Evaluation of the EU legislation on Blood, Tissues and Cells

Pharma Committee October 23, 2018

DG SANTE
Unit B4 – Medical Products: quality, safety, innovation

Health and Food Safety

Context

- Aim: assess whether EU Directives have **met their objectives** of ensuring safety and quality for blood (2002/98/EC) and for tissues and cells (2004/23/EC), and whether they **remain fit for purpose**

- Scope: **EU** activities on blood and blood components, haematopoetic stem cells (bone marrow, cord blood), IVF, replacement tissues, starting materials for manufacture (but NOT medicinal products or medical devices themselves)

- Relevance for pharmaceutical sector:
  - **Adequacy or BTC legislation when plasma, tissues or cells are used for manufacture of medicinal products**
  - **Coherence/borderlines between BTC and medicinal products**

- The evaluation is expected to provide a sound **evidence base by Q1 2019** which will be used to consider the need for any changes to the legislation.

INFOGRAPHIC

ORGANS, BLOOD, TISSUES & CELLS IN THE EU

BLOOD TRANSFUSION
25 MILLION / YEAR

BONE MARROW TRANSPLANTS
34 THOUSAND / YEAR

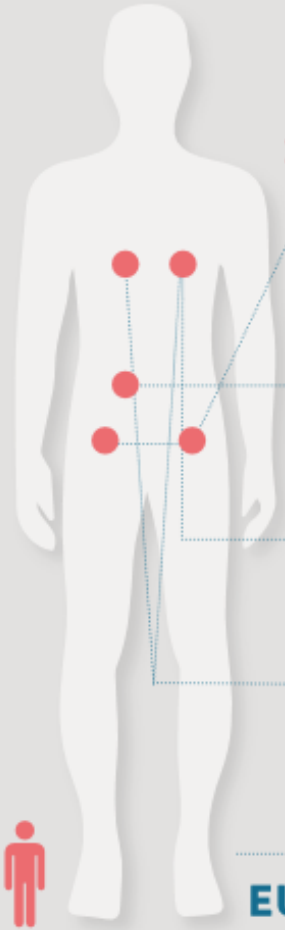
ASSISTED REPRODUCTION CYCLES
690 THOUSAND IN 2013

