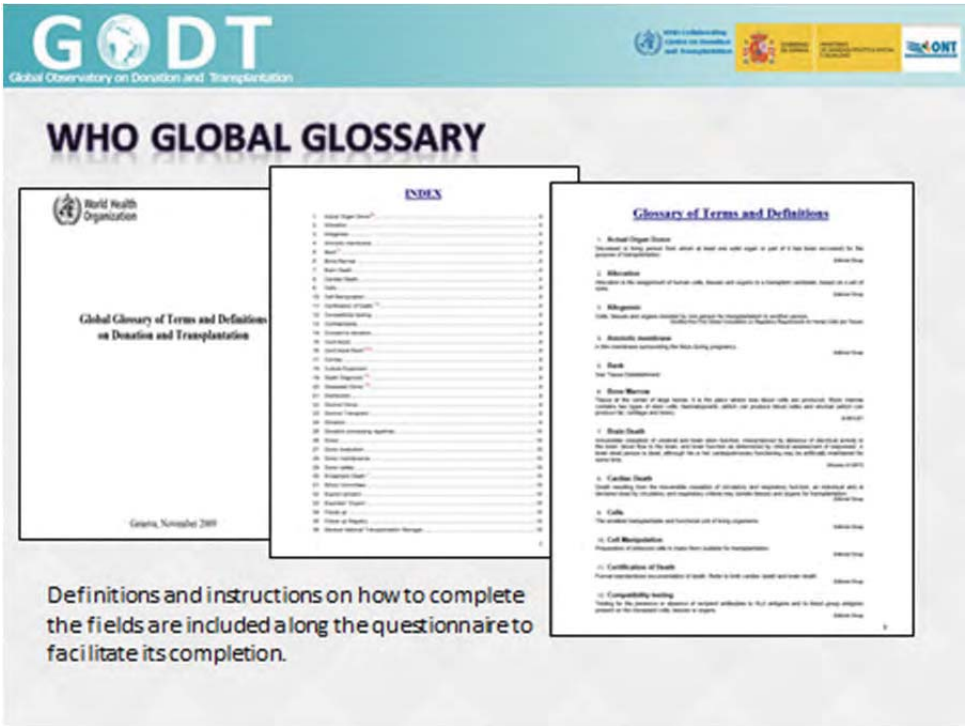

GODT
Global Observatory on Donation and Transplantation
Questionnaire II: Organs

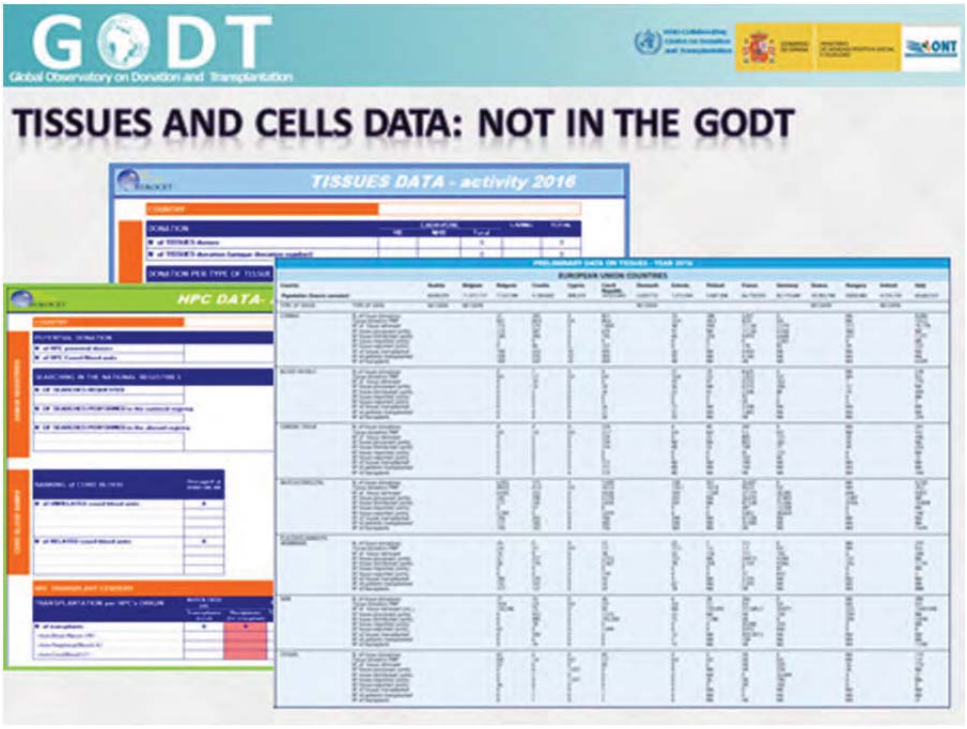

GODT
Global Observatory on Donation and Transplantation
Questionnaire III: Organs

