QUESTIONNAIRE FOR ADMINISTRATIONS, ASSOCIATIONS AND OTHER ORGANISATIONS

Fields marked with * are mandatory.

QUESTIONNAIRE FOR ADMINISTRATIONS[1], ASSOCIATIONS AND OTHER ORGANISATIONS[2]

GENERAL CONTEXT

The European Commission is conducting a comprehensive evaluation of the Union legislation on blood and on tissues and cells - Directives 2002/98/EC and 2004/23/EC, respectively ('the Main Directives') and their implementing (technical) Directives ('the Implementing Directives'), examining their functioning across the EU. In particular the evaluation is assessing the extent to which the Directives have met their original objectives and whether they remain fit for purpose, taking into account any relevant changes that have occurred since their adoption. The evaluation is expected to provide a sound evidence base which will be used to consider the need for any changes to the legislation.

The main objective of the Directives was to ensure a high level of human health protection through setting safety and quality standards for blood, tissues and cells for implementation by those providing these services and those overseeing them on behalf of citizens. Specifically, **the legislation aimed**:

- To ensure availability of safe blood, tissues and cells for EU citizens that need them;
- To provide citizens with transparent systems that would enhance public confidence, whether citizens are engaged as potential donors or recipients;
- Define clear lines of accountability for ensuring safety and quality both at service provider and health authority levels.

The specific objectives led to legislation with the following **operational objectives**:

1. To define technical safety and quality requirements for all stages of the chain from donor to recipient;

2. To ensure effective regulatory oversight of the blood, tissues and cells sectors;

3. To achieve a degree of harmonisation of safety and quality at Union level and facilitate EU-wide exchanges;

4. Establish a high level of legal certainty at Union level, i.e., to clarify how does the legislation on blood, tissues and cells relate to other Union legislation;

5. To achieve Union sufficiency through the encouragement of voluntary and unpaid donation and a strong public sector.

To achieve operational objective 1, the intention was to define legally binding minimum requirements for professionals that would address issues such as donor selection, testing, processing, storage and distribution and for blood establishments that would have to meet organisational provisions for personnel, quality management etc. These provisions would be adapted in line with scientific, technological and epidemiological changes, so that the public can support and trust in safety and quality in all steps from donation to application.

To achieve operational objectives 2 and 3, the legislation included provisions for the establishment of national competent authorities for each sector, working in an effective network across the Union. The authorities were tasked to establish programmes of inspection, authorisation and vigilance that would increase confidence and trust in safety and quality of blood, tissues and cells, including those circulating between Member States and those imported from outside the Union. The Commission would support the network through the organisation of meetings, the collection and publication of data and the provision of shared platforms for information exchanges (rapid alerts). This was to help ensure that risks are mitigated and unsafe activities are prevented.

Specific objective 4 was to be achieved through providing a clear legal scope and definitions of the blood, tissues and cells to be regulated by these sets of legislation.

To achieve operational objective 5, the legislation requires Member States to encourage voluntary and unpaid donation and the achievement of sufficiency through this type of donation. This aimed to increase public support and willingness to donate and reduce dependence on supply from 3rd countries.

The achievement of all 5 objectives would be supported via actions funded by the Public Health Programme.

OBJECTIVE OF THE CURRENT SURVEY

The aim of this targeted consultation is to gather detailed views and opinions to feed into the Evaluation of the blood, tissues and cells legislation. In particular, the survey seeks views and opinions on whether the legislation achieved its original objectives and to what extent it continues to be adequate today, taking into account any relevant technological, epidemiological, organisational or societal changes that have

occurred since its adoption. Views and opinions are also sought on the costs and burdens of implementing the legislation at an EU level and whether these have been justified by the results achieved and on the coherence of the Directives with other relevant EU legislation.

This questionnaire is addressed to administrations, associations, tissue and blood establishments, manufacturers of medicinal products using blood, cells or tissues as starting materials, and other organisations. Citizens are asked to fill in a separate non-specialised questionnaire, which can be found here: https://ec.europa.eu/eusurvey/runner/eulbtc

[1] For the purpose of this survey, administrations refer to both public administrations and private administrations with public service obligations

[2] For the purpose of this survey, associations and other organisations refer to professional associations, trade associations, professional,, academic and scientific societies and organisations representing the interests of specific stakeholders.

INFORMATION ABOUT THE RESPONDENT

Please provide the following information on your organisation/association/administration.

Select the country where your organisation/association/administration is based:

- ○ Austria
- ○ Belgium
- ○ Bulgaria
- ○ Croatia
- ○ Cyprus
- ○ Czech Republic
- ◉ Denmark
- ○ Estonia
- ○ Finland
- ○ France
- ○ Germany
- ○ Greece
- ○ Hungary
- ○ Ireland
- ○ Italy
- ○ Latvia
- ○ Lithuania
- ○ Luxembourg
- ○ Malta
- ○ Netherlands
- ○ Poland
- ○ Portugal
- ○ Romania

- ○ Slovak Republic
- ○ Slovenia
- ○ Spain
- ○ Sweden
- ○ United Kingdom
- ○ Other

Name of your organisation/association/administration:

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Danish Society for Clinical Immunology (DSCI) and the Organization of
Transfusion Centers in Denmark (OTCD).
Danish Society for Clinical Immunology is the Scientific society for
transfusion medicine and clinical immunology in Denmark. The Organization of
Transfusion Centers in Denmark is a formalized collaboration of the regional
blood banks in Denmark with main focus on performance in blood banking.
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Please indicate whether your organisation/association/administration is listed in the Transparency Register?[3]

[3] In the interest of transparency, organisations and associations have been invited to provide the public with relevant information about themselves by registering in Transparency Register and subscribing to its Code of Conduct. If the organisation or association is not registered, the submission will be published separately from the registered organisations/associations.

