Contribution ID: ab2f37c0-b16d-4b6e-960e-240127fb2ec7
Date: 15/04/2021 14:58:37

Online Public Consultation on the Revision of the EU Legislation on Blood, Tissues and Cells

Fields marked with * are mandatory.

Introduction

The European Commission has conducted a comprehensive evaluation of the blood, tissues and cells (BTC) legislation, examining its functioning across the EU and published its findings in October 2019. In particular the evaluation assessed the extent to which the Main Directives met their original objectives and whether they remain fit for purpose, given all that has changed in the intervening period.

The evaluation of the legislation, published in October 2019, confirmed that **the legislation had improved safety and quality of blood, tissues and cells used for transfusion, transplantation or medically assisted reproduction**. The evaluation also highlighted a number of gaps and short-comings which will be addressed by a revision of the legislation to ensure the framework is up-to-date, fit for purpose and future-proof.

The Commission has launched an initiative to revise the legislation, addressing the identified shortcomings. The initiative aims to:

- update the legislation to provide a more flexible alignment with scientific and technological developments
- tackle the (re-)emergence of communicable diseases, including lessons learnt from the COVID-19 pandemic
- focus on the increasing commercialisation and globalisation of the sector.

This public consultation will be an important source of information for the process that will lead to the revision. The consultation does not address changes to other EU legal frameworks but it does explore if there are specific products that do not fall clearly under the blood, tissues and cells framework or the medicines and/or medical device frameworks.
Please note that a more in-depth and technical consultation is open in parallel to this one, for organisations that are directly involved in or impacted by these activities and have a good knowledge of the current legislation. If you are such an organisation, you should complete **both this consultation and the targeted one**, available on the Santé web pages.
An external contracted study will also gather evidence and views to support the Impact Assessment.

About you

* Language of my contribution

- ○ Bulgarian
- ○ Croatian
- ○ Czech
- ○ Danish
- ○ Dutch
- ◉ English
- ○ Estonian
- ○ Finnish
- ○ French
- ○ German
- ○ Greek
- ○ Hungarian
- ○ Irish
- ○ Italian
- ○ Latvian
- ○ Lithuanian
- ○ Maltese
- ○ Polish
- ○ Portuguese
- ○ Romanian
- ○ Slovak
- ○ Slovenian
- ○ Spanish
- ○ Swedish

* I am giving my contribution as

- ○ Academic/research institution
- ◉ Business association
- ○ Company/business organisation
- ○ Consumer organisation
- ○ EU citizen
- ○ Environmental organisation
- ○ Non-EU citizen
- ○ Non-governmental organisation (NGO)
- ○ Public authority

- Trade union
- Other

* First name

Andreea

* Surname

Iordache

* Email (this won't be published)

andreea.iordache@efpia.eu

* Organisation name

255 character(s) maximum

EFPIA (European Federation of Pharmaceutical Industries and Associations)

* Organisation size

- Micro (1 to 9 employees)
- Small (10 to 49 employees)
- Medium (50 to 249 employees)
- Large (250 or more)

Transparency register number

255 character(s) maximum

Check if your organisation is on the transparency register. It's a voluntary database for organisations seeking to influence EU decision-making.

38526121292-88

* Does your organisation work in any of the following fields?

between 1 and 12 choices

- Blood collection and/or blood banking
- Plasma collection for manufacture of medicinal products
- Tissue or cell donation or banking for transplantation
- Tissue or cell donation or banking for assisted reproduction
- Transfusion of blood and blood components
- Clinical application of tissues or cells - transplantation

- [ ] Clinical application of tissues or cells - assisted reproduction
- [ ] Government oversight of blood or tissue establishments (inspection, authorisation, vigilance)
- [ ] Medical ethics
- [x] Pharmaceutical industry – plasma derived medicinal products
- [x] Pharmaceutical industry – other BTC derived medicinal products
- [ ] Non-industrial developers of blood, tissue or cell based medicinal products
- [ ] Representation of donors of blood, tissues or cells
- [ ] Representation of patients treated with blood tissues or cells or products manufactured from them
- [ ] Government oversight of medicinal products
- [ ] Government oversight of medical devices
- [ ] Research using blood, tissues or cells
- [ ] Other field relevant to this consultation
- [ ] No direct activity in this field

* Country of origin

Please add your country of origin, or that of your organisation.