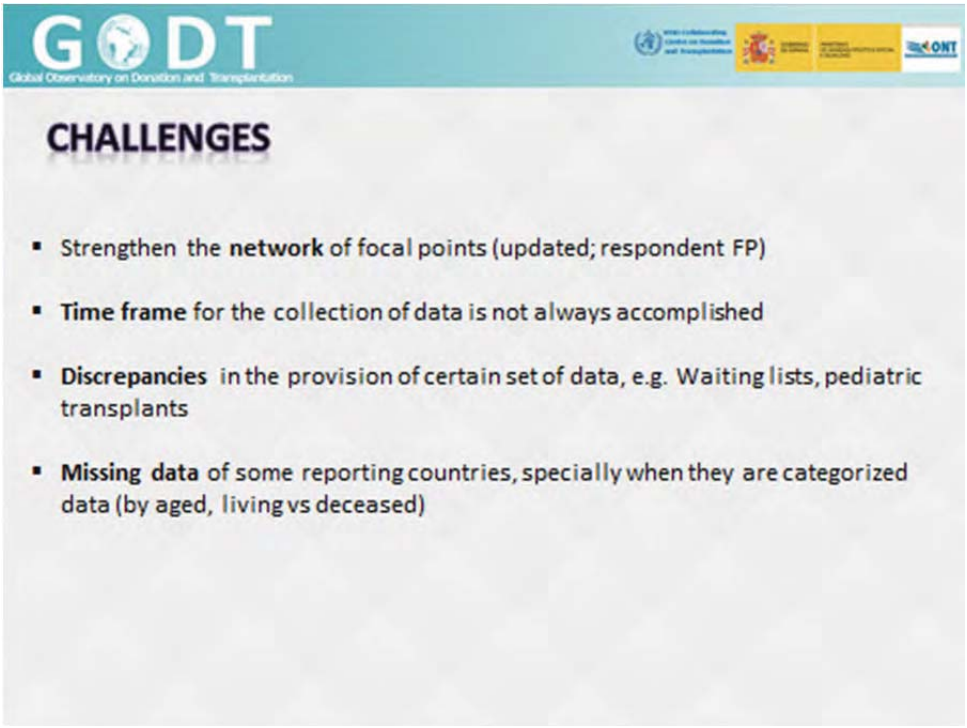

GODT
Global Observatory on Donation and Transplantation
Questionnaire IV: Organs

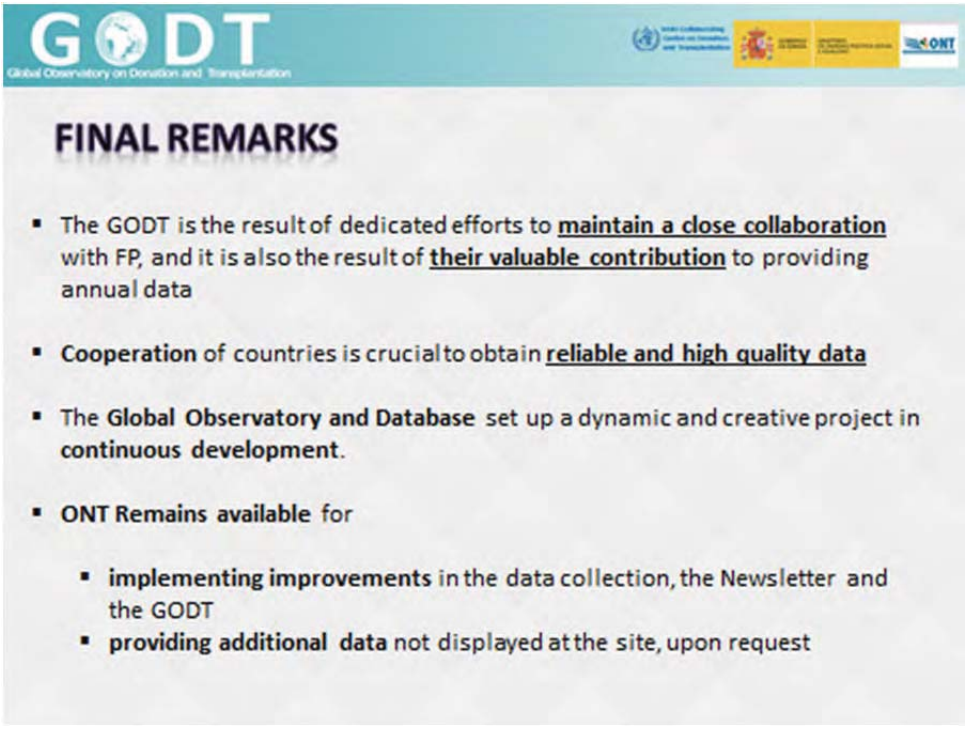

GODT
Global Observatory on Donation and Transplantation
WORKFLOW: COLLECTION AND DATA MANAGEMENT
Data collection
• Ad-hoc questionnaire sent to official FP at each country
• Initial request: each year in Q1 (Newsletter Transplant) / in Q3 other WHO countries
• Reminders (E-mail)
• Data reception
Data management
• Data quality checking / queries
• Data entry
Data Analysis
• Calculation of country, regional and global rates, other calculation
• More detailed analyses
• Creation of charts, bar charts and WHO official maps
Publication of data
• Immediate availability of annual data on the GODT website
• Newsletter Transplant, RCIDT Newsletter, annual report of data worldwide
• Presentations/ response to specific requests

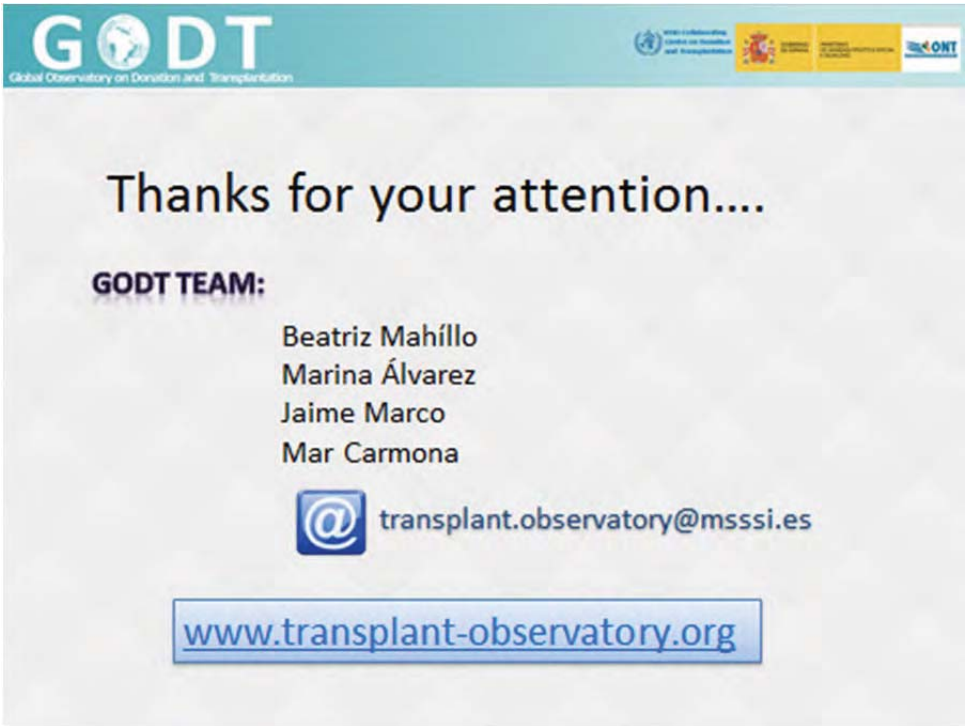

GODT
Global Observatory on Donation and Transplantation
PUBLICATION OF GLOBAL DATA. GODT ANNUAL REPORT
2015 Report