- ○ Yes
- ◉ No

The name of a contact person (please note that the name will not be made public and is meant for follow-up clarification only):

```
Betina Sorensen
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Please enter your e-mail address (this data will not be made public):

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betina.sorensen@skejby.rm.dk
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Do you consent to the Commission publishing your replies

- ◉ Yes (On behalf of my organisation/association/administration I consent to the publication of our replies and any other information provided, apart from my personal information, and declare that none of it is subject to copyright restrictions that prevent publication)
- ○ No (The replies provided by my organisation/association/administration will not be published but may be used internally within the Commission. Note that even if this option is chosen, your contribution may still be subject to 'access to documents' requests.)(As set out in Regulation (EC) No 1049/2001, any EU citizen, natural, or legal person has a right of access to documents of the EU institutions, including those which they receive, subject to the principles, conditions and limits defined in this Regulation).

SECTION I: CHARACTERISATION OF THE RESPONDENT

* 1.1. Main field of work of the responding organisation/association/administration

- ○ a) EU Public administration (Ministry of Health, competent authority etc.)
- ◉ b) Blood/Tissue Establishment and or/ Donor recruitment and procurement/collection
- ○ c) Patients
- ○ d) Donors
- ○ e) Healthcare provision (clinical use of blood, tissues, cells or medicinal products derived from these substances)
- ○ f) Manufacturers of downstream products using blood, tissues or cells as a starting material
- ○ g) Equipment or service provision
- ○ h) Academic or scientific research/development
- ○ i) Public administration outside the EU
- ○ j) Ethics
- ○ k) Other

*1.2. Please specify the geographic coverage of your organisation/association/administration

- ○ a) International/European
- ◉ b) National
- ○ c) Regional/local

*1.3. Are you an organisation/association/administration representing the interests of the stakeholders mentioned in question 1.1?

- ◉ Yes
- ○ No

*1.4. Please specify which sector is of interest for your organisation/association/administration *(one or more answers possible):*

- ☑ a) Blood and blood components
- ☑ b) Tissues for transplant
- ☑ c) Cells for transplant
- ☐ d) Tissues or cells for assisted reproduction
- ☑ e) Blood and/or blood components for the manufacture of medicinal products
- ☑ f) Tissues and/or cells for the manufacture of medicinal products
- ☑ g) Other

*1.4.a. For *Blood and blood components*, please specify which of the following is of most interest *(one or more answers possible):*

- ☑ i) Blood and blood components for transfusion
- ☑ ii) Other

*1.4.a.ii. If other, please specify:

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Plasma for fractionation
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*1.4.b. For *Tissues for transplant*, please specify which of the following is of most interest *(one or more answers possible):*

- ☑ i) Corneas and other tissues for eye surgery

- [x] ii) Bone and/or soft tissues for reconstructive surgery
- [ ] iii) Skin
- [ ] iv) Heart valves and other cardiovascular tissues
- [ ] v) Other tissues

* 1.4.c. For *Cells for transplant*, please specify which of the following is of most interest *(one or more answers possible):*

- [x] i) Bone marrow and/or peripheral blood stem cells
- [x] ii) Cord blood for allogeneic transplantation
- [ ] iii) Cord blood for family or own use
- [x] iv) Other cells

* 1.4.c.iv. If other cells, please specify:

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In-vitro Medical devices manufacturing from blood components
Cell: donor lymphocyt infusion, mononuclear cells for phototherapy
ATMP
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* 1.4.d. For *Tissues or cells for assisted reproduction*, please specify which of the following is of most interest *(one or more answers possible):*

- [ ] i) Sperm banking
- [ ] ii) In vitro fertilisation
- [ ] iii) Fertility preservation
- [x] iv) Other

* 1.4.d.iv. If other, please specify:

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not involved
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* 1.4.g. If *other*, please specify:

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not involved
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* 1.5. Please specify the main activity in which you or your organisation is involved *(one or more answers possible):*

- [x] i) Donor recruitment
- [x] ii) Donor evaluation (medical history review)
- [x] iii) Donation/procurement/collection
- [x] iv) Donor testing
- [x] v) Processing
- [x] vi) Storage
- [x] vii) Distribution
- [x] viii) Import
- [x] ix) Other

*1.5.ix. If other, please specify:

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Donor health
ATMP: the manufacturing process (cell expansion)
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IMPORTANT INSTRUCTIONS:

> If you wish to provide answers to this questionnaire for **both** the blood and the tissues & cells sectors, please answer all questions.

> If you wish to provide answers **only for the blood and blood components** sector please reply only to Sections II to VI.

> If you wish to provide answers **only for the tissues and cells** sector, please go immediately to Section VII and answer all questions from Sections VII to XI.

> If you wish to **upload documents** providing evidence that supports your responses, please do so in Section XII at the end of the questionnaire.

SECTION II: QUESTIONS ON EFFECTIVENESS – BLOOD AND BLOOD COMPONENTS

2.1. In your opinion to what extent has the legislation:

	A. To a great extent	B) To some extent	C) To a limited extent	D) No impact	D) I don't know
a) increased the quality and safety of blood and blood components?	○	◉	○	○	○
b) achieved a high level of human health protection for **recipients** of these substances	○	◉	○	○	○
c) achieved a high level of human health protection for **donors** of these substances?	○	○	◉	○	○

2.1.1. General comments on Safety and Quality of blood and blood components

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On the EU-level it has provided a framework that has driven improvements in the
quality and safety of blood for recipients, but to a lesser extent increased
safety for donors. Impact has been negligible in Denmark, which already had
high international standards for collection and processing of blood (blood and
blood components were regarded as medicinal products before the implementation
of the the EU directive).
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2.1.2.General comments on Human health protection for recipients or donors of these substances:

2.2. To your knowledge has the legislation led to any unintended effects (positive or negative)?

- (●) Yes
- ( ) No

2.2.1. If yes, please describe:

POSITIVE:
Common standards between countries
NEGATIVE:
Having guidelines put into legislation has meant that any change has been difficult, if not impossible. Therefore, changes that might increase safety or supply cannot be implemented.
