Contribution ID: 0f8fb7f5-ef69-4669-91ba-d291cd86efd9
Date: 15/04/2021 14:57:04

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

Fields marked with * are mandatory.

Introduction

The Commission has launched an initiative to revise the EU legislation on blood, tissues and cells (**BTC**), addressing a number of shortcomings identified in an evaluation of the legislation published in 2019. 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 **Targeted Consultation** supplements a Public Consultation that is open in parallel on the European Commission Have your Say portal. It is targeted at **organisations** (not individuals) that are **directly involved in or impacted by the fields concerned and are familiar with the current legislation** and its implementation. It will feed into the Impact Assessment process that will lead to the revision of the EU legislation on blood, tissues and cells. The scope of the impact assessment, and of this consultation, is limited to the EU legislation on blood, tissues and cells. Thus, it does not address possible changes to other EU legal frameworks, such as those for advanced therapy medicinal products, other medicinal products or medical devices, but it does explore issues at the borderlines between the blood, tissues and cells frameworks and those other regulated frameworks. If your organisation is among those targeted in this consultation, you are advised to complete **both** surveys, as questions in the Public Consultation are not repeated here or, in some cases, the topics are addressed again but explored in more depth in this survey. An external contracted study will also gather evidence and views to support the Impact Assessment.

Apart from the first section entitled 'About you', you are not obliged to answer all survey questions. You are advised to answer **only those questions for which you have experience or expertise**. Please note also that not all the shortcomings identified in the evaluation of the BTC legislation are addressed in this consultation. Some shortcomings are considered more appropriate for exploration in participatory workshops organised in the context of the external study.

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

* Organisation name

255 character(s) maximum

EFPIA (European Federation of Pharmaceutical Industries and Associations)

* Organisation scope

- ◉ International
- ○ Local
- ○ National
- ○ Regional

* Organisation size

- ○ Micro (1 to 9 employees)

- (●) Small (10 to 49 employees)
- ( ) Medium (50 to 249 employees)
- ( ) Large (250 or more)

Transparency register number (if applicable)

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.

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Which of the following best describes the work of your organisation?

- ( ) 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
- ( ) Standards setting
- ( ) Pharmaceutical industry – plasma derived medicinal products
- (●) 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

* Country where the organisation is based or where it has its main office

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

- ( ) Afghanistan
- ( ) Djibouti
- ( ) Libya
- ( ) Saint Martin

- Åland Islands
- Albania
- Algeria
- American Samoa
- Andorra
- Angola
- Anguilla
- Antarctica
- Antigua and Barbuda
- Argentina
- Armenia
- Aruba
- Australia
- Austria
- Azerbaijan
- Bahamas
- Bahrain
- Bangladesh
- Barbados
- Belarus
- Belgium
- Belize
- Dominica
- Dominican Republic
- Ecuador
- Egypt
- El Salvador
- Equatorial Guinea
- Eritrea
- Estonia
- Eswatini
- Ethiopia
- Falkland Islands
- Faroe Islands
- Fiji
- Finland
- France
- French Guiana
- French Polynesia
- French Southern and Antarctic Lands
- Gabon
- Georgia
- Germany
- Ghana
- Liechtenstein
- Lithuania
- Luxembourg
- Macau
- Madagascar
- Malawi
- Malaysia
- Maldives
- Mali
- Malta
- Marshall Islands
- Martinique
- Mauritania
- Mauritius
- Mayotte
- Mexico
- Micronesia
- Moldova
- Monaco
- Mongolia
- Montenegro
- Montserrat
- Saint Pierre and Miquelon
- Saint Vincent and the Grenadines
- Samoa
- San Marino
- São Tomé and Príncipe
- Saudi Arabia
- Senegal
- Serbia
- Seychelles
- Sierra Leone
- Singapore
- Sint Maarten
- Slovakia
- Slovenia
- Solomon Islands
- Somalia
- South Africa
- South Georgia and the South Sandwich Islands
- South Korea
- South Sudan
- Spain
- Sri Lanka

- Benin
- Bermuda
- Bhutan
- Bolivia
- Bonaire Saint Eustatius and Saba
- Bosnia and Herzegovina
- Botswana
- Bouvet Island
- Brazil
- British Indian Ocean Territory
- British Virgin Islands
- Brunei
- Bulgaria
- Burkina Faso
- Burundi
- Cambodia
- Cameroon
- Canada
- Cape Verde
- Cayman Islands
- Central African Republic
- Chad
- Gibraltar
- Greece
- Greenland
- Grenada
- Guadeloupe
- Guam
- Guatemala
- Guernsey
- Guinea
- Guinea-Bissau
- Guyana
- Haiti
- Heard Island and McDonald Islands
- Honduras
- Hong Kong
- Hungary
- Iceland
- India
- Indonesia
- Iran
- Iraq
- Ireland
- Morocco
- Mozambique
- Myanmar /Burma
- Namibia
- Nauru
- Nepal
- Netherlands
- New Caledonia
- New Zealand
- Nicaragua
- Niger
- Nigeria
- Niue
- Norfolk Island
- Northern Mariana Islands
- North Korea
- North Macedonia
- Norway
- Oman
- Pakistan
- Palau
- Palestine
- Sudan
- Suriname
- Svalbard and Jan Mayen
- Sweden
- Switzerland
- Syria
- Taiwan
- Tajikistan
- Tanzania
- Thailand
- The Gambia
- Timor-Leste
- Togo
- Tokelau
- Tonga
- Trinidad and Tobago
- Tunisia
- Turkey
- Turkmenistan
- Turks and Caicos Islands
- Tuvalu
- Uganda