GODT
Global Observatory on Donation and Transplantation
WHO GLOBAL GLOSSARY
World Health Organization
Global Glossary of Terms and Definitions on Donation and Transplantation
INDEX
Glossary of Terms and Definitions
Definitions and instructions on how to complete the fields are included along the questionnaire to facilitate its completion.

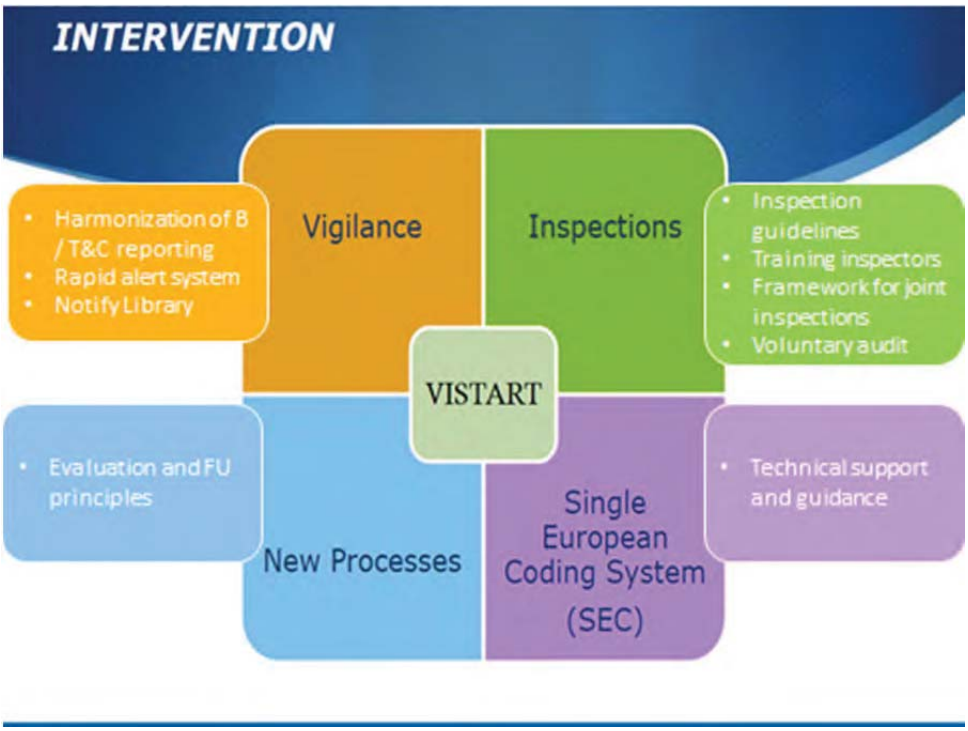

GODT
Global Observatory on Donation and Transplantation
TISSUES AND CELLS DATA: NOT IN THE GODT
TISSUES DATA - activity 2016
HPC DATA


GODT
Global Observatory on Donation and Transplantation
CHALLENGES
Strengthen the network of focal points (updated; respondent FP)
Time frame for the collection of data is not always accomplished
Discrepancies in the provision of certain set of data, e.g. Waiting lists, pediatric transplants
Missing data of some reporting countries, specially when they are categorized data (by aged, living vs deceased)


GODT
Global Observatory on Donation and Transplantation
ONT
FINAL REMARKS
The GODT is the result of dedicated efforts to maintain a close collaboration with FP, and it is also the result of their valuable contribution to providing annual data
Cooperation of countries is crucial to obtain reliable and high quality data
The Global Observatory and Database set up a dynamic and creative project in continuous development.
ONT Remains available for
implementing improvements in the data collection, the Newsletter and the GODT
providing additional data not displayed at the site, upon request


GODT
Global Observatory on Donation and Transplantation
ONT
Thanks for your attention....
GODT TEAM:
Beatriz Mahíllo
Marina Álvarez
Jaime Marco
Mar Carmona
transplant.observatory@msssi.es
www.transplant-observatory.org

- **The vigilance expert sub-group – are the SARE denominators fit for purpose? - George Galea (on behalf of the EU Vigilance Expert Sub-Group; VES)**



Funded by the European Commission

VISTART

Vigilance Expert Subgroup

Formed by SANTE, February 2017
Vigilance experts for Blood, Tissues and Cells, nominated by the national competent authorities

Technical expertise to **support annual SARE reporting** for Blood, tissues and cells e.g. improvement of Common Approach/reporting template (B/TC) analysis, publication of annual SARE summaries

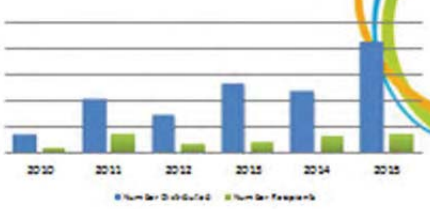
functioning of the Rapid Alert platforms for Blood (RAB) and Tissues and Cells (RATC)

other vigilance and surveillance activities.

Funded by the European Commission

VISTART

Scale of the Denominator problem



- Twenty one countries provided data regarding the number of tissues and cells *processed* in 2015
- For non-reproductive tissues and cells, only 24 countries reported data on units distributed on recipients.
- For reproductive tissues and cells, only 14 countries reported data on units distributed and 10 countries only on number of recipients.
- 13 Member States reported no recipient SAR in 2015.
- These data, suggest that SAR reporting still needs to be improved at national level.