Country-specific parameters e.g. local epidemiology cannot be taken into account, when taking decisions on blood safety. As an example, syphilis screeing in Denmark has not been performed since the 80'es du to low incidence of syphilis.

2.3. In your experience, have there been barriers preventing effective implementation of the legislation?

- (●) Yes
- ( ) No

2.3.1. If yes, please describe:

Not barriers preventing implementation, but it has caused significant regulatory burden, when multiple inspections are required e.g. for tissue and cells as well as blood. The directives were meant to cover all kinds of blood products, but e.g. plasma for fractionation is now regulated under GMP.

2.4. In your opinion, do the rules on oversight (inspection, authorisation, vigilance) effectively ensure full application of the legislation?

- (●) Yes
- ( ) No

2.5. What, if any, are the challenges to maintaining compliance with the legislation? *(more than one can be selected)*

- [ ] a) Limited Competent Authority resources
- [ ] b) Limited resources at Blood Establishment level
- [x] c) Requirements too stringent/detailed
- [ ] d) Requirements not specific enough
- [x] e) Lack of clarity regarding scope
- [ ]

f) Definitions inadequate

☐ g) Other

2.5.1. For any of the options selected in 2.5., please provide details

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c) - the legislation is too detailed and stringent and as noted in 2.2.1, the
legislative process has meant that changes cannot be made when indicated. Some
requirements are unwieldly or unrealistic, such as that for the donor
information leaflet to be read each time.
e) - some components are not included, such as serum eye drops
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2.6. To what extent, if any, has the legislation impacted on patient access to blood or blood components?

- ○ A) Increased patient access
- ◉ B) No impact on access
- ○ C) Reduced patient access
- ○ D) I don't know

2.6.1.General comments on patient access to these substances

SECTION III: QUESTIONS ON RELEVANCE – BLOOD AND BLOOD COMPONENTS

3.1. To what extent do you think the legislation is sufficiently adapted to:

	A) Fully adapted	B) Minor developments not addressed	C) Significant developments not addressed	D) Not suited to current situation	E) I don't know
a) developments related to donor eligibility (history screening)?	○	○	○	◉	○
b) scientific/technical developments related to donor testing for transmissible diseases?	○	○	○	◉	○
c) scientific developments related to blood and blood component processing (preparation and microbial inactivation), storage and distribution?	○	○	○	◉	○
d) epidemiological developments?	○	○	○	◉	○

3.1.a. If you answered B, C or D, please explain

Donor selection and donor vigilance - the directive should only contain general principles, details should be regulated by the CoE guideline (for detailed deferral criteria and methods for risk assessement).
Blood safety measures should be risk-based and proportionate.

3.1.b. If you answered B, C or D, please explain

NAT - methodology of the test (individual donation or pool) should not be defined by the directive (e.g. Directive 2014/110/EU); only the limits of pathogen detection in IU/mL should be included in the directive

3.1.c. If you answered B, C or D, please explain

Scientific developments cannot be included due to the fact that there are no regular updates of the directive. The process of revising directives is very lengthy and lacks flexibility.
EU should Consult not only the national competent authorities, but also Experts from the field.

Components list should be locally defined according to need and demand. Equally quality monitoring of components should be according to requirements guided by the CoE guideline.

3.2.Have there been developments to which the legislation is not adequately adapted other than those listed above?

- (●) Yes
- ( ) No

3.2.1. If yes, please describe.

VNRD: Donation for all labile blood components must come from voluntary, non-remunerated donors.The "non-remuneration" should be defined according to the Nuffield Council on Bioethics.

Self-sufficiency: Labile products seem not to be a problem in most EU member states including Denmark. Plasma for fractionation: Blood establishments should be encouraged to develop efficient plasmapheresis collection programs
In general: Self-sufficiency for plasma for fractionation should be applied at member state level - not EU-wide to be effective

For COLLECTION of blood, plasms and other substances of human origin, absence of profit should be emphasized.

3.3. To what extent do you think the legislation is sufficiently adapted to societal changes in the sector such as commercialisation/internationalisation?

	A) Fully adapted	B) Minor changes not addressed	C) Significant changes not addressed	D) Current situation not reflected by the legislation	E) I don't know
a) Commercialisation	○	○	◉	○	○
b) Internationalisation	○	○	○	◉	○

3.3.a. If you answered B, C or D, please explain

The directives should give more emphasis on VNRD and the absence of profit, when collecting substances of human origin.

3.3.b. If you answered B, C or D, please explain

Epidemiology of transfusion-transmitted infections is different across EU, and so are the risks for TTI and the required tests and referral rules.

3.4. Have there been societal changes in the sector **other** than commercialisation or internationalisation which are not adequately reflected or addressed in the legislation?

- ◉ Yes
- ○ No

3.4.1. If yes, please describe.

Problems concerning VNRD and self-sufficiency, see 3.2.1.
Donor protection should be intensified.

3.5. Are you aware of any gaps in terms of substances of human origin (substances not listed in Section 1 question 1.4) or activities (e.g. research, biobanking or other activities not listed in Section 1 question 1.5) that are not regulated by the Directives or other EU legislation?

- ◉ Yes
- ○ No

3.5.1. If yes, please describe.

Some substances of human origin are not regulated, e.g. serum eye drops, fibrin glue, platelet rich plasma, starting or raw material for ATMP (e.g. platelet lysate). This is due to the scope of directive 2002/98/EC (article 2: "this directive shall apply to the collection and testing of human blood and blood components, whatever their intended purpose, and to their processing, storage, and distribution when intended for transfusion), which limits the directive to blood components intended for transfusion. This definition should be changed.

There should be a mechanism to include new and emerging blood products, such as serum eye drops, e.g. either as new directives or in the CoE guideline. Similarly, other products manufactured from labile components, which are not used for direct transfusion e.g. fibrin glue, platelet rich plasma should be considered.

3.6. Do you consider that there are substances or activities falling within the scope of the Directive 2002/98/EC that should be removed?

- ○ Yes
- ◉ No

3.7. General comments on the relevance of the legislation today

The directives are not adaptable to the evolution of scientific knowledge and innovation due to the fact, that they do not encompass all relevant topics and that there are no regular updates.

SECTION IV: QUESTIONS ON EFFICIENCY – BLOOD AND BLOOD COMPONENTS