- Chile
- China
- Christmas Island
- Clipperton
- Cocos (Keeling) Islands
- Colombia
- Comoros
- Congo
- Cook Islands
- Costa Rica
- Côte d'Ivoire
- Croatia
- Cuba
- Curaçao
- Cyprus
- Czechia
- Democratic Republic of the Congo
- Denmark
- Isle of Man
- Israel
- Italy
- Jamaica
- Japan
- Jersey
- Jordan
- Kazakhstan
- Kenya
- Kiribati
- Kosovo
- Kuwait
- Kyrgyzstan
- Laos
- Latvia
- Lebanon
- Lesotho
- Liberia
- Panama
- Papua New Guinea
- Paraguay
- Peru
- Philippines
- Pitcairn Islands
- Poland
- Portugal
- Puerto Rico
- Qatar
- Réunion
- Romania
- Russia
- Rwanda
- Saint Barthélemy
- Saint Helena Ascension and Tristan da Cunha
- Saint Kitts and Nevis
- Saint Lucia
- Ukraine
- United Arab Emirates
- United Kingdom
- United States
- United States Minor Outlying Islands
- Uruguay
- US Virgin Islands
- Uzbekistan
- Vanuatu
- Vatican City
- Venezuela
- Vietnam
- Wallis and Futuna
- Western Sahara
- Yemen
- Zambia
- Zimbabwe

* Your first name

Andreea

* Your family name

Iordache

* Email

andreea.iordache@efpia.eu

Do you wish to be informed regarding further Commission events or publications related to this topic?

- (●) Please keep me informed regarding the BTC revision process
- ( ) Do **not** use this email address to contact me except for confirmation of my submission to this consultation

The Commission will publish all contributions to this targeted consultation. You can choose whether you would prefer to have your details published or to remain anonymous when your contribution is published. **For the purpose of transparency, the 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.

* **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**
  The name of your organisation, the field(s) that your organisation works in, the country where your organisation is based and your contribution will be published as received. Your personal name will not be published. Please do not include any personal data in the contribution itself.
- (●) **Public**
  Your name, the name of your organisation, the field(s) that your organisation works in, the country where your organisation is based and your contribution will be published as received. Please do not include any personal data in the contribution itself.

☑ I agree with the personal data protection provisions

SECTION A

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

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. These substances do not meet the defined scope and definitions of the basic acts for blood and for tissues and cells. Please note that this section does not address those substances that might border or fall under other frameworks (medicinal products or medical devices). Such borderline substances are addressed below in the innovation section.

Q1 Should the scope and/or definitions of the revised legislation be drafted to include any of the following?

	No - exclude from the scope of BTC legislation	Include donation, procurement /collection and testing only in the BTC scope	Include all steps up to clinical use and vigilance in the BTC scope	No answer
Blood used for clinical purposes other than transfusion (e.g. platelet rich plasma or serum eye drops)	○	◉	○	○
Blood, tissues or cells used for non-clinical research or teaching	○	○	○	◉
Other	◉	○	○	○

You selected 'Other'. Please describe

1000 character(s) maximum

The legislation aims to cover the use of human tissues for human application and for research.Companies established internal rules and guidance for use of human tissues in research accounting for the regulations governing the use of such material. The legislation would benefit from limiting its scope to the human application of those defined human tissues. The emphasize aims to harmonize established framework for BTC with less stringent requirements if applied for non-clinical research and teaching purpose.
Revision of the BTC legislation should clearly exclude cells and tissues when substantially manipulated or when used in a different essential function as they are already regulated as ATMP.ATMP quality, safety and efficacy requirements are already defined in Regulation 1394/2007 and connected Directives and European guidance prepared by experts from all member states at EMA, according to the highest principles of public health protection, ensuring EU and global harmonisation.

Q2 Should the legislation include in its scope substances of human origin that do not meet the definitions of blood, tissues or cells (e.g. breast milk or intestinal microbiota) but are applied to patients?

- ○ Yes
- ○ No
- ◉ No answer

Q3 If you have further comments on the extension of the BTC scope to substances not currently included (apart from substances that border other frameworks such as advanced therapy medicinal products or medical devices), please enter them here.