○ Afghanistan	○ Djibouti	○ Libya	○ Saint Martin
○ Åland Islands	○ Dominica	○ Liechtenstein	○ Saint Pierre and Miquelon
○ Albania	○ Dominican Republic	○ Lithuania	○ Saint Vincent and the Grenadines
○ Algeria	○ Ecuador	○ Luxembourg	○ Samoa
○ American Samoa	○ Egypt	○ Macau	○ San Marino
○ Andorra	○ El Salvador	○ Madagascar	○ São Tomé and Príncipe
○ Angola	○ Equatorial Guinea	○ Malawi	○ Saudi Arabia
○ Anguilla	○ Eritrea	○ Malaysia	○ Senegal
○ Antarctica	○ Estonia	○ Maldives	○ Serbia
○ Antigua and Barbuda	○ Eswatini	○ Mali	○ Seychelles
○ Argentina	○ Ethiopia	○ Malta	○ Sierra Leone

- Armenia
- Aruba
- Australia
- Austria
- Azerbaijan
- Bahamas
- Bahrain
- Bangladesh
- Barbados
- Belarus
- Belgium
- Belize
- Benin
- Bermuda
- Bhutan
- Bolivia
- Bonaire Saint Eustatius and Saba
- Bosnia and Herzegovina
- Botswana
- Bouvet Island
- Brazil
- British Indian Ocean Territory
- British Virgin Islands
- Falkland Islands
- Faroe Islands
- Fiji
- Finland
- France
- French Guiana
- French Polynesia
- French Southern and Antarctic Lands
- Gabon
- Georgia
- Germany
- Ghana
- Gibraltar
- Greece
- Greenland
- Grenada
- Guadeloupe
- Guam
- Guatemala
- Guernsey
- Guinea
- Guinea-Bissau
- Guyana
- Marshall Islands
- Martinique
- Mauritania
- Mauritius
- Mayotte
- Mexico
- Micronesia
- Moldova
- Monaco
- Mongolia
- Montenegro
- Montserrat
- Morocco
- Mozambique
- Myanmar /Burma
- Namibia
- Nauru
- Nepal
- Netherlands
- New Caledonia
- New Zealand
- Nicaragua
- Niger
- Singapore
- Sint Maarten
- Slovakia
- Slovenia
- Solomon Islands
- Somalia
- South Africa
- South Georgia and the South Sandwich Islands
- South Korea
- South Sudan
- Spain
- Sri Lanka
- Sudan
- Suriname
- Svalbard and Jan Mayen
- Sweden
- Switzerland
- Syria
- Taiwan
- Tajikistan
- Tanzania
- Thailand
- The Gambia

- Brunei
- Bulgaria
- Burkina Faso
- Burundi
- Cambodia
- Cameroon
- Canada
- Cape Verde
- Cayman Islands
- Central African Republic
- Chad
- Chile
- China
- Christmas Island
- Clipperton
- Cocos (Keeling) Islands
- Colombia
- Comoros
- Congo
- Cook Islands
- Costa Rica
- Côte d’Ivoire
- Croatia
- Haiti
- Heard Island and McDonald Islands
- Honduras
- Hong Kong
- Hungary
- Iceland
- India
- Indonesia
- Iran
- Iraq
- Ireland
- Isle of Man
- Israel
- Italy
- Jamaica
- Japan
- Jersey
- Jordan
- Kazakhstan
- Kenya
- Kiribati
- Kosovo
- Kuwait
- Nigeria
- Niue
- Norfolk Island
- Northern Mariana Islands
- North Korea
- North Macedonia
- Norway
- Oman
- Pakistan
- Palau
- Palestine
- Panama
- Papua New Guinea
- Paraguay
- Peru
- Philippines
- Pitcairn Islands
- Poland
- Portugal
- Puerto Rico
- Qatar
- Réunion
- Romania
- Timor-Leste
- Togo
- Tokelau
- Tonga
- Trinidad and Tobago
- Tunisia
- Turkey
- Turkmenistan
- Turks and Caicos Islands
- Tuvalu
- Uganda
- Ukraine
- United Arab Emirates
- United Kingdom
- United States
- United States Minor Outlying Islands
- Uruguay
- US Virgin Islands
- Uzbekistan
- Vanuatu
- Vatican City
- Venezuela
- Vietnam