4.1. Did application of the legislation bring costs for you, your organisation or the stakeholders represented by your organisation that would not have been incurred without EU legislation?

- ◉ A) No additional costs
- ○ B) Minor additional costs
- ○ C) Significant additional costs
- ○ D) I don't know

4.1.doc. If you have specific examples of data that support your response, please upload as a separate document in Section XII at the end of the questionnaire.

4.2. Are you aware of particular administrative or other burdens for **specific groups** of operators apart from your organisation or the organisations you represent?

- ◉ A) No additional costs
- ○ B) Minor additional costs
- ○ C) Significant additional costs

- ○ D) I don't know

4.2.doc. If you have specific examples of data that support your response, please upload it as a separate document in Section XII at the end of the questionnaire.

4.3.General comments on the costs of implementing the legislation:

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The directive should be flexible enough to medical progress and developments
and have a principle- or frame-based approach, rather than a detail-based
approach.
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SECTION V: QUESTIONS ON COHERENCE – BLOOD AND BLOOD COMPONENTS

5.1. To what extent do you consider Directives 2002/98/EC, 2004/33/EC, 2005/61/EC and 2005/62/EC to be consistent and coherent within their own provisions?

- ◉ A. Full consistency across all blood and blood component Directives
- ○ B. Minor inconsistencies between some of the Directives
- ○ C. Significant inconsistencies between some of the Directives
- ○ D. Major inconsistencies between many of the Directives
- ○ E. I don't know

5.2. To what extent do you consider the legislation on blood and blood components to be consistent and coherent with other legislation on substances of human origin (i.e. on organs and on tissues and cells)?

- ○ A. Full consistency across all blood and blood component Directives
- ○ B. Minor inconsistencies between some of the Directives
- ◉ C. Significant inconsistencies between some of the Directives
- ○ D. Major inconsistencies between many of the Directives
- ○ E. I don't know

5.2.bcd. If you answered B, C or D, please explain

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There does appear to be a lack of coherence or common standards between the
blood directives and the tissue and cells directives with higher manufacturing
standards including the requirement to inspect GMP for blood, but not tissues
applied to the former. Perhaps due to cross-reference to Eudralex.
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5.2.C. In which of the following provisions do you see inconsistencies?

- ☐ Scope
- ☐ Definitions
- ☑ Regulatory borderlines
- ☐ Oversight provisions – inspection and authorisation
- ☐ Oversight provisions - Vigilance
- ☐ Donor selection provisions

- [ ] Blood establishment or hospital blood bank provisions
- [ ] Other

5.3. To what extent do you consider that the legislation to be coherent and consistent with other relevant Union legislation?

	A. Blood legislation is fully consistent and coherent	B. There are **some minor** inconsistencies or incoherencies in the blood legislation in relation to the other legislation	C. There are **some significant** inconsistencies or incoherencies in the blood legislation in relation to the other legislation	E. I don't know
a) Legislation on Communicable Diseases	◉	○	○	○
b) Legislation on Medical Devices	○	○	◉	○
c) Legislation on Medicinal Products	○	◉	○	○

5.3.b.BC. If you answered B or C for *Legislation on Medical Devices*, please explain

When products from blood for topical/non-transfusion use (such as fibrin glue in surgical setting, serum for ophthalmic use) are produced in hospital setting, they are not covered by the blood directives, but only by the medical devices legislation. However, the medical devices legislation can only guarantee the safety of the device used to produce the product, but not the quality and safety of the blood product itself.

5.3.c.BCD. If you answered B or C for *Legislation on Medicinal Products*, please explain

Role of Good Practice Guideline vs GMP's for blood establishments. Is compliance with the GPG's equivalent to complicance with GMP's?
Blood establishments produce and release human plasma intended both for transfusion and manufacturing of medicinal products. One set of rules is desirable.

5.3.b.C. For *Legislation on Medical Devices*, in which of the following provisions do you see inconsistencies?

- [ ] Testing or reporting requirements
- [ ] Vigilance and Surveillance communication requirements within or between Member States
- [ ] Role/mandate of EU agencies
- [ ] Other

5.3.c.B. For *Legislation on Medicinal Products*, in which of the following provisions do you see inconsistencies?

- [ ] Testing or reporting requirements
- [ ] Vigilance and Surveillance communication requirements within or between Member States
- [ ] Role/mandate of EU agencies
- [x] Other

5.3.c.B. If Other, please specify

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Good Practice Guidelines vs GMP-guidelines. Blood establishments should only
refer to GPG.
Status of blood products not for transfusion should be clarified (e.g. serum
eye drops, platelet rich plasma). They should not be considered medicinal
products, but included in the scope of the blood directive.
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5.4. To what extent do you consider that the legislation to be coherent and consistent with other relevant Union legislation regarding EU Charter of Fundamental Rights?

- ( ) A. Blood legislation is fully consistent and coherent
- (•) B. There are some minor inconsistencies or incoherencies in the blood legislation in relation to the Charter
- ( ) C. There are some significant inconsistencies or incoherencies in the blood legislation in relation to the Charter
- ( ) E. I don't know

5.4.BC. If you answered B or C for *EU Charter of Fundamental Rights*, please explain

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More coherence needed with other EU legislation outside health, e.g.
antidiscrimination legislation and data protection legislation.

The EU charter of Fundamental Rights states in article 3 (Right to integrity of
the person) that "in the fields of medicine and biology, the following must be
respected in particular: (...) - the prohibition on making the human body and
its parts as such source of financial gain". However, in the field of blood
donation, Directive 2002/98/EC Article 20 on voluntary and unpaid blood
donation only "encourages" voluntary and unpaid blood donations, without making
it an obligation. In our view, paid donations is contrary to the principle
stated in the EU charter of Fundamental Rights, and voluntary, non-remunerated
blood donation should be an obligation in all EU member states.
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5.4.B. *For EU Charter of Fundamental Rights*, in which of the following provisions do you see inconsistencies?

- [x] eligibility
- [ ] Consent
- [x] Donor reimbursement/compensation
- [x] Donor protection
- [ ] Supply practices (allocation, pricing etc.)
- [x] Other

5.4.B. If Other, please specify