1000 character(s) maximum

Q4 The European Commission has proposed reinforcing the mandate of ECDC, including a role in routine surveillance of communicable disease test results among BTC donors in the EU. Do you have comments on this proposal?

1000 character(s) maximum

We believe that 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.

Q5 Should scope and technical quality and safety rules differ for different types of **donation settings**?

	Exclude from scope	Include with lighter requirements compared to unrelated allogeneic	Include with the same requirements as allogeneic unrelated settings compared to unrelated allogeneic	No answer
Autologous BTC not processed or stored (used immediately)	○	○	○	◉
Autologous BTC processed but not stored (used almost immediately)	○	○	○	◉

Autologous BTC stored	○	○	○	◉
Allogeneic related (family donor) BTC not stored	○	◉	○	○
Allogeneic related (family donor) BTC stored	○	○	◉	○
BTC collected for medically assisted reproduction from a couple that are in a sexual relationship, not stored	○	○	○	◉
BTC collected for medically assisted reproduction from a couple that are in a sexual relationship, stored	○	○	○	◉
Other	◉	○	○	○

You selected 'Other'. Please descibe the donation setting you are referring to.

500 character(s) maximum

Autologous BTC should be regulated by using practical and suitable approaches implemented and leveraging existing accreditation or certification programs (FACT-JACIE international standards) and their recognition across member states should be ensured.

Q6 Should the **processing** of BTC that are not stored be regulated regardless of the donation setting?

	No	Yes with less stringent requirements	Yes with the same requirements as for BTC processed in authorised establishments	No answer
BTC removed, processed **in** the surgical room and reapplied **during surgery**?	◉	○	○	○
BTC removed, processed **outside** the surgical room and reapplied during surgery?	○	◉	○	○
BTC removed, processed and reapplied **at the bedside** (non-ATMP)	○	○	◉	○
Gametes processed (e.g. sperm washing) for immediate use in a partner in IVF clinics?	○	○	○	◉

Other	○	○	○	○

Q7 The following terms are currently defined in the basic act for **blood** (Directive 2002/98/EC). Do you consider that any of these should be revised?

- ☐ blood
- ☐ blood component
- ☐ blood product
- ☐ autologous transfusion
- ☐ blood establishment
- ☐ hospital blood bank
- ☐ serious adverse event
- ☐ serious adverse reaction
- ☐ blood component release
- ☐ deferral
- ☐ distribution
- ☐ haemovigilance
- ☐ inspection
- ☐ none

Q8 Are there additional terms related to **blood** that should be defined in a basic act ?

- ○ Yes
- ○ No
- ○ No answer

Q9 The following terms are defined in the basic act for **tissues and cells** (Directive 2004/23/EC). Do you consider that any of these should be revised?

- ☐ cells
- ☐ tissue
- ☐ donor
- ☐ donation
- ☐ organ
- ☐ procurement
- ☐ processing
- ☐ preservation

- [ ] quarantine
- [ ] storage
- [ ] distribution
- [ ] human application
- [ ] serious adverse event
- [ ] serious adverse reaction
- [ ] tissue establishment
- [ ] allogeneic use
- [ ] autologous use
- [ ] none

Q10 Are there additional terms related to **tissues and cells** that should be defined in a basic act?

- ( ) Yes
- (•) No
- ( ) No answer

Q11 Does the description and role of the **Responsible Person** in a blood or tissue establishment need to be improved?

- (•) Yes
- ( ) No
- ( ) No answer

Please explain how it should be improved

1000 character(s) maximum

Harmonisation across MS is required, currently there is large divergence, with requirements spanning from requirement of manufacturing licence to none

Q12 Do you consider that a role for **physicians** in blood or tissue establishments should be defined in a basic act?

- ( ) Yes

- (●) No
- ( ) No answer

Q14 If you consider that there are **other key personnel roles** in blood and tissue establishments that should be defined in a basic act, please give details here.

1000 character(s) maximum

The EU legislation includes many technical rules to be followed by blood and tissue establishments. 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 establishments 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 competent 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.

Q15 Which of the proposed policy options is most appropriate to define and update each of the following technical rules? You may choose different options for different aspects.