Cuba	Kyrgyzstan	Russia	Wallis and Futuna
Curaçao	Laos	Rwanda	Western Sahara
Cyprus	Latvia	Saint Barthélemy	Yemen
Czechia	Lebanon	Saint Helena Ascension and Tristan da Cunha	Zambia
Democratic Republic of the Congo	Lesotho	Saint Kitts and Nevis	Zimbabwe
Denmark	Liberia	Saint Lucia	

The Commission will publish all contributions to this public consultation. You can choose whether you would prefer to have your details published or to remain anonymous when your contribution is published. **Fo r the purpose of transparency, the type of respondent (for example, 'business association, 'consumer association', 'EU citizen') country of origin, organisation name and size, and its transparency register number, are always published. Your e-mail address will never be published.** Opt in to select the privacy option that best suits you. Privacy options default based on the type of respondent selected

* Contribution publication privacy settings

The Commission will publish the responses to this public consultation. You can choose whether you would like your details to be made public or to remain anonymous.

Anonymous

Only organisation details are published: The type of respondent that you responded to this consultation as, the name of the organisation on whose behalf you reply as well as its transparency number, its size, its country of origin and your contribution will be published as received. Your name will not be published. Please do not include any personal data in the contribution itself if you want to remain anonymous.

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Organisation details and respondent details are published: The type of respondent that you responded to this consultation as, the name of the organisation on whose behalf you reply as well as its transparency number, its size, its country of origin and your contribution will be published. Your name will also be published.

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The BTC evaluation findings

An evaluation of the BTC legislation was published on 11 October 2019. Although the evaluation concluded that the legislation had increased safety and quality of blood, tissues and cells in the EU, a number of shortcomings and gaps were identified.

Q1 To what extent are the findings of the evaluation still valid one year since the publication of the evaluation?

at most 8 answered row(s)

	Valid	Partially valid	Partially invalid	Invalid	No answer
* Technical requirements for safety and quality are not up-to-date	◉	○	○	○	○
* There are substances of human origin that should be in the scope of the legislation but currently are not (breast milk, fecal microbiota, serum eye drops etc.)	○	○	○	○	◉
* Divergent national approaches to oversight by authorities leads to unequal protection and lack of inter-Member State trust and barriers to BTC exchange	◉	○	○	○	○
* Donors of blood, tissues and cells are not adequately protected by the legislation	○	○	○	○	◉
* Children born from medically assisted reproduction techniques are not adequately protected	○	○	○	○	◉
* The requirements for authorising new ways of preparing and using blood, tissues and cells are not adequate, particularly because demonstration of efficacy and safety in the recipient is not required.	◉	○	○	○	○
* There are sometimes difficulties in defining the borderlines for novel BTC (used in transfusion, transplantation or assisted reproduction) with other regulatory frameworks	○	◉	○	○	○
* Current legislation has not proven adequate to protect EU patients from the risk of shortages or sudden supply disruption	◉	○	○	○	○

Do you have additional insights on any of these topics that were not adequately highlighted in the evaluation?

at most 8 choice(s)

- [ ] Technical requirements for safety and quality are not up-to-date
- [ ] There are substances of human origin that should be in the scope of the legislation but currently are not (breast milk, fecal microbiota, serum eye drops etc.)
- [ ] Divergent national approaches to oversight by authorities leads to unequal protection and lack of inter-Member State trust
- [ ] Donors of blood, tissues and cells are not adequately protected by the legislation
- [ ] Children born from medically assisted reproduction techniques are not adequately protected
- [x] The requirements for authorising new ways of preparing and using blood, tissues and cells are not adequate, particularly because demonstration of efficacy and safety in the recipient is not required.
- [x] There are sometimes difficulties in defining the borderlines for novel BTC (used in transfusion, transplantation or assisted reproduction) with other regulatory frameworks
- [ ] Current legislation has not proven adequate to protect EU patients from the risk of shortages or sudden supply disruption

Please describe the additional information, specifying which problem you refer to

1500 character(s) maximum

It needs to be made clear the differentiation with ATMPs. Substantially manipulated tissues and cells as well as those used in a different essential function are regulated as Advanced Therapy Medicinal Products (ATMP). The quality, safety and efficacy have to be demonstrated and requirements are defined in EU legislation and connected European guidance. Further, the concept of "novel BTC" is not clear. The borderline between ATMP and other regulatory frameworks has clear published principles of demarcation.