```
The current encouragement to VNRD is not sufficiently in line with the
principle set in the Charter of "the prohibition on making the human body and
its parts as source of Financial gain". Donor compensation section should fit
with the commercial development and manufacturing of ATMP's.

Donor deferral should be able to be modified  in response to risk assessements.

Donor vigilance should be included in the directive
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5.5. To what extent do you consider that Directive 2002/98/EC, together with Directive 2001/83/EC, form an **effective** framework for ensuring the safety and quality of plasma derived medicinal products?

- (●) A. Adequately ensures the safety of the manufactured products
- ( ) B. The requirements in the blood legislation need minor modification to ensure safety and quality of manufactured products
- ( ) C. The requirements in the blood legislation need significant modification to ensure safety and quality of manufactured products
- ( ) D. The requirements in the blood legislation major modification to ensure safety and quality of manufactured products
- ( ) E. I don't know

5.6.To what extent do you consider that Directive 2002/98/EC, together with Directive 2001/83/EC, form an **efficient (cost effective)** framework for ensuring the safety and quality of plasma derived medicinal products?

- (●) A. The framework is optimally efficient
- ( ) B. The blood legislation introduces minor inefficiencies or unjustified burdens
- ( ) C. The blood legislation introduces significant inefficiencies or unjustified burdens
- ( ) D. The blood legislation introduces major inefficiencies or unjustified burdens
- ( ) E. I don't know

5.6. To your knowledge, is the legislation coherent with other relevant international / third country approaches to the regulation of the quality and safety of blood and blood components?

- (●) Yes
- ( ) No

5.7.General comments on Coherence:

SECTION VI: QUESTIONS ON EU ADDED VALUE – BLOOD AND BLOOD COMPONENTS

6.1. To what extent has the legislative framework at EU level added value to the regulation of blood and blood components across the EU-28 in a manner that could not have been achieved by measures taken at national or global level?

- ○ A) Only EU legal provisions could have achieved the current safety and quality level
- ◉ B) EU legal provisions have greatly improved/accelerated what would have been achieved at national /global level
- ○ C) EU legal provisions have somewhat improved/accelerated what would have been achieved at national /global level to a small extent
- ○ D) The same outcome would have been reached without EU legal provisions
- ○ E) I don't know

6.2. To what extent do stricter national measures pose an obstacle to exchange of supplies between Member States?

- ○ A) No impact on inter-MS supply
- ◉ B) Minor negative impact on inter-MS supply
- ○ C) Significant negative impact on inter-MS supply
- ○ D) I don't know

6.3.General comments on EU Added Value:

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EU legislation secures minimum standards, but it must take into account dynamic
scientific and technological achievements, epidemiological changes, differences
between member states, experience and knowledge of experts, and promote
evidence-based decisions and risk-based thinking. In most cases, Denmark follow
recommendations by the Council of Europe Blood Guide and the country has high
level national guidelines.