	Option 1 Professionals	Option 2 Expert bodies	Option 3 EU legislation	Other	No answer
Donor age limit rules	○	◉	○	○	○
Donor/donor family consent rules	○	◉	○	○	○
Rules regarding donor medical and behavioural history screening	○	◉	○	○	○
Rules for deferral/exclusion and mandatory testing for communicable diseases	○	◉	○	○	○
Rules for genetic testing of gamete donors	○	◉	○	○	○
Rules for donor protection and follow up	○	◉	○	○	○
Donor reimbursement/compensation rules	○	○	◉	○	○
Air quality requirements for processing environments	○	○	○	◉	○
Rules on storage temperatures and time limits for different BTC processed in different ways	○	○	○	◉	○
BTC critical characteristics and quality control tests for release for clinical use	○	○	○	◉	○
Requirements for traceability systems (including coding and labelling)	○	○	○	◉	○
BTC allocation rules (priority etc.) and distribution rules	○	○	○	◉	○
Rules on distribution channels (on request of health care professionals, via signed agreements with health care professionals, via internet etc.)	○	○	○	◉	○
Requirements for serious adverse reaction and event reporting to BE/TE and assessment by BE/TEs or clinicians	○	○	◉	○	○
Requirements for adverse reaction and event reporting to the authority by BE/TEs or others	○	○	◉	○	○

Rules for the follow up of patients treated with BTC or children born from medically assisted reproduction, if introduced in legislation.	○	○	○	○	◉
Requirements for quality management	○	○	◉	○	○
Requirements for contingency/ emergency plans	○	◉	○	○	○
Rules on the risk assessment of significant changes or innovation by BEs/TEs, if introduced	○	◉	○	○	○
Requirements for activity data (e.g. donations, distribution) reporting to the national competent authority	○	◉	○	○	○
Other	◉	○	○	○	○

You chose 'other' for one or more of the rules. Please describe the alternative option you propose, specifying the rule/requirement you are referring to.

2000 character(s) maximum

Implementation of a combination of Policy Option 2 and 3 will be a huge step forward to have:
The Commission laying down a Regulation to have a harmonized EU framework defining the regulatory requirements;
Only high-level principles should be outlined in EU law with adoption of technical details set by expert bodies.
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;
From an ATMP perspective, requirements on quality testing and management as established in the GMP for ATMPs are applicable and are considered sufficient. Additional overlapping requirements from a BTC perspective should be avoided to ensure there are clear boundaries between ATMP and BTC frameworks.
Mutually accepted inspections by e.g. focus inspectorates and EU level audits of national control systems audits of national control systems.

Q16 If option 2, or a combination including option 2 is implemented, which rules should be defined by **ECDC**?

- ☐ Rules for donor deferral/exclusion to prevent transmission of communicable diseases
- ☐ Requirements for donor selection questionnaires in relation to communicable disease transmission risk
- ☐ Communicable diseases to be screened in donors routinely and in specific circumstances
- ☐ Communicable disease testing methods to be applied (e.g. serology, NAT etc.)
- ☐ Rules for test kit selection and validation
- ☐ Rules on confirmatory testing of initially reactive tests
- ☐ Rules for testing laboratory good practice
- ☐ Rules on reporting of positive donor testing results to competent authorities or ECDC, if required by legislation
- ☐ Rules on donor sample archiving, if required by legislation

- [ ] Requirements for validation of existing or new microbial inactivation technologies
- [ ] Rules on combining measures (donor questionnaires, testing, microbial inactivation) to achieve required safety levels of BTC
- [x] Other

You selected 'Other'. Please describe other rules/requirements that you consider should be defined by reference to **ECDC**

1000 character(s) maximum

The definition of rules should be done at EU level by competent authorities in collaboration with expert bodies such as EDQM and ECDC. Potentially a formalization of the expert group of Competent Authorities on Substances of Human Origin.

Q17 If option 2, or a combination including option 2, is implemented, which parts of **EDQM guidance** should be referenced in EU legislation?

- [ ] Good Practice Guidelines (GPG) for blood (as currently)
- [ ] Good Practice Guidelines (GPG) for tissues and cells
- [ ] Blood component monographs
- [ ] Tissue and cells component monographs
- [ ] The entire EDQM blood guide
- [ ] The entire EDQM tissue and cell guide
- [ ] The EDQM tissue and cell guide excluding Section C
- [x] Other specific sections in the EDQM guides
- [ ] No answer

You selected 'Other'. Please list the sections of the guides that you consider should be referenced

1000 character(s) maximum

The definition of rules should be done at EU level by competent authorities in collaboration with expert bodies such as EDQM and ECDC. Potentially a formalization of the expert group of Competent Authorities on Substances of Human Origin.

Q18 What do you consider to be the appropriate role(s) of **professional and scientific associations** in the setting of technical rules for BTC?

- [ ] They should define their standards independently and those standards should be taken into account by those setting the rules for the EU
- [x] They should be formally consulted on all rule changes by those setting the rules for the EU
- [ ] They should be represented in expert committees established to support those setting the rules for the EU
- [ ] Their standards should be considered for direct referencing in EU legislation
- [ ] Other

Q19 Can you propose an expert body that sets standards for **genetic testing** of gamete or embryo donors?