Funded by the European Commission

VISTART

SAR Denominators- key issue to relate SAR into context

- Numbers processed ->SAE denominator
- Numbers distributed/issued
- Numbers grafted/recipients

Accuracy and options dependent on

- *National reporting structures*
- *Type of tissue*
- *Processing methodology*
- *Agreement on units*

Funded by the European Commission

VISTART

SAR denominators commonality is critical:

- When there is significant lack of data-the 'incidence of SAR' are more of a reflection of the effectiveness and completeness of the national vigilance and reporting systems.
- only when commonly agreed data is used -the % of SARs calculated individually, will allow for bench-mark the data.

Funded by the European Commission

VISTART
VIGILANCE AND INSPECTION FOR THE SAFETY OF TRANSFUSION ASSISTED REPRODUCTION AND TRANSPLANTATION

VES Rapporteurs: work plan

Review of proposals for harmonization/improvement of vigilance data quality

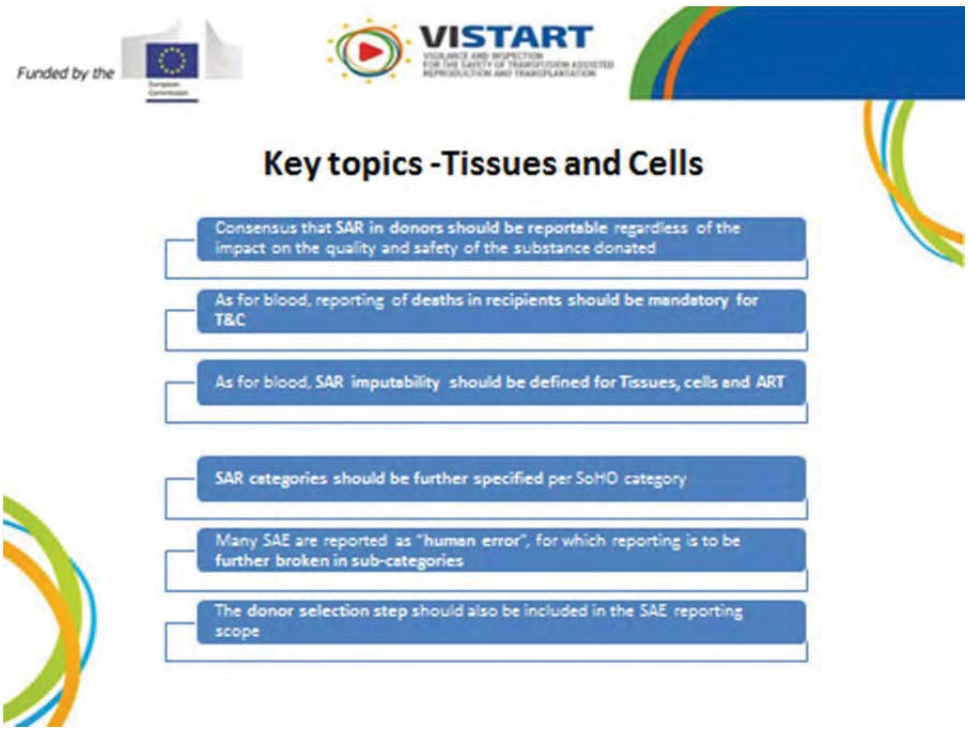
- Sources: minutes of VES meeting, VISTART recommendations
- Domain: Blood, Tissues and Cells
- Change required in: Common Approach, reporting template, Directive

