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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

German Medical Association / Bundesärztekammer

* 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.

89648243865-50

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

You selected 'Other'. Please describe the relevant work of your organisation to this consultation

Text of 1 to 1000 characters will be accepted

Determination of state of science regarding human cells and tissues in national guidelines; on the basis of its legal mandate, determination of the generally accepted state of science and technology for the preparation of blood and blood components and for the use of blood components in national guidelines.

* 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
- Åland Islands
- Albania
- Algeria
- American Samoa
- Andorra
- Angola
- Anguilla
- Antarctica
- Antigua and Barbuda
- Argentina
- Armenia
- Aruba
- Australia
- Austria
- Azerbaijan
- Djibouti
- Dominica
- Dominican Republic
- Ecuador
- Egypt
- El Salvador
- Equatorial Guinea
- Eritrea
- Estonia
- Eswatini
- Ethiopia
- Falkland Islands
- Faroe Islands
- Fiji
- Finland
- France
- Libya
- Liechtenstein
- Lithuania
- Luxembourg
- Macau
- Madagascar
- Malawi
- Malaysia
- Maldives
- Mali
- Malta
- Marshall Islands
- Martinique
- Mauritania
- Mauritius
- Mayotte
- Saint Martin
- 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

- 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
- Brunei
- Bulgaria
- Burkina Faso
- Burundi
- 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
- Haiti
- Heard Island and McDonald Islands
- Honduras
- Hong Kong
- Mexico
- Micronesia
- Moldova
- Monaco
- Mongolia
- Montenegro
- Montserrat
- Morocco
- Mozambique
- Myanmar /Burma
- Namibia
- Nauru
- Nepal
- Netherlands
- New Caledonia
- New Zealand
- Nicaragua
- Niger
- Nigeria
- Niue
- Norfolk Island
- Northern Mariana 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
- Timor-Leste
- Togo
- Tokelau
- Tonga

- 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
- Cuba
- Curaçao
- Cyprus
- Hungary
- Iceland
- India
- Indonesia
- Iran
- Iraq
- Ireland
- Isle of Man
- Israel
- Italy
- Jamaica
- Japan
- Jersey
- Jordan
- Kazakhstan
- Kenya
- Kiribati
- Kosovo
- Kuwait
- Kyrgyzstan
- Laos
- Latvia
- 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
- Russia
- Rwanda
- Saint Barthélemy
- 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
- Wallis and Futuna
- Western Sahara
- Yemen

- Czechia
- Democratic Republic of the Congo
- Denmark
- Lebanon
- Lesotho
- Liberia
- Saint Helena Ascension and Tristan da Cunha
- Saint Kitts and Nevis
- Saint Lucia
- Zambia
- Zimbabwe

* Your first name

Rudolf

* Your family name

Reibel

* Email

bruessel@baek.de

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

- From the point of view of the German Medical Association, and within our responsibility (please compare our answer to the following question above "Which of the following best describes the work of your organsiation?"), it seems very unfavorable to combine questions about the already existing extensive regulatory networks for blood alone with further ones, e. g. different tissues and different cells. Technical answers, differentiated according to BTC are hardly possible. We recommend holding separate consultations.

- Use of only one method for systematic quality assurance for preparation/manufacturing/use of blood, blood components and blood products in EU Directives is essential. Currently, it is almost impossible to follow different instructions and regulations because there is no conclusive system.

(Please see our full text answer in the annex attached to our response)

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

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	○	○	○	○

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

Please give details of the definition(s) you think should be revised and why.