OTHER TISSUES :
HEART VALVES | SKIN | BONE | CORNEA

PLASMA FOR MANUFACTURING MEDICINES
8 MILLION LITRES / YEAR

FROM DONOR TO RECIPIENT

DONATION → COLLECTION → TESTING → PROCESSING → STORAGE → DISTRIBUTION → APPLICATION



ORGAN TRANSPLANTS

20 638	KIDNEY
7 762	LIVER
2 254	HEART
1 916	LUNG

OTHERS
- PANCREAS
- SMALL BOWEL
- HAND
- FACE

TOTAL IN 2016
33.4 THOUSAND

59 THOUSAND
PATIENTS ON WAITING LISTS ON 31/12/2016

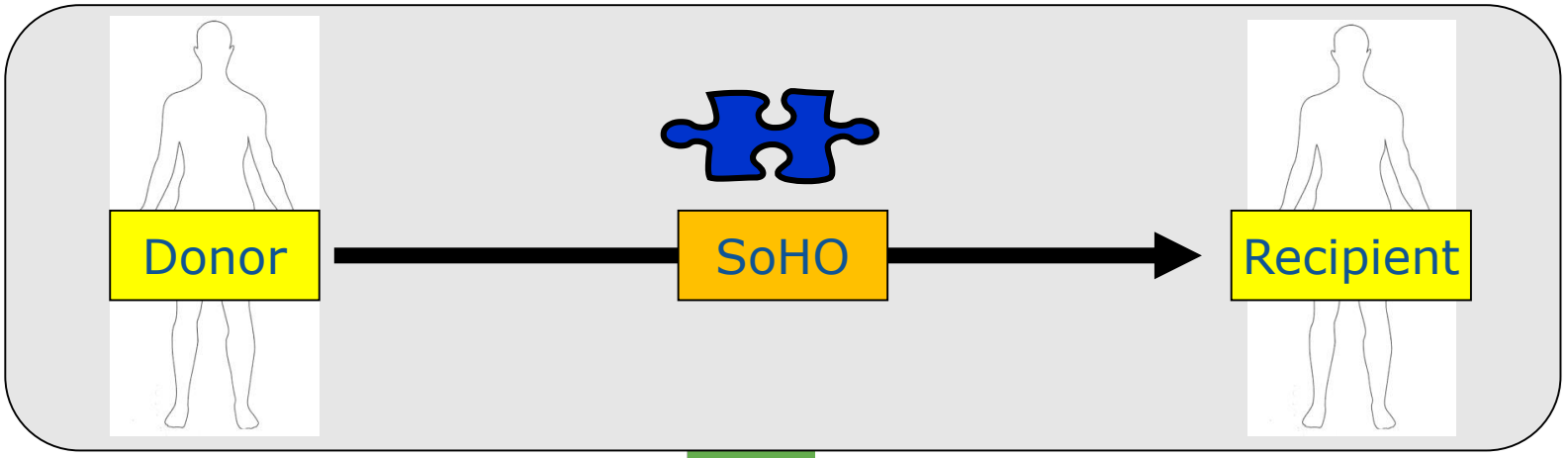
EU ACTION PLAN ORGANS

EU legal framework
Main acts

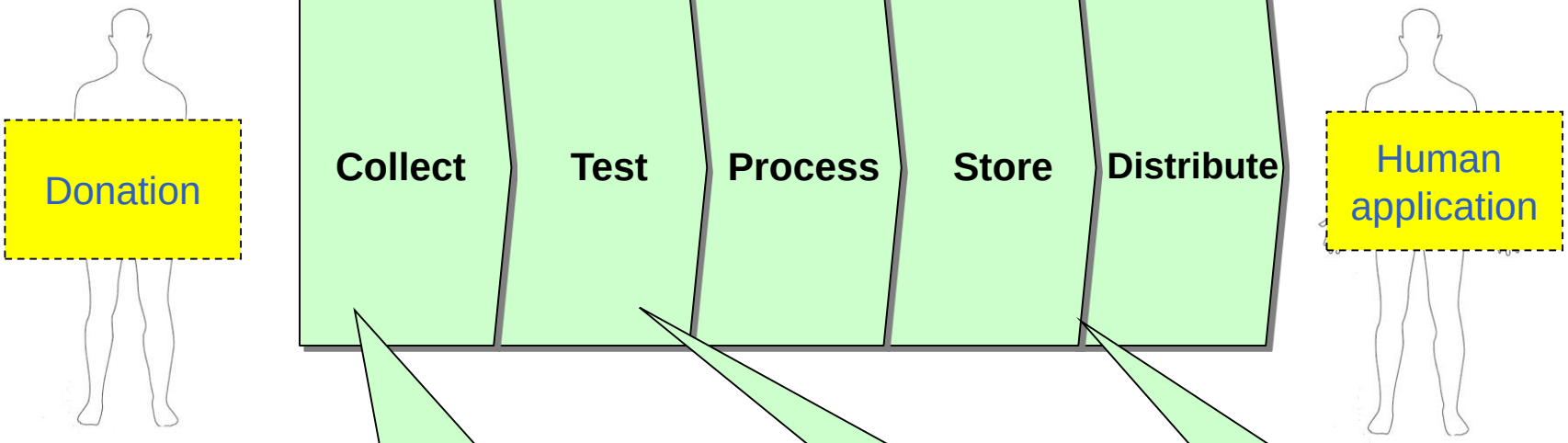
2002

2004

2010



EU legal mandate: safety and quality



① **Medical Professionals**

Selection/deferral, consent…

HIV, Hepatitis B, Hepatitis C..

Quality requirements

② **National Competent Authorities**

Oversight: vigilance, traceability, accreditation, inspection…

③ **European Commission**

EU-level support: rapid alerts, traceability system…

The Member States transpose and implement the legislation

Oversight is the role of the National Competent Authorities (NCA) – some are medicinal product regulatory agencies and others are not