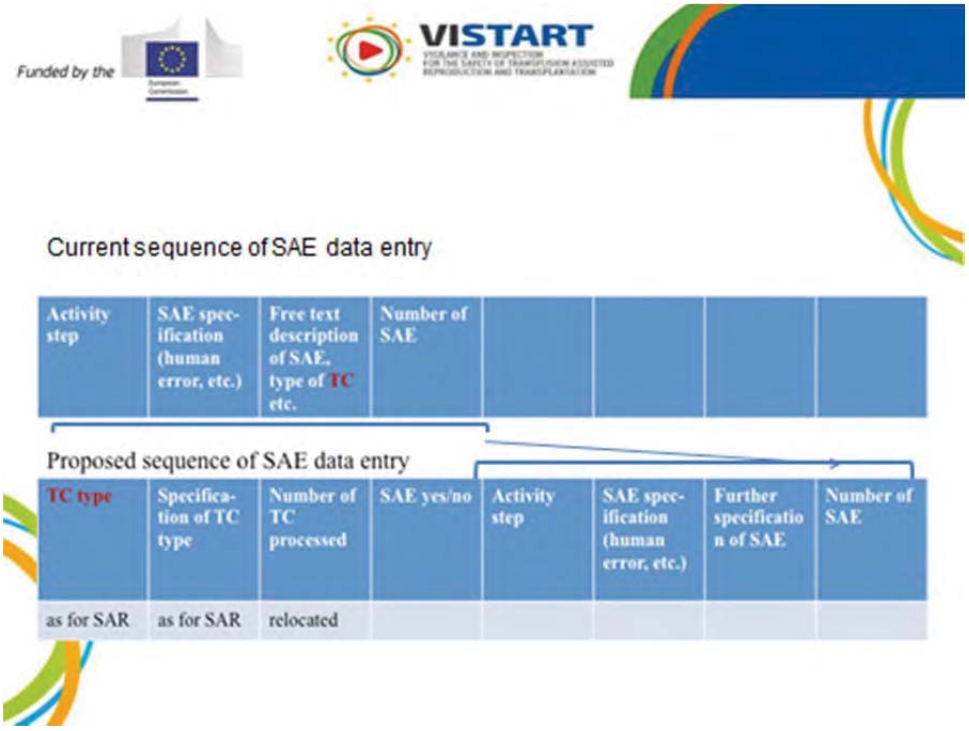
44 proposals identified

Funded by the European Commission

VISTART
VIGILANCE AND INSPECTION FOR THE SAFETY OF TRANSFUSION ASSISTED REPRODUCTION AND TRANSPLANTATION

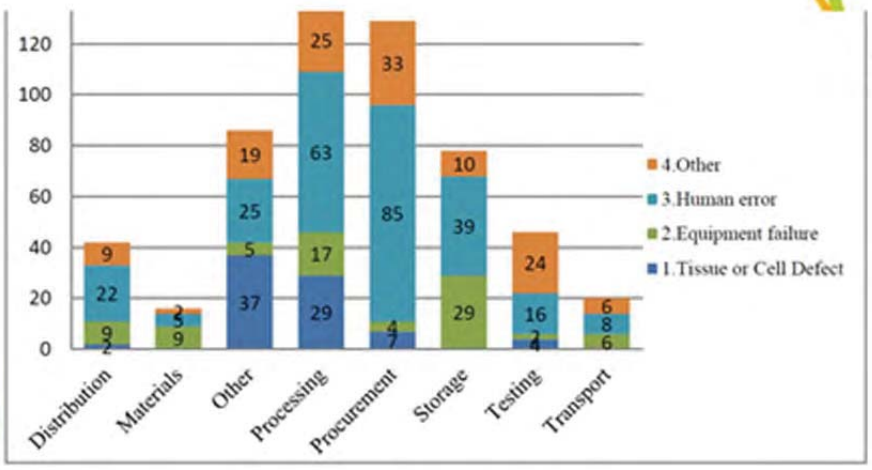
14		V	B, TC	10	SAE reporting criteria	Blood SSBT Sentinel Events definition	x			3			
15	M	V	B	2	SAE denominators	Cryoprecipitate & granulocytes should be included	x	x		4	Proposal to include further breakdown of platelet concentrates and of TC according to EUTC composition not supported by EDQM/VES		Cryoppt is already covered as "plasma" and Granulocytes/ buffy coats can be added as "Other", though no objections to further defining individual components. However, this does add additional burden to reporting establishments if they have to provide specific "issue" data for an ever growing list of component types.
16	M		B, TC	2	SAE denominators	There should be a differentiation between components which have had a viral inactivation step applied and those which have not. (Applies also to TC)	x			4	*Do not understand why. An SAEE or SAE should be reported irrespective of the component tissue used.*		See comment above
17	M		B, TC	2	SAE denominators	There should be a differentiation between components that have been leucodepleted and those that have not. (Applies also to TC)	x			4			See comment above
18	M		B, TC	2	SAE denominators	Include percent of more detailed product types (not SAE per type)	x			4	*I think denominators are difficult to agree on, would welcome a broader discussion. In the UK we struggle with Annual Activity data which at best is very approximate!*		Not sure what is meant here. A "product" as defined by the Directive is not covered. See comment above relating to additional burden on reporters to provide more detailed information.


Funded by the
VISTART
Key topics -Tissues and Cells
Consensus that SAR in donors should be reportable regardless of the impact on the quality and safety of the substance donated
As for blood, reporting of deaths in recipients should be mandatory for T&C
As for blood, SAR imputability should be defined for Tissues, cells and ART
SAR categories should be further specified per SoHO category
Many SAE are reported as "human error", for which reporting is to be further broken in sub-categories
The donor selection step should also be included in the SAE reporting scope


Funded by the
VISTART
Current sequence of SAE data entry
Activity step
SAE specification (human error, etc.)
Free text description of SAE, type of TC etc.
Number of SAE
Proposed sequence of SAE data entry
TC type
Specification of TC type
Number of TC processed
SAE yes/no
Activity step
SAE specification (human error, etc.)
Further specification of SAE
Number of SAE
as for SAR
as for SAR
relocated