- ( ) Yes
- (•) No

Q20 Please provide details of any other expert bodies that could be considered to define technical safety and quality rules for reference in EU legislation if option 2 is implemented, describing the technical quality and safety criteria in which they are expert

1000 character(s) maximum

Q21 Do you have comments regarding the process (e.g. participation, transparency, consultation, evidence basis) that should be followed for updating guidance by ECDC, EDQM or other expert bodies if option 2 is adopted?

- (●) Yes
- ( ) No

Please provide your comments here

1000 character(s) maximum

Policy options leveraging technical standards developed by relevant expert bodies at EU level such as ECDC and EDQM and leveraging EURO GTP I and II will ensure a dynamic system that can more easily adapt to changes in the current state of science. Decision on adoption of standards should remain with competent authorities through EU level coordination.
Public consultation step should be incorporated whenever new standards are created or existing standards are updated.

Q22 If policy option 3 is implemented, how can EU legislation be kept up to date most efficiently?

- ( ) Revised legislation is proposed by the European Commission following guidance published by expert bodies
- ( ) The European Commission establishes a series of expert scientific committees to continuously review evidence and propose changes
- ( ) The European Commission incorporates technical experts in its relevant policy team to review evidence and update legislation
- (●) Other

You selected 'Other'. Please describe

1000 character(s) maximum

Both answers 1 and 3:
- Revised legislation is proposed by the European Commission following guidance published by expert bodies
- The European Commission incorporates technical experts in its relevant policy team to review evidence and update legislation

Q23 Please enter here any further comments you may have on how technical safety and quality rules can be kept up to date with science, technology and epidemiology

2000 character(s) maximum

SECTION B

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 create barriers to the exchange of blood, tissues and cells between Member States.

Q24 Would adding any of the following general principles in EU legislation increase confidence in oversight practice?

- [ ] Independence from the regulated sector
- [x] Adequate administrative capacity
- [x] Lack of personal conflicts of interest of inspectors at each inspection
- [x] Legal mandate of inspectors (to issue orders to cease activity, to seize documentation and/or samples, etc.)
- [x] Transparency to citizens
- [ ] Other
- [x] Skill and competence of inspectors and other authority officials

Q24.1 You selected 'Transparency to citizens'. Which of the following aspects of transparency would you consider appropriate for inclusion in EU legislation?

Publication of national aggregated annual reports of inspection, authorisation and vigilance activities

10

Publication of individual results of blood and tissue establishment inspections /authorisations

5

Publication of the details of serious non-compliances, cessation orders or the detection of illegal practice of significance to public health

5

Q24.2 You selected 'Competence of authority officials'. How can competence of authority officials be promoted/ensured by EU legislation?

- [x] Specific qualification requirements
- [x] Regular participation in international training events (e.g. PIC/S)
- [x] Certification in an EU training programme
- [x] Assessment of competence by EU auditors
- [ ] Certification in a national training programme
- [x] Participation in multi-country inspections or mutual audits
- [ ]
- [ ] Other

- [ ] Requirements for regular participation in EU organised training events
- [ ] Regular participation in national training events

Q24.3 How can the administrative capacity (resources) of an authority be promoted /strengthened by EU legislation?

- [ ] Requirements for specific staff numbers per population size
- [ ] Assessment of the adequacy by EU auditors
- [x] Participation in multi-country inspections or mutual audits
- [x] Sharing of inspector resources between Member States
- [ ] Other

The current legislation describes the key requirements for authorisation of blood and tissue establishments. The following questions explore how these might be improved in revised legislation

Q25 Which of the following should be considered in revised legislation?

	Yes	No	No answer
Ensure competence of BE/TEs by defining a minimum level of BE/TE activity per year for maintenance of BE/TE authorisation	○	○	◉
Evaluation of aggregated outcome data to demonstrate good quality (e.g. number of live births for an IVF centre) for renewal of BE/TE authorisation	○	○	◉
Required mutual acceptance of national authorisations	◉	○	○
Required justification for non-acceptance of authorisations by other MS	◉	○	○
Authorisation by a multi-country inspection team for BTC distribution outside of the Member State	◉	○	○
Special authorisations for import (into the EU) as currently exists for tissues and cells	◉	○	○
Recognition of accreditation/certification by international organisations for relevant requirements (e.g. JACIE, ISO)	◉	○	○
Other	○	○	○

Q26 There is a Commission hosted public platform with a compendium of authorised tissue establishments, indicating the activities for which they are authorised. Should there be one for Blood establishments too?

- ◉ Yes

- ○ No
- ○ No answer

Q27 The current legislation does not require inspection or authorisation of the following entities by competent authorities. Should this be added in revised legislation?