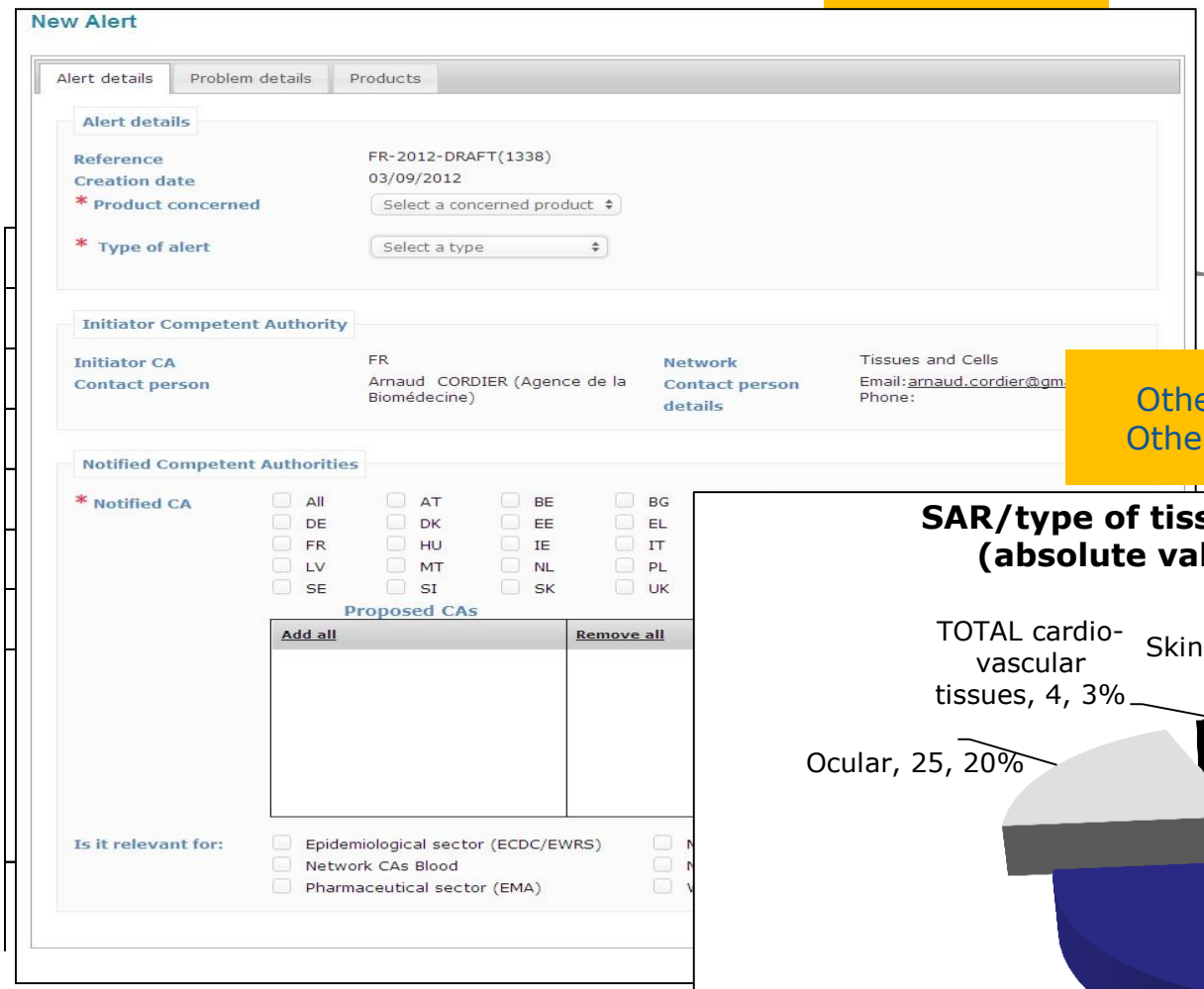
- *PEI (DE)*
- *HTA, MHRA and HFEA (UK)*
- *CNT and CNS (IT)*
- *ANSM and ABM (FR)*
- *ONT and MoH (ES)*
- *HPRA (IE)*
- *etc.*