2000 character(s) maximum

Incongruencies in definitions as well as in language versions within the EU legislation should be removed:

Unprecise or absent definitions and lack of clarification, e. g. Annex III to Directive 2004/33/EC (CJEU case C-528/13 (Léger)).
Unprecise or absent definitions and lack of clarification, e. g. Annex III to Directive 2004/33/EC:
Different national interpretation of deferral criteria for donors as well as differences in the official language version lead to confusion concerning, e. g. "sexual behaviour". Consistent regulations and official language versions are needed in order to adhere to the principle of legal certainty.
Linguistic differences between the official laguage versions, e. g. Directive 2004/33/EC:
EN "high risk" - DE hohes Risiko
EN "risk" - DE hohes Risiko (correct translation would be: Risiko)
Thus, it remains unclear in the German language version what kind of risk is being addressed.

An exception for preparation and use of blood prepared by mechanised auto-transfusion during the same surgical procedure is needed, in analogy to Directive 2004/23/EC, Article 2, "2. This Directive shall not apply to:
(a) tissues and cells used as an autologous graft within the same surgical procedure;".

There are multiple examples of inconsistencies in definitions, e. g. "retracing", "retraceability", between different EU Directives. In order to keep regulations consistent, it is necessary that all EU Directives use the same definitions.

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

Please give details of the definition(s) you think should be revised and why

2000 character(s) maximum

In Germany, human cells and tissues are considered "drugs". European legislation was implemented in different laws and regulations, which lead to confusing regulations. Still it is doubtful whether human transplants are "drugs", because there are completely different requirements for drugs on the one hand and for human transplants on the other hand. As a consequence, the differentiation between the definitions of "cell", "tissue" and "organ" has major implications in German legislation. Human reproductive cells were excluded from being "drugs" in German legislation. Furthermore, legislation for haematopoietic stem cells in Germany is different depending to their origin. While haematopoietic stem cells received from peripheral blood or cord blood are regulated in drug law, haematopoietic stem cells received from bone marrow are regulated in transplantation law. These different legislations lead to inconsistent regulations in Germany.

The systematic of donor and recipient, which is fitting well for all human transplants like cornea and haematopoietic stem cells, does not fit for human reproductive cells. Also, human reproductive cells are not "transplanted" in the narrower sense. Therefore, human reproductive cells should especially be excluded from European Directives 2004/23/EC, 2006/17/EC and 2006/86/EC.

(Please see our full text answer in the annex attached to our response)

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

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

As the development of EU Directives is a long process, EU Directives are not able to quickly address, e. g. newly developed methods, current epidemiological developments or new infectious diseases. Therefore, EU Directives can only be and should only be a legal framework. Detailed regulations for these issues should be reserved for national regulations.

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
- [ ] Other

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
- [ ] Other specific sections in the EDQM guides
- [ ] No answer

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
- [ ] 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

Transparency of an expert board to recommend early and expedite measures appears necessary.

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

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
- Adequate administrative capacity
- Lack of personal conflicts of interest of inspectors at each inspection
-

- [ ] Legal mandate of inspectors (to issue orders to cease activity, to seize documentation and/or samples, etc.)
- [ ] Transparency to citizens
- [ ] Other
- [ ] Skill and competence of inspectors and other authority officials

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	○	○	◉

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

Problems arise with the 24-hour regimen for post mortal blood sampling (see 2006/17/EC, Annex II, 2.4). Due to this regimen, potential tissue donations cannot be performed. According to data from Lions Cornea Bank Baden-Württemberg, 84 potential donors in 2011, 36 potential donors in 2012, 47 potential donors in 2013, 94 potential donors in 2014, 87 potential donors in 2015, and 141 potential donors in 2016 were lost due to the 24-hour-regimen. Overall, 489 potential donors, which means almost 1000 potential corneal transplants, were lost in the last six years without reason. According to an interview of six German cornea banks (Aachen, Freiburg, Kiel, Köln-Merheim, LMU München, Münster as well as Deutsche Gesellschaft für Gewebetransplantation (DGFG)) by Deutsche Ophthalmologische Gesellschaft (DOG), more than 3.000 potential donors were lost between 2012 an 2016 due to the 24-hour-regimen. Current data indicate that blood sampling is possible within 48 h postmortal. Therefore, a correction of 2006/17/EC, Annex II, 2.4 should urgently be taken into consideration and should be revised considering scientific evidence.