Funded by the European Commission

VISTART



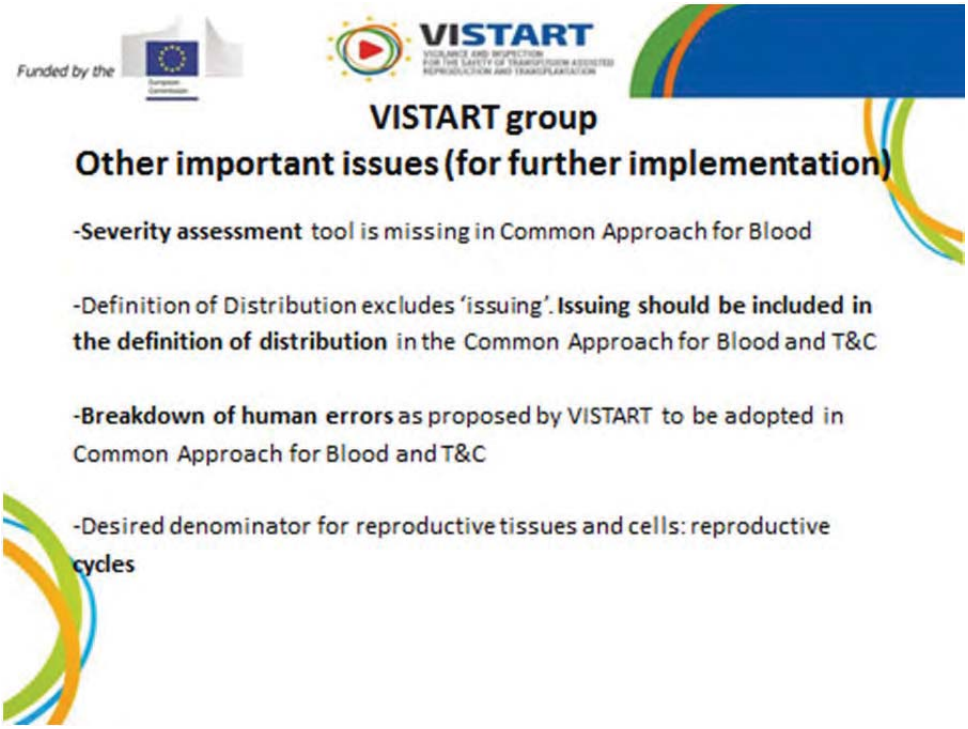
Funded by the European Commission

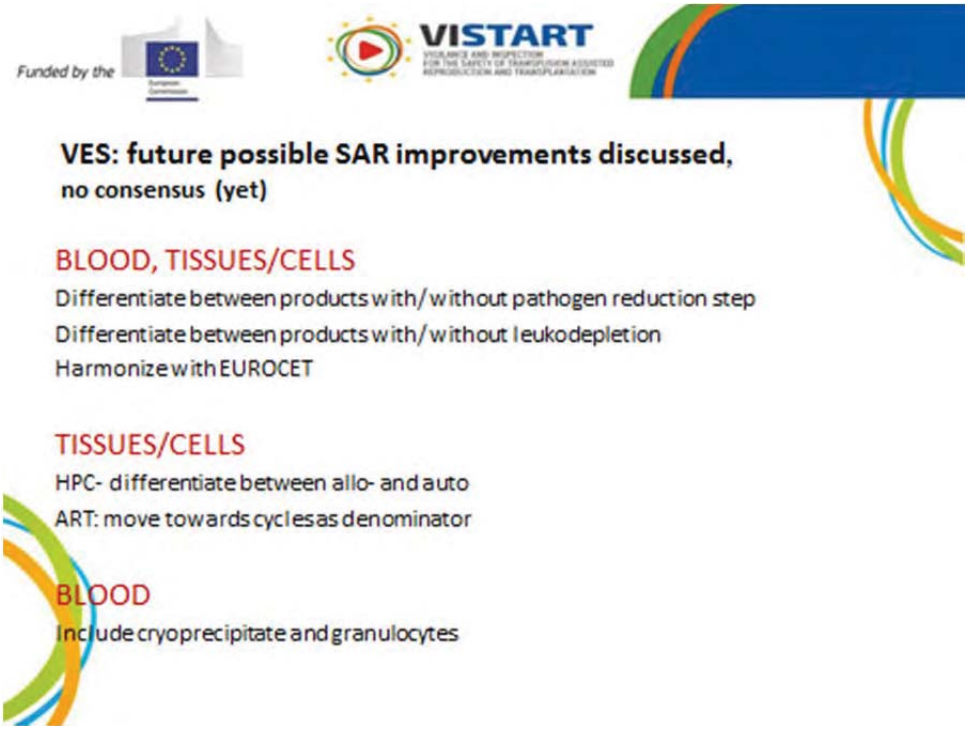
VISTART

VES: future improvements

1. Clarify and agree on proposals for next round (Vigilance Expert Subgroup in consultation with SANTE)
2. Competent Authority approval
3. Members of Vigilance Expert Subgroup draft texts for Common Approach & Templates → circulated for approval before 2019 reporting exercise

Level 1	Level 2			Depending on complexity:
"Quick fix"			2018	Develop consensus & proposal
		2018	2019	Advance notice
2017	2018	2019	2020	SARE reporting (Establishments)
2018	2019	2020	2021	Commission data collection

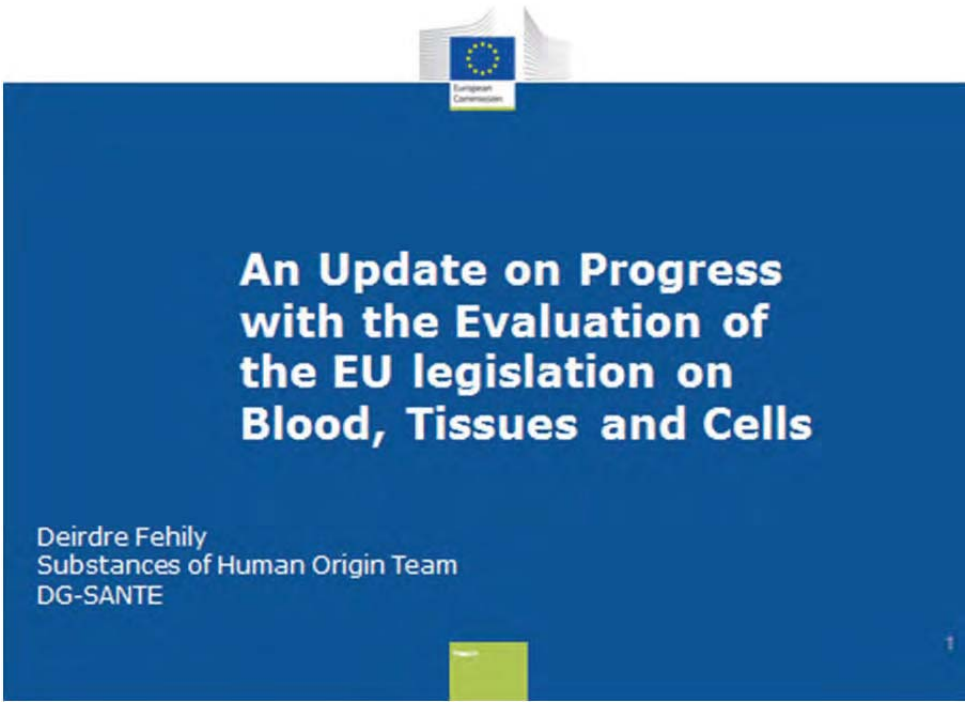

Funded by the
VISTART
VISTART group
Other important issues (for further implementation)
-Severity assessment tool is missing in Common Approach for Blood
-Definition of Distribution excludes 'issuing'. Issuing should be included in the definition of distribution in the Common Approach for Blood and T&C
-Breakdown of human errors as proposed by VISTART to be adopted in Common Approach for Blood and T&C
-Desired denominator for reproductive tissues and cells: reproductive cycles


Funded by the
VISTART
VES: future possible SAR improvements discussed,
no consensus (yet)
BLOOD, TISSUES/CELLS
Differentiate between products with/without pathogen reduction step
Differentiate between products with/without leukodepletion
Harmonize with EUROCET
TISSUES/CELLS
HPC- differentiate between allo- and auto
ART: move towards cycles as denominator
BLOOD
Include cryoprecipitate and granulocytes