Ensure oversight – inspection, authorisation, vigilance

HANDLING ALERTS - SAR

European Commission

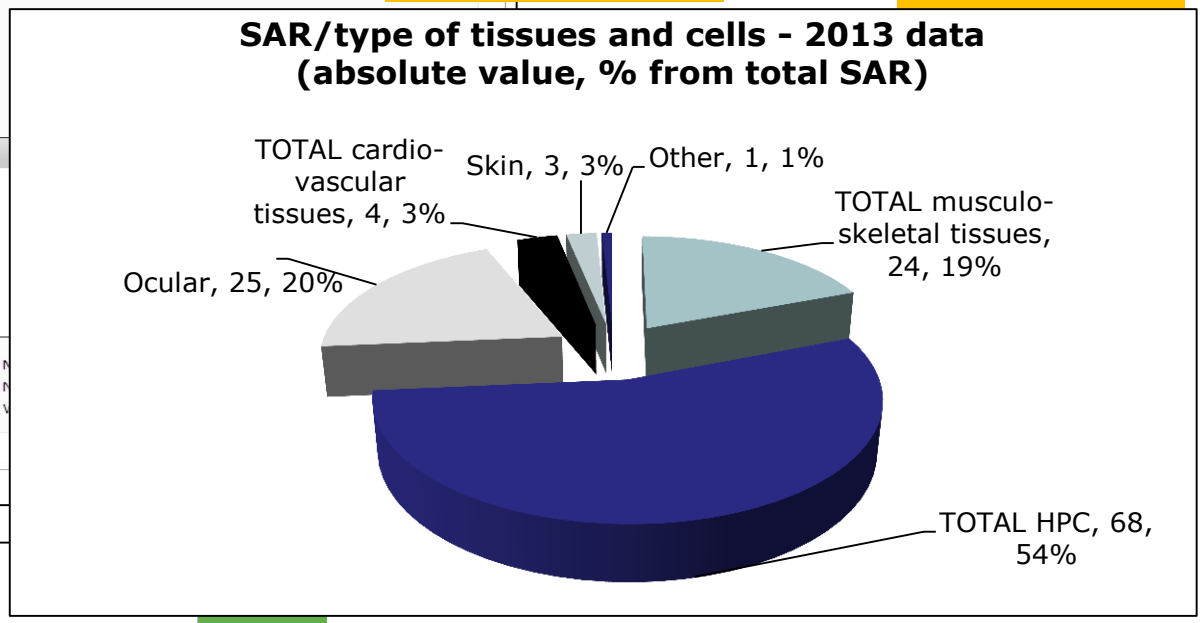
ANNEX III



National Competent Authorities

Other NCA's Other sectors

European Commission



The Evaluation
Following Better Regulation Rules

Assessment Criteria

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

OPEN PUBLIC CONSULTATION RESULTS

SUBMISSIONS BY 158 ORGANISATIONS

European Commission

Health and Food Safety Directorate General

Twitte

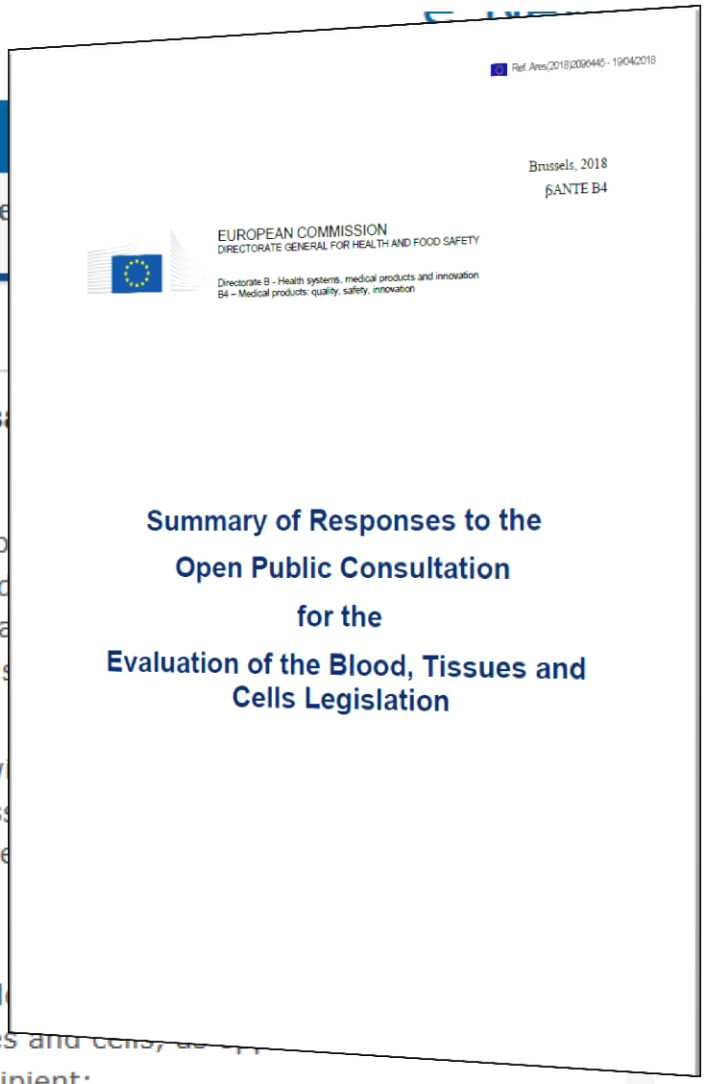
Public Health

EU legislation makes Blood, Tissues and Cells s with developments, Public Consultation finds