	Yes	No	No answer
National bone marrow registries	○	◉	○
The international bone marrow registry (WMDA)	○	◉	○
Organ procurement organisations and other teams that do donor family interviewing and selection for donation after death	○	◉	○
Tissue and cell procurement establishments	○	◉	○
Donor testing laboratories – inspected and authorised for blood, not usually for T&C	◉	○	○
Other critical laboratories – bacteriology, HLA, genetic testing	○	◉	○
Other third party critical suppliers	○	◉	○
Commercial BTC distributors and brokers	○	◉	○
Clinical outcome registries (when used for secondary purposes related to oversight)	○	◉	○
Blood and tissue establishments in third countries supplying the EU	○	◉	○
Other	◉	○	○

You selected 'Other'. Please describe the other entities that you consider should be authorised

1500 character(s) maximum

The practical and suitable approaches should be implemented using existing accreditation or certification programmes (FACT-JACIE international standards) and their recognition across member states should be ensured.

Q28 How should the requirements for national authorities be defined and updated?

	Full details in EU legislation	Guidance by EU Expert Group of authorities or its Expert sub-groups (VES, IES, Coding)	Other	No answer
Annual Vigilance reporting to the EU	○	◉	○	○
Procedures for rapid alert sharing with other Member States	◉	○	○	○
Annual donation and use reporting to the EU (if introduced in legislation)	◉	○	○	○
Procedures for inspection and for sharing inspection outcomes	○	◉	○	○
Procedures for TE/BE authorisation and sharing of authorisation information with Member States and citizens	◉	○	○	○
Procedures for authorising BTC preparation processes and sharing of process authorisation with other Member States and citizens, if introduced in legislation	◉	○	○	○
Other	○	○	○	○

Q29 Should the possibility for donors or patients to report adverse outcomes or complaints directly to the competent authority be required in legislation?

- ◉ Yes
- ○ No
- ○ No answer

Q30 Please describe here any further comments you may have on improving oversight of blood, tissue and cell activities

2000 character(s) maximum

SECTION C

Supporting innovation for patient benefit

The BTC evaluation found that innovation was not facilitated optimally. In particular, while the tissue and cell legislation includes some requirements for preparation process authorisation, the blood legislation only specifies the required characteristics of blood components for transfusion and does not require preparation process authorisation.

Strengthening the authorisation of preparation processes of BTC (non-ATMP)

Q31 Do you consider that new preparation processes or clinical uses for blood, tissues or cells (non-ATMP) should require a specific authorisation ?

- (●) Yes
- ( ) No
- ( ) No answer

Q32 If authorisation of preparation processes is introduced across blood, tissues and cells (non-ATMP), which of the following should apply?

	Fully agree	Partially agree	Disagree	No answer
Preparation process authorisation requirements should be proportionate to risk (see GAPP Joint Action)	(●)	( )	( )	( )
Initial authorisations should be conditional on collection and provision of clinical evidence on safety and effectiveness to a degree that is proportionate to the identified risks	(●)	( )	( )	( )
Authorisations should be required in the case of changes only to the mode of clinical application (non-ATMP)	( )	(●)	( )	( )
Clinical outcome registries could be used as one source of evidence of a safe and effective preparation process	(●)	( )	( )	( )
Preparation process authorisation should be granted according to intended clinical application	(●)	( )	( )	( )

Authorised preparation processes should be shared and recognised between Member States	◉	○	○	○
Authorised preparation processes should be listed in a public register/compendium	○	◉	○	○

Q33 If you consider that there are other key principles relating to preparation process authorisation that should be addressed in legislation please describe them.

1000 character(s) maximum

Clear definition of the term “substantial change” versus “significant change” in context of risk assessment connected with authorization of preparation process should be established in order to achieve harmonization across member states.

Q34 What would be your assessment of the cost and administrative burden of introducing a requirement for authorisation of new preparation processes or clinical uses for blood, tissues or cells (non-ATMP), including clinical studies proportionate to the assessed risk?

For competent authorities

5

For blood and tissue establishments

5

For clinical users

5

Q35 Please enter here any futher comments you may have on preparation process authorisation

2000 character(s) maximum

Defining whether, and if so which, BTC requirements should be applied to a substance /product

Member States are responsible for deciding the regulatory status of substances/products. They might classify them as blood, tissues and cells (Substances of Human Origin) or under another legal framework such as the pharmaceutical or medical device frameworks. The BTC evaluation identified that some substances/products are regulated under different frameworks (BTC, medicinal products, medical devices) in different Member States. 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). An equivalent advisory mechanism is not established in the current BTC legislative framework.

Q36 If an EU mechanism were introduced to advise on whether, and if so which, BTC requirements should apply to a substance/product, what is your view on the following statements regarding its possible role?

	Fully agree	Partially agree	Do not agree	No answer
It should advise on whether a substance/product should be subject to all, or certain, provisions of the BTC legislation	○	◉	○	○
It should **not** advise on the appropriate legislative framework when the BTC framework is not considered relevant	◉	○	○	○
The criteria it would apply should be defined in BTC legislation	○	◉	○	○
It should publish its advice	◉	○	○	○

Q37 If such an advisory mechanism were introduced, which of the following should be included in its composition?