In EU legislation the mechanism for revision and incorporation of medical
evidence into regulations is difficult and ineffective leading to failure of
the directives to keep up with developments in technology and emergent risks.

Blood establishments producing plasma for PDMP should be regulated by the blood
directives (GPG) only, not the GMP-guidelines on the top of the EU directives.
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SECTION VII: QUESTIONS ON EFFECTIVENESS – TISSUES AND CELLS

7.1. In your opinion...

	A. To a great extent	B. To some extent	C. To a limited extent	D. No impact	E. I don't know
To what extent has the legislation increased the quality and safety of tissues and cells?	○	◉	○	○	○
To what extent has the legislation achieved a high level of human health protection for **recipients** of these substances	○	◉	○	○	○

To what extent has the legislation achieved a high level of human health protection for **donors** of these substances?	○	○	◉	○	○

7.2. General comments on Safety and Quality of tissues and cells

It has given a framework with common minimal requirements for tissue and cells. Enables exchange of tissue and cells within EU and what to expect regarding quality and safety. The increased quality and safety has been less in tissue establishments established in existing blood establishments.

7.3. General comments on human health protection for recipients or donors of these substances

It has greatly increased the impact on protection of donors in some instances, but less in cases, where donors were handled by blood establishments.

Many different kinds of tissue and cells used in many different situations are covered by the same paragraphs. It does not always make sense, since indication and transplanted-related-mortality are very different, e.g. stem cells compared to bones.

Donor protection should be strenghtened.

7.4. To your knowledge has the legislation led to any unintended effects (positive or negative)?

- ◉ Yes
- ○ No

7.4.1. If yes, please describe.

POSITIVE:
Greater information cross-frontier sharing and consistency enabling exchange of tissue and cells
Better safety for donors and recipients in some instances, e.g. tissue and cells handled in clinical departments and commercial companies.
NEGATIVE:
Cost of implementation of the directives without significant increase in quality in centers already having national guidelines and quality control systems implemented, e.g. tissue and cells handled in existing blood establishments or in which accreditation programme exists (FACT-JACIE, WMDA).
Absence of revision.

7.5. In your experience, have there been barriers preventing effective implementation of the legislation?

- ◉ Yes
- ○ No

7.5.1. If yes, please describe.

Late implementation of some directives and late and poor translation to national legislation

Costs related to implementing the directives

7.6. In your opinion, do the rules on oversight (inspection, authorisation, vigilance) effectively ensure full application of the legislation?

- (●) Yes
- ( ) No

7.7. What, if any, are the challenges to maintaining compliance with the legislation?

- [ ] Competent Authority resources
- [ ] Limited resources at Tissue Establishment level
- [x] Requirements too stringent/detailed
- [ ] Requirements not specific enough
- [x] Lack of clarity regarding scope
- [x] Definitions inadequate
- [ ] Other

7.7.2. For any of the options selected above, please provide details

Technical directive too stringent/detailed and may be outdated too rapidly (e.g. blood dilution algorithm).

The scope and definitions do not include all cells, e.g. lymphocytes. Some border-line substances are not regulated, e.g. micriobioma

7.8. To what extent, if any, has the legislation impacted on patient access to tissues and cells?

- ( ) A. Increased patient access
- (●) B. No impact on access
- ( ) C. Reduced patient access
- ( ) D. I don't know

7.9. General comments on patient access to these substances

SECTION VIII: QUESTIONS ON RELEVANCE – TISSUES AND CELLS

8.1. To what extent do you think the legislation is sufficiently adapted to:

	A. Fully adapted	B. Minor developments not addressed	C. Significant developments not addressed	D. Not suited to current situation	E. I don't know
a) Developments related to donor eligibility (history screening)?	○	○	◉	○	○
b) Scientific/technical developments related to donor testing for transmissible diseases?	○	○	◉	○	○
c) Scientific developments related to tissue and cell processing (preparation and microbial inactivation), storage and distribution?	○	○	○	◉	○
d) Epidemiological developments?	○	◉	○	○	○

8.1.a. If you answered B, C or D to a), please explain

Donor eligibility criteria not evidence-based.

8.1.b. If you answered B, C or D to b), please explain

Not allowing for technical Developments. Lack of evidence-based approach.

8.1.c. If you answered B, C or D to c), please explain

Scientific developments cannot be addressed due to lack and delay of revision.

8.2.Have there been developments to which the legislation is not adequately adapted other than those listed above?

- (●) Yes
- ( ) No

8.2.1. If yes, please describe:

Developments in IT solutions not addressed, e.g. possibility of data sharing. IT Developments enable safe data sharing for exchange of products and information among centers national and international. No legislation, including the directive on data protection is sufficient adapted to those situations.

8.3. To what extent do you think the legislation is sufficiently adapted to societal changes in the sector such as commercialisation/internationalisation?

	A) Fully adapted	B) Minor changes not addressed	C) Significant changes not addressed	D) Current situation not reflected by the legislation	E) I don't know
a) Commercialisation	( )	(●)	( )	( )	( )
b) Internationalisation	( )	(●)	( )	( )	( )

8.3.a. If you answered B, C or D to a), please explain

The directives should give more emphasis to VNRD.

8.3.b. If you answered B, C or D to b), please explain

There is increasing exchange of data and products cross-frontier within EU and outside EU. The commission directive EU 2015/566 does not sufficiently consider the procedures and need for exchange of hematopoietic stem cells.