Q2 Select up to 4 problems to which you would give highest priority

at most 4 choice(s)

- [x] Technical requirements for safety and quality are not up-to-date

- [ ] There are substances of human origin that should be in the scope of the legislation but currently are not (breast milk, fecal microbiota, serum eye drops etc.)
- [x] Divergent national approaches to oversight by authorities leads to unequal protection and lack of inter-Member State trust
- [ ] Donors of blood, tissues and cells are not adequately protected by the legislation
- [ ] Children born from medically assisted reproduction techniques are not adequately protected
- [ ] The requirements for authorising new ways of preparing and using blood, tissues and cells are not adequate, particularly because demonstration of efficacy and safety in the recipient is not required.
- [ ] There are sometimes difficulties in defining the borderlines for novel BTC (used in transfusion, transplantation or assisted reproduction) with other regulatory frameworks
- [x] Current legislation has not proven adequate to protect EU patients from the risk of shortages or sudden supply disruption

Q3 How did, in your view, the Covid-19 pandemic influence the evaluation conclusions?

at most 8 answered row(s)

The pandemic made them:	Stronger	Unchanged	Weaker	No answer
* Technical requirements for safety and quality are not up-to-date	◉	○	○	○
* There are substances of human origin that should be in the scope of the legislation but currently are not (breast milk, fecal microbiota, serum eye drops etc.)	○	○	○	◉
* Divergent national approaches to oversight by authorities leads to unequal protection and lack of inter-Member State trust	◉	○	○	○
* Donors of blood, tissues and cells are not adequately protected by the legislation	○	◉	○	○
* Children born from medically assisted reproduction techniques are not adequately protected	○	○	○	◉

* The requirements for authorising new ways of preparing and using blood, tissues and cells are not adequate, particularly because demonstration of efficacy and safety in the recipient is not required.	○	◉	○	○
* There are sometimes difficulties in defining the borderlines for novel BTC (used in transfusion, transplantation and assisted reproduction) with other regulatory frameworks	○	◉	○	○
* Current legislation has not proven adequate to protect EU patients from the risk of shortages or sudden supply disruption	◉	○	○	○

Q4 Are there other lessons learned from the Covid-19 pandemic that should be taken into account in the revision of the BTC legislation? If so, please describe.

1500 character(s) maximum

·The availability of blood and blood products around the world are being heavily impacted by the current healthcare crisis because of temporary loss of donors due to imposed or voluntary self-isolation to help prevent the spread of the COVID-19 virus.
·COVID-19 has underscored the urgent need for the development, evaluation, and implementation of innovative approaches to optimize transfusion use and blood management in chronic diseases.
·The implementation of Patient Blood Management can help reduce the pressure on the blood supply and its concept should be included in the revision of the BTC legislation.
o PBM is an evidence-based bundle of care to optimize medical and surgical patient outcomes in acute and chronic settings by clinically managing and preserving a patient's blood
o around 2/3 of red blood cell transfusions are used in medical care of these chronic diseases
·By optimizing patients red cell mass, minimizing blood loss and bleeding and optimizing and harnessing the reserve of anemia, PBM leads to reduced mortality and morbidity, lower transfusion rates and increased hospital savings.
·PBM in the context of the ongoing blood shortage has been recommended by a number of organizations – from medical societies such as Society for the Advancement of Blood Management (SABM) to the European Centre for Disease Control (ECDC).

Keeping EU technical requirements up to date with scientific and medical knowledge and practice

The EU legislation includes many rules regarding technical issues such as who can donate, what tests must be carried out on donors, what quality criteria should be met for the blood, tissues and cells that are supplied to hospitals and clinics, which types of adverse occurrences should be notified to authorities, etc. According to the evaluation, many of these rules are currently out of date. The evaluation also concluded that the rules should be extended to include donor protection and the protection of children born from medically assisted reproduction.
The Commission is considering three possible options for setting and updating these technical rules:
1. By **professionals**: the blood and tissue centres would conduct their own risk assessments and establish rules based on the conclusions, together with professional society guidance. This process would be

reviewed for approval by inspectors from the national authority.
2. EU law would require that professionals follow the rules and guidance of named **expert bodies** such as ECDC and EDQM , in consultation with professional associations.
3. All detailed technical requirements would be described in **EU legislation** and kept up-to-date with regular amendments.