- ☑ Member State BTC competent authorities
- ☐ Patient representatives
- ☐ Blood and tissue establishment representatives

- [ ] Donor associations
- [ ] Health Technology Assessment bodies
- [x] Scientific experts
- [x] Clinical experts
- [ ] Others

Q38 If such a mechanism were introduced, who should be eligible to request advice on whether a substance/product should be subject to the BTC legislation (in part or in its entirety)?

- [x] National BTC competent authorities
- [x] Blood and tissue establishments
- [x] Researchers
- [x] Industry
- [x] Professional associations
- [ ] Others

Interaction between advisory mechanisms on regulatory status of substances/products

Q39 Does your organisation have experience of developing therapies that are at the borderlines with other EU regulated frameworks?

- (•) Yes
- ( ) No

From your experience, how easy have the following aspects been?

	Very easy	Rather easy	Rather complex	Very complex
Identifying the criteria setting the scope of the different legislative frameworks to understand which framework(s) applies to your substance/product	( )	(•)	( )	( )
Obtaining confirmation of the regulatory framework(s) to be applied (regulatory status) for the substance/product in your country	( )	(•)	( )	( )
Acceptance in other Member States of the regulatory status applied in your Member State (when you distribute the substance/product abroad)	( )	( )	(•)	( )
Obtaining guidance on regulatory status from EU level expert groups/committees (e.g. SOHO competent authorities expert group, Committee for Advanced Therapy Medicinal Products, the Medical Device Borderlines and Classification Group)	(•)	( )	( )	( )

Other	○	○	○	○

You indicated that some aspect was complex or you selected 'Other'. Please describe

1500 character(s) maximum

It is problematic to get harmonised view on some aspects of classification of borderline products between ATMP/BTC that is also recognised across member states.

Q40 If an EU mechanism is established to advise on whether, and if so which, requirements of the BTC legislation should apply to certain substances/products, should this mechanism interact with equivalent advisory structures in other frameworks (e.g. Committee on Advanced Therapy Medicinal Products and the Medical Device Classification and Borderlines Group)?

- ◉ Yes
- ○ No
- ○ No answer

Which of the following topics should be the subject of that interaction?

- ☑ Co-ordination regarding advice/recommendations on which regulatory framework should apply in borderline **cases**
- ☑ Coordination regarding the application of the regulatory status (scope) **criteri a** in the different legal frameworks to ensure coherent advice
- ☑ **Exchange of information** in circumstances where advice/recommendations from one mechanism has an impact on another framework
- ☐ Other

Q41 Do you or your organisation have experience of working with substances /products that are subject to provisions of more than one regulated frameworks (BTC, pharmaceutical products, medical devices)?

- ◉ Yes
- ○ No

Please indicate the borderline(s) with which you have experience

- [ ] BTC and plasma derived medicinal products
- [x] BTC and other classical medicinal products
- [x] BTC and advanced therapy medicinal products
- [x] BTC and medical devices
- [ ] BTC and food
- [ ] Other

Given your experience, how easy do you consider it is to comply with requirements across the frameworks?

	Easy to comply	Rather easy to comply	Rather challenging	Challenging
Meeting all technical provisions when more than one framework applies	○	○	◉	○
Inspection and authorisation procedures when more than one framework applies	○	○	◉	○
Vigilance reporting when more than one framework applies	○	○	◉	○
Other	○	○	○	○

You indicated that compliance with one or more type of requirement was challenging or that there were aspects other than those listed. Please describe

2000 character(s) maximum

Challenges are created with new legislation (medical device) that would require up-classification of blood bags system and create a risk with potential availability and consequences in shortages. Similar challenges are also posed by additional vigilance requirements as per new legislation. The interaction between the BTC legislation and other legislation needs to be considered.

Q42 Do you consider that blood competent authorities should be able to authorise storage of plasma that is collected for the manufacture of medicinal products?

- (●) Yes
- ( ) No
- ( ) No answer

Please explain your reasons

1000 character(s) maximum

As recently published in EU program of COVID-19 convalescent plasma collection and transfusion blood establishments complying with the donation, collection, processing, and testing criteria should be authorised by the competent authority. Authorization requirements should be harmonized across member states since some member states has put more stringent requirements.

Q43 To what extent do you consider the current blood donor selection and testing requirements appropriate for plasma collected for manufacture of plasma-derived medicinal products?

- ( ) Inappropriate
- (●) Somewhat inappropriate
- ( ) Appropriate
- ( ) No answer

Please explain what you consider is inappropriate

1000 character(s) maximum

Donor selection process differs across member states. It will be beneficial to have agreement on rules and practices for donor selection, differentiation between first time and repeated donor including type of donation. Different testing requirements across different member states. More stringent requirements create a complex and unclear situation that leads to challenging situation on distribution of these substances between member states.