8.4. Have there been societal changes in the sector **other** than commercialisation or internationalisation which are not adequately reflected or addressed in the legislation?

- (●) Yes
- ( ) No

8.4.1. If yes, please describe:

Donor protection should be intensified.

8.5. Do you consider that there are substances or activities falling within the scope of the Directive 2004/23/EC that should be removed?

- ( ) Yes
- (●) No

8.6. General comments on the relevance of the legislation today

Many border-line products do not fall within the scope and definitions of the directives, e.g. non-cellular materials from the human body such as microbioma and cultured cells, in which the function and purpose of the cells are not changed. In order to circumvent the delay in revision of directives relative to new developments, we suggest the scope to be changed to "tissue and cells from human organism intended for human application and which do not fall under the definitions of ATMP". Clear definition of ATMP is a prerequiste.

SECTION IX: QUESTIONS ON EFFICIENCY – TISSUES AND CELLS

9.1. Did application of the legislation bring costs for you, your organisation or the stakeholders represented by your organisation that would not have been incurred without EU legislation?

- ( ) A) No additional costs
- ( ) B) Minor additional costs
- (●) C) Significant additional costs
- ( ) D) I don't know

9.1.bc.If you answered B or C to the previous question, do you consider that the costs were justified by the benefits for patients?

- ( ) A) Costs fully justified by benefits
- (●) B) Costs partially justified by benefits
- ( ) C) Costs not justified by benefits

- ○ D) I don't know

9.1.bc.bc. If you answered B or C, please explain

```
Fixed periods of inspections not always justified. Implementation of
requirements in cases where existing systems exists, e.g. Single European Code.

In Denmark, many tissue establishments already had an acceptable quality system
in place.
```

9.1.doc. If you have specific examples of data that support your response, please upload it as a separate document in Section XII at the end of the questionnaire.

9.2. Are you aware of particular administrative or other burdens for **specific groups** of operators apart from your organisation or the organisations you represent?

- ○ A) No additional costs
- ○ B) Minor additional costs
- ◉ C) Significant additional costs
- ○ D) I don't know

9.2.bc.If you answered B or C to the previous question, do you consider that the costs were justified by the benefits for patients?

- ○ A) Costs fully justified by benefits
- ◉ B) Costs partially justified by benefits
- ○ C) Costs not justified by benefits
- ○ D) I don't know

9.2.bc.bc. If you answered B or C, please explain

```
In Denmark, many tissue establishments already had an acceptable quality system
in place.
```

9.2.doc. If you have specific examples of data that support your response, please upload it as a separate document in Section XII at the end of the questionnaire.

9.3.General comments on the costs of implementing the legislation:

```
The cost-effectiveness of some measures has never been assessed and in a cost-
constraint health care environment, operational and financial impacts need to
considered against potential benefits.
```

SECTION X: QUESTIONS ON COHERENCE – TISSUES AND CELLS

10.1. To what extent do you consider Directives 2004/23/EC, 2006/17/EC, 2006/86/EC and 2015/566/EC to be consistent and coherent within their own provisions?

- (●) A. Full consistency across all tissue and cell Directives
- ( ) B. Minor inconsistencies between some of the Directives
- ( ) C. Significant inconsistencies between some of the Directives
- ( ) D. Major inconsistencies between many of the Directives
- ( ) E. I don't know

10.2. To what extent do you consider the legislation on tissues and cells to be consistent and coherent with other legislation on substances of human origin (i.e. on organs and on blood)?

- ( ) A. Full consistency across blood, tissues and cells and organs Directives
- (●) B. Minor inconsistencies between some of the Directives
- ( ) C. Significant inconsistencies between some of the Directives
- ( ) D. Major inconsistencies between many of the Directives
- ( ) E. I don't know

10.2.bcd. If you answered B, C or D, please explain

```
The directives on blood, tissue and cells, and organs, are basically covering
the same aspects, but still not consistent. This could be due to the fact, that
they are implemented at different times over many years, and scientific and
epidemiological devopments from the first implementation to the latest, have
not clearly been adressed.

Vigilance systems need to take into consideration that one donor can donate
many different kinds of substances.
```

10.2.B. In which of the following provisions do you see inconsistencies?

- [ ] Scope
- [x] Definitions
- [x] Regulatory borderlines
- [ ] Oversight provisions – inspection and authorisation
- [x] Oversight provisions - Vigilance
- [ ] Donor selection provisions
- [ ] Blood establishment or hospital blood bank provisions
- [ ] Other

10.2.C. In which of the following provisions do you see inconsistencies?

- [ ] Scope
- [ ] Definitions
- [ ] Regulatory borderlines
- [ ] Oversight provisions – inspection and authorisation
- [ ] Oversight provisions - Vigilance
- [ ] Donor selection provisions
- [ ] Blood establishment or hospital blood bank provisions
- [ ] Other

10.2.D. In which of the following provisions do you see inconsistencies?

- [ ] Scope
- [ ] Definitions
- [ ] Regulatory borderlines
- [ ] Oversight provisions – inspection and authorisation
- [ ] Oversight provisions - Vigilance
- [ ] Donor selection provisions
- [ ] Blood establishment or hospital blood bank provisions
- [ ] Other

10.3. To what extent do you consider that the legislation to be coherent and consistent with other relevant Union legislation?