Q5 Who should set out these technical rules to effectively achieve up-to-date safety and quality rules, based on good science? (Consider the time required to update the rules, including during crises, their quality as well as whether EU harmonisation is essential or not)

	Professionals	Expert bodies	EU law	No answer
* Rules on donor suitability and testing	○	◉	○	○
* Rules on donation frequency and donor monitoring.	○	◉	○	○
* Rules on quality management by providers of blood, tissues and cells (air quality requirements, documentation, quality control testing, training etc.)	○	◉	○	○
* Rules on the technical characteristics of blood, tissues and cells provided for patients (e.g. volume, cell numbers, labelling)	○	◉	○	○
* Criteria and templates for reporting and investigation of adverse reactions and events to authorities.	○	◉	○	○
* Rules for the development of new processing methods or new clinical uses of blood, tissues and cells	○	◉	○	○

Q6 In general, which of these options, in your view, would overall be most **cost-effective**?

	Very	Quite	Rather not	Not at all	No answer
* Professionals	○	○	○	○	◉
* Expert bodies	○	○	○	○	◉
* EU law	○	○	○	○	◉

The BTC evaluation showed that, over time, many new substances of human origin being used in patients do not fall within the scope of the BTC legislation. Some fall wholly or partially under other frameworks nationally and some are unregulated at the EU level.

Q7 In which of the following cases do you think that technical rules for safety and quality should be **included in the scope** of the BTC legislation?

	Only for donation and testing	For all aspects from donation to distribution	No answer
* Fecal microbiota transplants	○	○	◉
* Donated human breast milk	○	○	◉
* Serum eye drops	○	○	◉
* Blood, tissues or cells used for cosmetic/esthetic purposes	○	○	◉
* Blood, tissues or cells removed from a patient, processed and returned to the patient at the bedside or during their surgery, without falling under a different legislative framework	○	○	◉
Others	◉	○	○

Please provide a description of the other substances you consider should be included in this legislation and explain why.

Text of 1 to 2000 characters will be accepted

Blood, tissues or cells removed from a patient, processed and returned to the patient at the bedside or during their surgery, if substantially manipulated or used in a different essential function fall under the ATMP /medicines legislative framework. Under this ATMP legal framework, provisions for autologous substances are covered as well as for automated processes at the bed side - ATMP should be clearly excluded from the scope of this question as the quality, safety and efficacy requirements are already well defined in legislation and connected European guidance.

Q8 If you have further comments on the technical rules for safety and quality of blood, tissues and cells and other substances of human origin, please enter them here.

Text of 1 to 2000 characters will be accepted

• A centralised approach to setting technical rules would prevent disharmonization across EU Member States
• Capturing BTC technical standards in EU law would hinder regular and timely updates in line with scientific developments.The process for updating rules should be timely and responsive, driven by experts in the field and not reliant on a legislative process
• The composition and organisation of expert bodies responsible for this should be the subject of further consultation
• Implementation of a combination of Policy Option 2 and 3 will be a huge step forward to have:
• Only high-level principles should be outlined in EU law with adoption of technical details set by expert bodies, which should be subject to further consultation
• Definition of the quality and safety requirements should be kept with the expertise of competent authorities in collaboration with EDQM and ECDC or other EU body with relevant expertise and experience; Requirements on quality testing and management as established are applicable for BTC and are considered sufficient
• Mutually accepted inspections by e.g. focus inspectorates and EU level audits of national control systems
• A clear distinction between BTC and ATMP should be made. Autologous and allogeneic Tissues or cells when substantially manipulated or used for a different essential function, due to the inherent risks, fall under the ATMP/medicines legislative framework.ATMP should be clearly excluded from the scope of this question as the quality, safety and efficacy requirements are already defined and by no means the standards applied to cells and tissues that are ATMP should be lowered. Substantial manipulation cannot be assumed as having equivalent safety or efficacy in different manufacturing settings as the specific conditions of manufacture determine the safety or efficacy outcome. Also, cells used in a different essential function cannot be assumed to behave as in the original setting in terms of safety and efficacy

Improving oversight of blood, tissue and cell activities

The evaluation indicated that variable national approaches to oversight of blood, tissue and cell activities in Member States results in a lack of trust and creates barriers to the exchange of blood, tissues and cells between Member States.