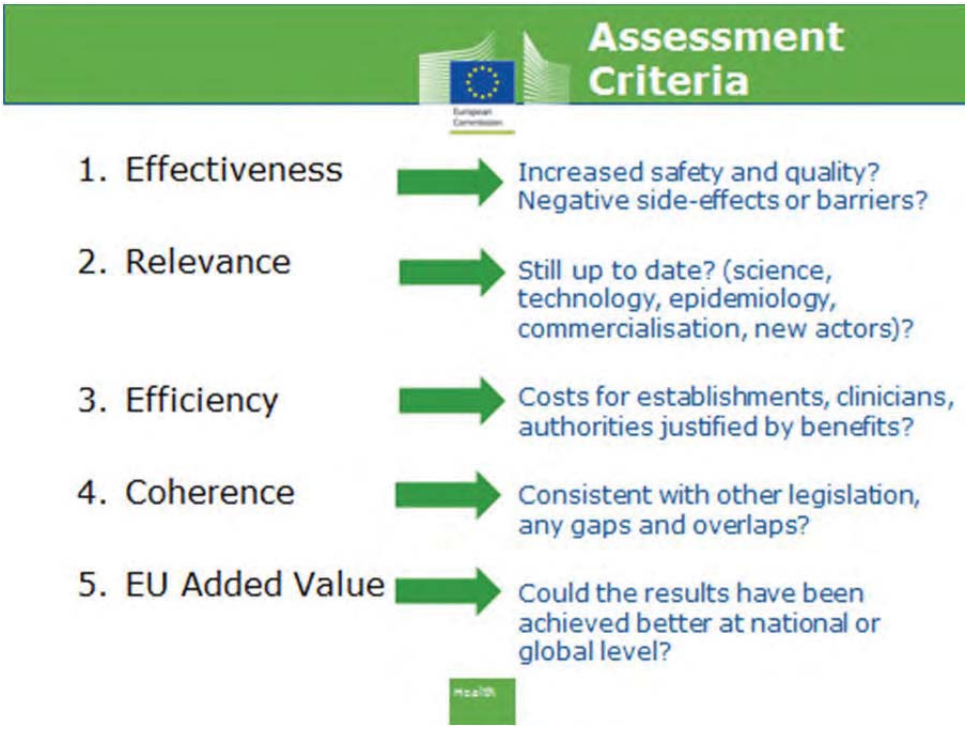

Funded by the
VISTART
Key issues:
• Commonality of denominators
These are key actors for ensuring not only traceability of tissues and cells, but also effective vigilance systems.
It is important to avoid overburdening reports with too much detail especially if SARs cannot be collected consistently.
• Improved tissue vigilance
Health professionals involved in the clinical application of tissues and cells and tissue establishment personnel should be encouraged to submit reports.
• These outcomes may contribute to the ongoing evaluation of the legal frameworks on blood, tissues and cells.
Improved legislation in any future revisions.

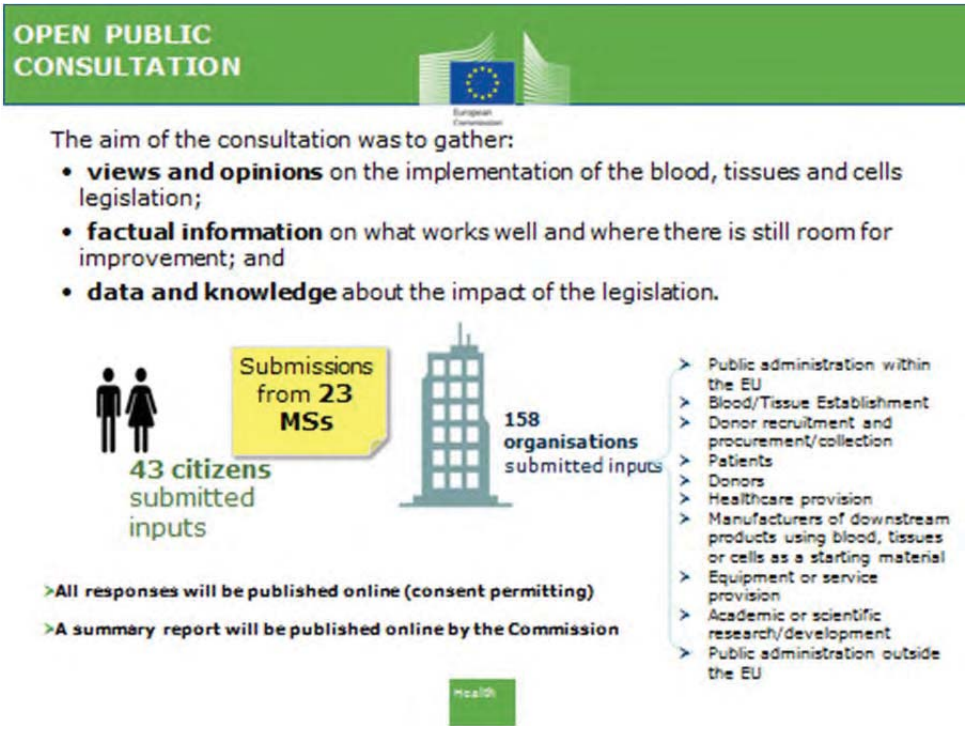

Funded by the
VISTART
THANK YOU!

- **An Update on progress with the evaluation of the EU legislation on Blood, Tissues and Cells - Deirdre Fehily (European Commission)**



- The purpose of the evaluation is to provide a comprehensive assessment of the directives, examining their **functioning across the EU**.
- In particular the evaluation is assessing the extent to which the Main Directives have met their **original objectives** and whether they remain **fit for purpose** looking also at the contribution of the Implementing Directives.
- The evaluation is expected to provide a sound **evidence base** which will be used to consider the need for any changes to the legislation.


Assessment Criteria
1. Effectiveness
Increased safety and quality? Negative side-effects or barriers?
2. Relevance
Still up to date? (science, technology, epidemiology, commercialisation, new actors)?
3. Efficiency
Costs for establishments, clinicians, authorities justified by benefits?
4. Coherence
Consistent with other legislation, any gaps and overlaps?
5. EU Added Value
Could the results have been achieved better at national or global level?