Q44 Have you experienced difficulties related to the BTC legislation when importing tissues or cells for the manufacture of ATMPs or importing manufactured ATMPs

- (●) Yes
- ( ) No
- ( ) No answer

Please explain and suggest how this might be resolved in revised BTC legislation

1000 character(s) maximum

In some instances, challenging donor traceability and different testing requirements including re-testing upon importing.

Q45 Have you experienced difficulties related to the BTC legislation when exporting tissues or cells for the manufacture of ATMPs, or exporting manufactured ATMPs?

- ( ) Yes
- (●) No
- ( ) No answer

Interplay between regulatory frameworks when more than one applies to a substance /product

Q46 To what extent do you consider that interplay between regulated frameworks (BTC, medicinal products, medical devices) would be improved by increased co-operation between authorities in the different sectors at **Member State level**?

5

Q47 To what extent do you consider that interplay between regulated frameworks (BTC, medicinal products, medical devices) would be improved by increased co-operation between authorities in the different sectors at **EU level**?

5

Q48 If you have general comments on other topics related to innovation in the BTC sector, please enter them here

2000 character(s) maximum

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 ATMPs under the pharmaceuticals framework ensures the highest standards of scientific evaluation are performed. This approach assures stability for future investment in novel cell and tissue-based medicines and should be maintained to protect public health.
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 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 frameworks that can help identify inefficiencies that would benefit from streamlining and set examples to help developers navigate the various requirements.
The revision of the Blood Directive is 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.

SECTION D

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. All 3 policy options under consideration include measures to monitor sufficiency of supply on a routine basis and an alert requirement in the case of sudden supply threats.

Q49 How would you rate the cost and administrative burden of implementing requirements for reporting and monitoring of activity data (e.g. donations, supply, shortages) nationally and at an EU level?

For blood and tissue establishments

5

For competent authorities

5

For hospitals/clinics that use blood, tissues and cells in patients

5

A significant reliance of the EU on the US for its supply of plasma for medicinal product manufacture is well documented and the international exchange of haematopoietic stem cells is understood and essential for matching purposes. Significant imports of some other BTC are also reported, notably corneas and bone.

Q50 How can the EU ensure sufficiency of BTC supply for EU patients without relying on imports from third countries?

	Yes	No	No answer
Investment in establishment equipment and staff	◉	○	○
Promotional donation campaigns	◉	○	○
More trust, collaboration and exchanges between Member States	◉	○	○
EU platforms for the exchange of BTC between Member State establishments	◉	○	○
More appropriate policies for use in clinical settings	○	○	◉
Reduced wastage	◉	○	○
Supply planning at the regional, national or EU level	◉	○	○
Provisions to allow export bans	○	○	◉
Other	○	○	○

Q51 How would you assess the burden (financial and administrative) of these measures for stakeholders and authorities?

	Low	Significant	High	No answer
Investment in establishment equipment and staff	○	○	○	◉
Promotional donation campaigns	○	○	○	◉
More trust, collaboration and exchanges between Member States	○	○	○	◉
EU platforms for the exchange of BTC between Member State establishments	○	○	○	◉
More appropriate policies for use in clinical settings	○	○	○	◉
Reduced wastage	○	○	○	◉
Supply planning at the regional, national or EU level	○	○	○	◉
Provisions to allow export bans	○	○	○	◉

Q52 If you have other comments on measures to support the achievement of BTC sufficiency, please enter them here

2000 character(s) maximum

A sufficient and sustainable supply of e.g. blood components in the event of outbreak caused by emerging situation should be established. Interaction between the BTC legislation and other legislation (e.g. medical device). Re-classification of existing medical devices and their usage in connection with BTC may create a risk in terms of availability of components with potential resulting in shortages. Implementation of automation and traceability using novel technologies should be implemented in the interest of donors and recipients' safety. Implementation of technologies providing greater level of safety should be prioritized.

Q53 How can it be ensured that BTC are allocated according to clinical need?

- Requirements for priority allocation rules at establishment level - led by clinicians
- Requirements for priority allocation rules at national level - led by clinicians
- Requirements for priority allocation rules at EU level - led by clinical expert committees
- No requirements - leave establishments collect and supply according to demand
- Other

Q54 If you have general comments on other topics related to the sufficiency of the BTC supply, please enter them here

2000 character(s) maximum

Future EU legislation should be designed and harmonized to foster innovation and its uptake.The revision of the Blood Directive is 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 PBM 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.
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 PBM.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.
PBM is not only valuable in the surgical setting, but also in medical care for chronic diseases (including cancer), especially as around 2/3 of red blood cell transfusions are used in medical care of chronic diseases.
PBM 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 PBM guidelines and WHO/EDQM guidance in the field, as well as educational efforts towards healthcare providers.

General comments and supporting documents

Q55 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.

2000 character(s) maximum

"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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