Q9 What would be the impact of introducing oversight principles for authorities in EU legislation. The principles might address independence of inspectors, conflicts of interest, and competency requirements for staff in authorities.

5

Q10 Would audits by the European Commission of Member State competent authority control systems (inspection, vigilance, reporting) improve trust and inter-Member State exchange of blood, tissues and cells?

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Q11 Would greater collaboration between Member State competent authorities (e. g. joint inspections, peer audits of inspections improve effectiveness of oversight and increase inter-Member state exchange of blood, tissues and cells?

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Q12 Would an EU programme of training of staff in national/regional authorities to agreed guidelines improve effectiveness of oversight and increase inter-Member state exchange of blood, tissues and cells?

5

* Q13 For questions 9 to 12, do you see any risks or potential negative impacts?

- (•) Yes
- ( ) No
- ( ) No answer

Please describe the risk or negative impact, specifying which question you refer to.

1500 character(s) maximum

Tissues or cells when substantially manipulated or used for a different essential function, due to the inherent risks, fall under the ATMP/medicines legislative framework. ATMP should be clearly excluded from the scope of these questions 9-12 as the medicines code includes mutually recognised inspection system, pharmacovigilance and data sharing between EU regulatory authorities.

Q14 If you have further comments on oversight of the blood, tissues and cells sector, please enter them here.

Text of 1 to 2000 characters will be accepted

Non-binding elements from the “Operational manual for competent authorities - inspection of tissue and cells procurement and tissue establishments” laid down principles for establishing regulatory system with aim to promote standardization of established regulatory systems in EU. Harmonization of inspections across member states and mutually accepted inspections are important milestones in standardization of the oversight system. This should also support a collaboration and recognition between member states.
Building up the expertise of competent authorities in collaboration with EDQM and ECDC or other EU body with relevant expertise and experience is very important step in harmonizing approach for BTC.
Note on the distinction of ATMPs, tissues or cells when substantially manipulated or used for a different essential function, due to the inherent risks, fall under the ATMP/medicines legislative framework. ATMP should be clearly excluded from the scope of this question.

Supporting innovation for patient benefit

The BTC evaluation found that innovation was not facilitated optimally. In particular, only laboratory validation of new processing methods is required (no animal or clinical studies to demonstrate safety and efficacy in the patient).

* Q15 Should legal requirements be introduced in EU legislation for demonstrating safety, quality and efficacy when blood, tissues or cells are prepared or used in new ways?

- ○ Yes
- ○ No
- ◉ No answer

* Q16 Are you aware of cases where blood, tissues and cells are used to treat patients, without proven clinical benefit?

- ◉ Yes
- ○ No

Please describe the case(s) you are aware of briefly

Text of 1 to 2000 characters will be accepted

This was highlighted in the EMA's recent warning against using unproven cell-based therapies (https://www.ema.europa.eu/en/documents/public-statement/ema-warns-against-using-unproven-cell-based-therapies_en.pdf) highlighted a December 2019 story in Polityka highlighted the use of stem cell therapies without proven benefit: (https://www.polityka.pl/tygodnikpolityka/nauka/1935142,1,sledztwo-polityki-zludne-terapie-komorkami-macierzystymi.read) and a report in Jan 2020 on clinics in the UK providing stem cell treatments without evidence of benefit: https://www.bbc.co.uk/news/health-51006333.

Member States are responsible for deciding the regulatory status of products/substances. They might classify as blood, tissues and cells (Substances of Human Origin) or under another legal framework such as the pharmaceutical or medical device frameworks. EU level regulatory advice can be sought on whether the legislation on Advanced Therapy Medicinal Products would apply (from the Committee for Advanced Therapies) and on whether the medical device legislation would apply (from an expert group of medical device authorities).

* Q17 Are you aware of cases where the regulatory classification of a substance of human origin is unclear?

- ○ Yes
- ◉ No

* Q18 Do you consider that there are substances/products being regulated under one legal framework but would be better regulated under another?

- ○ Yes
- ◉ No
- ○ No answer

Q19 How would you assess the impact of a new EU level structure or committee to advise Member States on whether a substance falls under the BTC legislation or not, equivalent to those for ATMPs and medical devices?