OPEN PUBLIC CONSULTATION
The aim of the consultation was to gather:
• views and opinions on the implementation of the blood, tissues and cells legislation;
• factual information on what works well and where there is still room for improvement; and
• data and knowledge about the impact of the legislation.
Submissions from 23 MSs
43 citizens submitted inputs
158 organisations submitted inputs
Public administration within the EU
Blood/Tissue Establishment
Donor recruitment and procurement/collection
Patients
Donors
Healthcare provision
Manufacturers of downstream products using blood, tissues or cells as a starting material
Equipment or service provision
Academic or scientific research/development
Public administration outside the EU
All responses will be published online (consent permitting)
A summary report will be published online by the Commission

Stakeholder Event 20.09.2017

- >200 participants
- Wide range of interests
- Strong statements from 20 panellists
- Lively open discussions

5 main themes

- Donors
- Regulatory oversight
- Availability and sufficiency
- Consistency and coherence
- A changing world

Stakeholder Event Summary Report

Health

External Study

- **Contractor** – ICF Consulting
  - Supporting the Commission in evaluating the legislation
  - Supported by **3 thematic experts**
  - Focusing on answering the evaluation questions
  - Independently documenting an evidence base
  - An independent study to be published by mid-2018
- **Commission** to bring together the work of the contractor, EC services and results of the public consultation in Commission Staff Working Document for publication by end 2018

Effectiveness

Some preliminary Stakeholder consultation messages

The legislation has helped increase safety and quality (Blood – 90%; Tissues and Cells – 99%)

But several provisions are not adequate or missing:

- Donor safety (donor reactions and donor follow-up, including long term)
- Clinical outcomes (post-transplant/transfusion/ART) – control of access to stem cell therapies of unproven efficacy – stem cell tourism
- Impact on supply/sufficiency (plasma, corneas)
- Voluntary Unpaid Donation (VUD) – unclear and varying interpretation – challenge when SoHO used for commercial manufacture of medicines
- Unclear Vigilance definitions and requirements – particularly for denominator reporting
- Value of professional standards, certification and training not reflected
- SEC implementation challenging - exemptions implemented differently in MS
- Need for specialist training of inspectors

Relevance

Some preliminary Stakeholder consultation messages

The legislation is not adaptable enough to manage risks and changes, such as:

- technological/ scientific
- epidemiological (WNV, Malaria, Zika, etc.)
- societal e.g. ageing, travel, migration

In particular, it is lacking in:

- procedures to keep legislation up to date
- provisions for the authorisation of novel/experimental treatments (increasing complexity of manipulation requires more specific requirements)
- clarity of scope (new SoHO, stakeholders, activities)
- provisions addressing specificities of subsectors (plasma, ART, HSC etc.)
- involvement of experts (EDQM, ECDC, professional societies, etc.)

While in some cases it is considered too specific:

- equivalent safety/quality can be achieved in different ways – cross reference professional standards

Efficiency

Some preliminary Stakeholder consultation messages

The legislation led to higher costs but it also brought benefits that justified the costs (Blood - 80%, Tissues and Cells - 88%)

Specific cost issues raised in relation to:

- smaller blood and tissue establishments that face higher costs
- GMP and air quality requirements [Tissues and Cells]
- Burdensome oversight rules (e.g., inspection planning/frequency, import requirements)

Insufficient attention is given to:

- assessing cost effectiveness of safety measures [Blood]
- re-evaluating technical criteria to ensure balance between safety and costs (e.g. testing, donor selection)

Coherence

Some preliminary Stakeholder consultation messages

The legislation within its own provisions is generally coherent. Incoherencies with other relevant EU legislation highlighted:

Borderlines and definitions (Medical Devices, Medicinal Products)

- Some SoHO fall under different legislations across Member States
- Classification mechanisms not adequate
- Some non-homologous ATMP are identical to T&C, same Safety & Quality standards should apply. T&C legislation the most appropriate
- Incoherence with Organ Directive for donor protection and VUD
- Communication between the sectors not optimal (e.g. for vigilance)
- No harmonisation of inspection requirements under different legislations
- Link to legislation on communicable diseases and role of ECDC
- EU charter of human rights and commercialisation (VUD and non-profit)
- Global standards needed for global distribution of HSC

EU Added Value

Some preliminary Stakeholder consultation messages

The legislation has helped increase safety and quality, harmonisation and confidence

Blood - 74% and Tissues and Cells - 64% of organisations believe that:

- **this could not have been achieved at national level, or**
- **might have happened but EU legislation sped up the process**

80% of the individual citizens that responded believe that the same results could not have been achieved without EU action.

- However, some say that certain sectors were already well organised therefore limited value for those sectors (particularly HSC).
- EU Added Value limited by more stringent national requirements and by national limits placed on donor recruitment.

20/09/2017

Timeline

Key elements	Estimated timing
Roadmap consultation	Q1 2017
Public consultation	Q3 2017
Publication of submissions summary results	Q2 2018
External contract	Q2 2017 – Q3 2018
(Desk-based research focus groups, interviews, targeted survey)	
Commission evaluation report	Q4 2018

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https://ec.europa.eu/health/blood_tissues_organs/policy/evaluation_en

LIST OF ATTENDING EXPERTS

List of the participants

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ACRONYMS

CD-P-TO	European Committee on Organ Transplantation (EDQM, Council of Europe)
CNT	Italian Centro Nazionale Trapianti (Italy)
EATB	European Association of Tissue Banks
EBA	European Blood Alliance
EBMT	European Society for Blood and Marrow Transplantation
EC	European Commission
EDQM	European Directorate for the Quality of Medicines & HealthCare
EEBA	European Eye Banking Association
ESHRE	European Society for Human Reproduction and Embryology
EU	European Union
GODT	Global Observatory on Organ Donation and Transplantation (WHO)
HTA	Health Technology Assessment
ONT	National Transplant Organisation (Spain)
SARE	Serious Adverse Events and Reactions
VES	EU Vigilance Expert Subgroup
WHO	World Health Organization
WMDA	World Marrow Donor Association