	A. Tissue and cell legislation is fully consistent and coherent	B. There are **some minor** inconsistencies or incoherencies in the tissue and cell legislation in relation to the other legislation	C. There are **some significant** inconsistencies or incoherencies in the tissue and cell legislation in relation to the other legislation	E. I don't know
a) Legislation on Communicable Diseases	○	○	○	◉
b) Legislation on Medical Devices	○	○	○	◉
c) Legislation on Medicinal Products	○	○	◉	○

10.3.c.BCD. If you answered B C or D for *Legislation on Medicinal Products*, please explain

Not clear distinction between definitions and border-line products. Slightly modified cells may well be classified as medicinal products, which results in unnecessarily, heavily increasing demands for manufacturing practice, not possible to fulfill for many tissue establishments. This can lead to restricted access to new treatments.

10.3.c.C. For *Legislation on Medicinal Products*, in which of the following provisions do you see inconsistencies?

- [ ] Testing or reporting requirements
- [x] Vigilance and Surveillance communication requirements within or between Member States
- [x] Role/mandate of EU agencies
- [ ] Other

10.4. To what extent do you consider that the legislation to be coherent and consistent with other relevant Union legislation regarding EU Charter of Fundamental Rights?

- ○ A. Tissue and cell legislation is fully consistent and coherent
- ◉ B. There are some minor inconsistencies or incoherencies in the tissue and cell legislation in relation to the Charter
- ○ C. There are some significant inconsistencies or incoherencies in the tissue and cell legislation in relation to the Charter
- ○ E. I don't know

10.4.BC. If you answered B or C for *EU Charter of Fundamental Rights*, please explain

```
The EU charter of Fundamental Rights states in article 3 (Right to integrity of
the person) that "in the fields of medicine and biology, the following must be
respected in particular: (...) - the prohibition on making the human body and
its parts as such source of financial gain". However, in the field of donation
of tissue and cells, Directive 2004/23/EC only "encourages" voluntary and
unpaid donations, without making it an obligation. In our view, paid donations
is contrary to the principle stated in the EU charter of Fundamental Rights,
and voluntary, non-remunerated donation should be an obligation in all EU
member states.
```

10.4.B. *For EU Charter of Fundamental Rights*, in which of the following provisions do you see inconsistencies?

- ☐ eligibility
- ☐ Consent
- ☐ Donor reimbursement/compensation
- ☑ Donor protection
- ☐ Supply practices (allocation, pricing etc.)
- ☑ Other

10.4.B. If Other, please specify

```
Donor vigilance should be included in the directives.
```

10.5. To what extent do you consider that Directive 2004/23/EC, together with Directive 2001/83/EC, form an **effective** framework for ensuring the safety and quality of medicinal products manufactured from tissues and cells?

- ◉ A. Adequately ensures the safety of the manufactured products
- ○ B. The requirements in the tissue and cell legislation need minor modification to ensure safety and quality of manufactured products
- ○ C. The requirements in the tissue and cell legislation need significant modification to ensure safety and quality of manufactured products
- ○ D. The requirements in the tissue and cell legislation major modification to ensure safety and quality of manufactured products
- ○ E. I don't know

10.6.To what extent do you consider that Directive 2004/23/EC, together with Directive 2001/83/EC, form an **efficient (cost effective)** framework for ensuring the safety and quality of medicinal products manufactured from tissues and cells?

- (●) A. The framework is optimally efficient
- ( ) B. The tissue and cell legislation introduces minor inefficiencies or unjustified burdens
- ( ) C. The tissue and cell legislation introduces significant inefficiencies or unjustified burdens
- ( ) D. The tissue and cell legislation introduces major inefficiencies or unjustified burdens
- ( ) E. I don't know

10.6. To your knowledge, is the legislation coherent with other relevant international / third country approaches to the regulation of the quality and safety of tissues and cells?

- (●) Yes
- ( ) No

10.7.General comments on Coherence:

SECTION XI: QUESTIONS ON EU ADDED VALUE – TISSUES AND CELLS

11.1. To what extent has the legislative framework at EU level added value to the regulation of tissues and cells across the EU-28 in a manner that could not have been achieved by measures taken at national or global level?

- ( ) A. Only EU legal provisions could have achieved the current safety and quality level
- (●) B. EU legal provisions have greatly improved/accelerated what would have been achieved at national /global level
- ( ) C. EU legal provisions have somewhat improved/accelerated what would have been achieved at national /global level to a small extent
- ( ) D. The same outcome would have been reached without EU legal provisions
- ( ) E. I don't know

11.2. To what extent do stricter national measures pose an obstacle to exchange of supplies between Member States?

- ( ) A. No impact on inter-MS supply
- (●) B. Minor negative impact on inter-MS supply
- ( ) C. Significant negative impact on inter-MS supply
- ( ) D. I don't know

11.3. General comments on EU Added Value:

EU legislation secures minimum standards, but it must take into account dynamic scientific and technological achievements, epidemiological changes, differences between member states, experience and knowledge of experts, and promote evidence-based decisions and risk-based thinking.

In EU legislation the mechanism for revision and incorporation of medical evidence into regulations is difficult and ineffective leading to failure of the directives to keep up with developments in technology and emergent risks.

SECTION XII: Uploading of Documents with Supporting Evidence

Upload documents as pdf files. Please include the Section and Question number in the name of the file along with an abbreviation of your organisation's name.

Please upload your file

Please upload your file

Please upload your file

Contact

Deirdre.FEHILY@ec.europa.eu