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If you have further comments on your answer please enter them here

2000 character(s) maximum

There is a risk a new EU structure or committee for classification may duplicate existing mechanisms and add further complexity in the system. A new EU level structure or committee to advise on whether a substance falls under the BTC legislation should coordinate with existing mechanisms at EMA such as ATMP classification procedure (https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/advanced-therapies/advanced-therapy-classification) and Innovation Task force (https://www.ema.europa.eu/en/human-regulatory/research-development/innovation-medicines). Use of existing frameworks is encourage with potential optimization. An integrated system would ensure transparency of decision making and avoid potential opportunities for 'shopping around' between systems for an opinion. The creation of a new classification structure also increases the risk of discrepancies if the decision at EU level is not binding to all EU MS. If a substance is considered an ATMP, due to the fact that medicines are more stringently regulated as product, process and use, it should not be possible to request also a classification as BTC.

* Q20 If an EU level structure or committee as described in Q19 were established, do you consider that it should co-ordinate decisions with the equivalent committees in the medicinal product and medical device frameworks?

- (●) Yes
- ( ) No
- ( ) No answer

* Q21 Are the donation, procurement and testing provisions for blood, tissues and cells that are used to manufacture medicinal products or medical devices adequate?

- ( ) Very inadequate
- (●) Somewhat inadequate
- ( ) Adequate
- ( ) Somewhat too stringent
- ( ) Much too stringent
- ( ) I don't know

Please describe the specific provisions you consider should be changed and why.

2000 character(s) maximum

Requirements could be better risk-adapted, for example, tissues and cells collected for autologous use should have not have the same donor eligibility testing requirements applied as for tissues and cells intended for allogeneic use. It can also be challenging to comply with potentially overlapping requirements across frameworks such as inspection and vigilance reporting requirements.
The practical and suitable approaches should be implemented leveraging existing accreditation or certification programmes (FACT-JACIE international standards) and their recognition across member states should be ensured.

Q22 If you have further comments on the subject of innovation in blood, tissues and cells please enter them here.

Text of 1 to 2000 characters will be accepted

Future EU legislation should be designed and harmonized to help foster innovation and its uptake. The definition of an advanced therapy medicinal product (ATMP) is clearly elaborated in Regulation 1394/2007 and Annex I, Part IV of Directive 2001/83/EC. The current approach of regulating these products under the pharmaceuticals framework ensures the highest standards of scientific evaluation are performed. This approach also assures stability for future investment in novel cell and tissue-based medicines.
Nevertheless, there can be challenges in identifying which requirements from which framework apply at a specific timepoint in the development and manufacturing lifecycle. There can even be challenges in determining whether material falls under the Blood Directive or the Tissues and Cells Directive before entering ATMP manufacturing process.
Navigating the interplay between different regulatory frameworks can present challenges. A centralized approach to establishing and maintaining technical standards is a first step for BTCs in streamlining the current system. Another suggestion could be to establish a series of roadmaps for different innovative therapy ‘models’ that sit at the interface of different regulatory framework and can set examples to help developers navigate the various requirements.
The revision of the Blood Directive is also an opportunity to embed Patient Blood Management (PBM) principles. This approach optimises the care of patients who might need a blood transfusion while decreasing the amount of blood needed. The inclusion of Patient Blood Management in the Blood Directive, and its implementation across Europe in both the acute and the chronic setting, can improve patient outcomes while safeguarding the blood supply.

Sufficiency of supply of blood, tissues and cells

Although an objective of the BTC legislation was to ensure a sustainable supply of critical blood, tissues and cells, the evaluation showed that there are dependencies on certain Member States and on third countries for certain substances, in particular plasma for the manufacture of medicinal products. In addition, it was highlighted that there is a lack of legal provisions to ensure appropriate emergency measures in the event of sudden supply interruptions.

Q23 What effect would mandatory EU monitoring and **routine** reporting of sufficiency data (mandatory reporting of donations, distribution, import, export and use by BTC establishments to national authorities and to the Commission) have?

Additional costs and administrative burden for establishments and authorities

5

Transparency for citizens

5

Q24 What effect would sharing of reported donation and supply monitoring data on an EU platform have?