The open public consultation evaluating the EU legal framewo found that that the majority of the respondents, who included groups, such as professional societies, donor and patient orga consider that the legislation had made blood, tissues and cells

Most respondents find that the legislation is not up-to-date w epidemiological or societal developments and that the proces enough to adapt to them. They also believe that some require inadequate, among them:

- Inadequate provisions for the protection of the living d
- Lack of requirements to ensure quality of blood, tissues and cells, as
- Lack of demonstration of safety and efficacy in the recipient;
- Absence of provisions for ensuring sufficiency of supply.


Ref. Ares(2018)2096445 - 19/04/2018

Brussels, 2018
SANTE B4

EUROPEAN COMMISSION
DIRECTORATE GENERAL FOR HEALTH AND FOOD SAFETY

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

Summary of Responses to the Open Public Consultation for the Evaluation of the Blood, Tissues and Cells Legislation

Stakeholder Event 20.09.2017

European Commission

- >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

Report published online

Targeted consultation meetings

- FIODS
- IPOPI/PLUS
- EPA
- EHC
- IHN
- PPTA
- IPFA
- EBA
- EBMT
- WMDA
- ESHRE
- EATB

- CoReSoHO
- EHA
- EEBA
- Fertility Europe
- Cryos Int
- Medtech
- FDA
- AABB
- AATB
- ISCT
- ECA ATMP group

1. Donor Safety and vigilance
2. Plasma Supply
3. Recipient follow-up
4. Testing requirements (e.g. WNV)
5. Assisted Reproduction topics – genetic testing and transmission, sperm delivery etc.
6. Pathogen* inactivation
7. Medical devices*

Published Summary Minutes

*not yet published

Summary minutes of meetings with Stakeholders

All Events

Blood

Blood - Meetings with Stakeholders

25 June 2018
Meeting with Medtech Europe

19 June 2018
Meeting with the Plasma Protein Therapeutics Association (PPTA)

17 April 2018
Meeting with the International Plasma Fractionators Association (IPFA)

03 April 2018
Meeting with the European Blood Alliance

09 March 2018
Meeting with the American Association of Blood Banks (AABB)

08 March 2018
Meeting with the U.S. FDA Center for Biologics Evaluation and Research

20 September 2017
Stakeholder Event - Evaluation of the EU legislation on blood, tissues and cells

15 September 2017
Meeting with the Plasma Protein Therapeutics Association (PPTA)

22 June 2017

e-newsletter Thu, 10/11/2018

0 goals reachable if we stay the course

Latest updates

European Day of Organ Donation and Transplantation: Number of transplants in EU continues to rise
Released 12 October 2018

Agenda - Meeting of Competent authorities for blood and blood components (10-11 October 2018)
Released 04 October 2018

Summary minutes - Meeting with Medtech Europe (25 June 2018)
Released 14 September 2018

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Highlights

Effectiveness

Emerging messages (non-exhaustive)

European Commission

The legislation has helped increase safety and quality but several provisions are not adequate or are missing:

- Donor safety (e.g. reporting of serious reactions, long-term follow-up)
- VUD and compensation (many interpretations, deviation single market, …)
- Mandatory evaluation of T&C quality (as opposed to safety)
- Risk-basis for technical requirements (different means possible)
- Genetic testing for gamete donors
- Some requirements negatively impact supply/sufficiency (plasma, corneas)
- Other supply issues are not covered (e.g., US dependency for plasma or emergency preparedness)
- Specifications for authorities: skill levels, independence, inspection frequency, vigilance definitions…
- Unclear Vigilance definitions and requirements
- Clinical outcomes/efficacy requirements missing or insufficient (post-transplant/transfusion/ART) – concerns regarding claims and stem cell tourism
- No recognition/use of professional standards and accreditation

Relevance

European Commission

Emerging messages (non-exhaustive)

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

- Technological innovation
- Scientific knowledge
- Epidemiological changes (WNV, Malaria, Zika, etc.)
- Societal changes e.g. ageing, migration, same-sex couples

In particular, it is lacking in provisions to address:

- changing risks and technology – safety and effectiveness (many examples)
- underused potential for pathogen inactivation and automation
- authorisation of novel/experimental treatments – e.g., need for clinical follow-up data to demonstrate safety and quality
- clarity of scope (new SoHO, stakeholders, activities – e.g., point-of-care)
- provisions addressing specificities of subsectors (plasma, ART, etc.)
- involvement of experts (EDQM, ECDC, professional societies, etc.)
- provisions for emergency preparedness (e.g. role of ECDC, continuity of critical supply – blood and plasma)
- tools to address commercialisation/internationalisation
- definitions to reflect gender rights

Efficiency

European Commission

Emerging messages (non-exhaustive)

The legislation led to higher costs but it also brought benefits that justified the costs

Specific cost issues raised in relation to:

- GMP and air quality requirements [Tissues and Cells – NB ART]
- Donor testing requirements (certain tests, certain sectors and sampling time limits)
- Use of CE marked vs in-house devices – cost/benefit ?
- Smaller scale BE/TE's face relatively higher (investment) costs
- Burdensome oversight rules (e.g., inspection planning/frequency) – no differentiation for the size and complexity of the Blood or Tissue Establishment)

Insufficient attention is given to:

- Assessing cost -effectiveness of safety measures
- Re-evaluating technical criteria to ensure balance between safety, costs (e.g. testing, donor selection) and supply/access – taking into account variations in GDP per capita and different local risks

Coherence - OPC

European Commission

Coherence of legislation on Blood & Blood components with …

… own provisions (n=86)

- Fully consistent (56%)
- Minor/significant inconsistencies between Directive 2002/98/EC, Directive 2004/33/EC and Directive 2005/61/EC (29%)

… Legislation communicable diseases (n=86)

- Minor /significant inconsistencies (21%)

… Legislation medical devices (n=84)

- Minor (12%)/significant (15%) inconsistencies (27%)

… Legislation medicinal products (n=82)

- Minor (37%)/ significant (12%) inconsistencies (total 49%)

… EU charter of Fundamental Rights (n=85)

- Minor /significant inconsistencies (35%)

Coherence – issues

European Commission

Incoherencies with relevant EU legislation highlighted and issues raised:

- Key borderline definitions (Medical Device, Medicinal Products legislation – particularly ATMP) - no provisions for EU level classification
- Some S&Q rules for BTC not adequate when used for ATMP, PD
- Sub-optimal communication and alignment between sectors (e.g., for vigilance, or double/gaps in inspection)
- No link to legislation on communicable diseases and role of ECDC
- Questions on correctness link to EU charter of human rights and commercialisation (VUD – body as source of financial gain)
- Inadequate alignment of requirements with international bodies (FDA, WHO, PIC/S)

EU Added Value

Emerging messages (non-exhaustive)

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

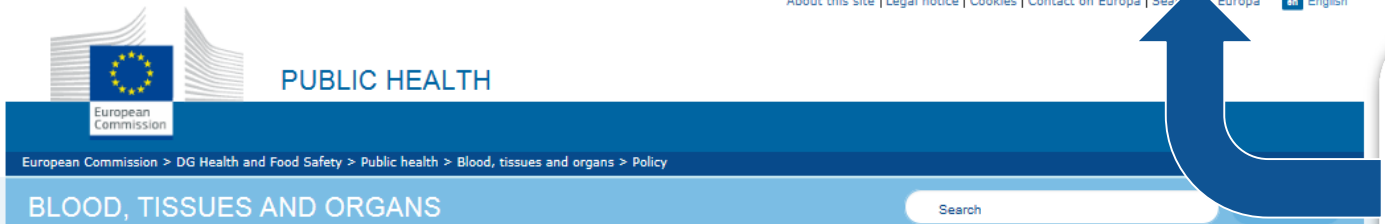
Blood - 74% and Tissues and Cells - 64% of organisations believe that:

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

Factors highlighted that limit the EU added value:

- Differing interpretations at national level ➔ lack of clarity for stakeholders
- Application of more stringent national requirements ➔ barrier for exchange
- Lack of adaptability of the technical requirements

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



- OPC summary – online
- Minutes Stakeholder event - online
- Meetings NCA's, multi- and bilateral meetings stakeholders – online
- Independent study – to be published together with the Evaluation Report
- Evaluation Report – Q1 2019

Follow the Evaluation process here!

Any comments, suggestions, relevant information or data that might be missing?

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or

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