Additional costs and administrative burden for establishments and authorities

5

Information for policy makers (for vigilance and sufficiency measures)

5

Q25 What would be the impact of mandatory rapid notification to the national authority, and by them to other Member State authorities, in the case of a sudden significant drop in supply due to an incident or other crisis?

5

* Q26 What other measures could be introduced in legislation to address a sudden drop in supply due to a crisis?

- [x] Co-operative actions between blood and tissue establishments
- [x] Notification to the national authority with a response at Member State level
- [ ] Notification to the EU level with collective response co-ordination
- [x] Other
- [ ] No answer

Please describe

1000 character(s) maximum

We strongly believe that the directive should also contribute to best managing the existing blood supply by encouraging Member States to introduce policies aimed at driving hospitals to implement Patient Blood Management.
Patient Blood Management standards should be developed by ECDC and/or EDQM, that could then inform harmonized PBM guidelines across Member States. Further, the ECDC could have a strong role to play in monitoring and routine reporting of sufficiency data and recommending various options such as the implementation of Patient Blood Management to best manage existing supplies. ECDC could also monitor how Member States are implementing PBM practices.

Some blood and tissue establishments and competent authorities have in place preparedness/contingency plans for emergencies such as infectious disease outbreaks, natural disasters or military conflicts.

* Q27 What would be the effect of making such **preparedness/contingency plans** mandatory?

- ○ It would raise many concerns
- ○ It would raise some concerns
- ○ It would have no impact
- ◉ It would bring some improvements
- ○ It would bring many improvements
- ○ No answer

Q28 If you have further comments on the topic of ensuring a sustainable supply of essential blood, tissues and cells. Please list any other measure you consider would support this objective.

Text of 1 to 2000 characters will be accepted

It is strongly believe that the directive should also contribute to best managing the existing blood supply by encouraging Member States to introduce policies aimed at driving hospitals to implement Patient Blood Management.
PBM is an evidence-based bundle of care to optimize medical and surgical patient outcomes by clinically managing and preserving a patient's blood
By optimizing patients red cell mass, minimizing blood loss and bleeding and optimizing and harnessing the reserve of anemia, PBM leads to reduced mortality and morbidity, lower transfusion rates and increased hospital savings.
Patient Blood Management standards should be developed by ECDC and/or EDQM, that could then inform harmonized PBM guidelines across Member States. This will support optimization of clinical practice of transfusion as per WHO guidance. This will also support patient safety while conserving the blood supply. In the COVID-19 context, this is now even more important to help improve patient outcomes while managing the impact of the crisis on blood supplies.
Implementation of PBM would require monitoring & data collection across Europe, including types of uses, indications, observance of patient blood management guidelines and WHO/EDQM guidance in the field, as well as educational efforts towards healthcare providers.

General comments and supporting documents

Q29 If you have general comments on other topics related to the revision of the EU legislation on blood, tissues and cells, please enter them here.

Text of 1 to 2000 characters will be accepted

Our responses have been given from perspective that only BTC requirements for donation, procurement and testing are relevant for collection of material destined for ATMP manufacture. Revision of the BTC legislation should clearly exclude cells and tissues when substantially manipulated or when they are used in a different essential function as they are already regulated as Advanced Therapy Medicinal Products (ATMP). A risk-based approach should be applied to requirements for demonstrating safety, quality and efficacy of new BTC methods. Review would ensure there are no gaps in the legal framework could be exploited to circumvent regulatory requirements. Assessment would ensure that innovative BTC methods are adhering to the right regulatory requirements and importantly that any new methods that create a product meeting the definition of the legislation. If it is identified that a product meets the definition of an ATMP it should be regulated under the ATMP/medicines legislative framework. ATMP quality, safety and efficacy requirements are already defined in the Regulation 1394/2007, and connected Directives and European guidance prepared by experts from all member states at the European Medicines Agency (EMA), according to the highest principles of public health protection, ensuring harmonisation within the EU and aligned with other parts of the regulated world.

"EFPIA calls on the EMA to quickly issue the update of the position statement on Creutzfeldt-Jakob disease and plasma-derived and urine-derived medicinal products, following the public consultation closed in October 2019, to address critical issues that may arise in different Member States."

You may upload one supporting document to your submission here.

Only files of the type pdf,txt,doc,docx,odt,rtf are allowed

THANK YOU FOR YOUR CONTRIBUTION!

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