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

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
- ☐ Scientific experts
- ☐ 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)?

- ☐ National BTC competent authorities
- ☐ Blood and tissue establishments
- ☐ Researchers
- ☐ Industry
- ☐ 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

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

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

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

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

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

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

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

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

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

Linguistic differences between the official language versions, e. g. Directive 2004/33/EC:
EN "high risk" - DE hohes Risiko
EN "risk" - DE hohes Risiko (correct translation would be: Risiko)
Thus, it remains unclear what kind of risk is being addressed in the German language version.

Unprecise or absent definitions and lack of clarification, e. g. Annex III to Directive 2004/33/EC:
Different national interpretation of deferral criteria for donors as well as differences in the official language version lead to confusion concerning, e. g. "sexual behaviour". Consistent regulations and official language versions are needed in order to adhere to the principle of legal certainty.

An exception for preparation and use of blood prepared by mechanised auto-transfusion during the same surgical procedure is needed, in analogy to Directive 2004/23/EC, Article 2, "2. This Directive shall not apply to:
(a) tissues and cells used as an autologous graft within the same surgical procedure;".

There are multiple examples of inconsistencies in definitions, e. g. "retracing", "retraceability", between different EU Directives. In order to keep regulations consistent, it is necessary that all EU Directives use the same definitions.

You may upload one supporting document to your submission here.

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

7980448b-1e31-4e38-8790-217cac8b8f06/Annex__Response_German_Medical_Association_2021-04-15.pdf

THANK YOU FOR YOUR CONTRIBUTION!

Contact

Contact Form

Annex, German Medical Association response to the
Targeted Consultation on the Revision of the EU Legislation on Blood, Tissues and Cells,
15 April 2021

German Medical Association answer to Question 1 (full text):

- From the point of view of the German Medical Association, and within our responsibility (please compare our answer to the following question above "Which of the following best describes the work of your organsiation?"), it seems very unfavorable to combine questions about the already existing extensive regulatory networks for blood alone with further ones, e. g. different tissues and different cells. Technical answers differentiated according to BTC are hardly possible. We recommend holding separate consultations.

- Use of only one method for systematic quality assurance for preparation/manufacturing/use of blood, blood components and blood products in EU Directives is essential. Currently, it is almost impossible to follow different instructions and regulations because there is no conclusive system. Also, uniform and conclusive safety/quality standards in Europe are needed for testing of blood products. Some (newly developed) methods of treatment are subject to the EU legislation regarding the preparation and use of blood and blood components, e. g. photopheresis. These newly developed methods should not be covered by EU Directives, as the regulations are not suitable for these newly developed methods. Regulations prohibit medical treatment needed by patients.

German Medical Association answer to Question 9 (full text):

In Germany, human cells and tissues are considered "drugs". European legislation was implemented in different laws and regulations, which lead to confusing regulations. Still it is doubtful whether human transplants are "drugs", because there are completely different requirements for drugs on the one hand and for human transplants on the other hand. As a consequence, the differentiation between the definitions of "cell", "tissue" and "organ" has major implications in German legislation. Human reproductive cells were excluded from being "drugs" in German legislation. Furthermore, legislation for haematopoietic stem cells in Germany is different depending to their origin. While haematopoietic stem cells received from peripheral blood or cord blood are regulated in drug law, haematopoietic stem cells received from bone marrow are regulated in transplantation law. These different legislations lead to inconsistent regulations in Germany.

The systematic of donor and recipient, which is fitting well for all human transplants like cornea and haematopoietic stem cells, does not fit for human reproductive cells. Also, human reproductive cells are not "transplanted" in the narrower sense. Therefore, human reproductive cells should especially be excluded from European Directives 2004/23/EC, 2006/17/EC and 2006/86/EC.

Regulations are partly out of place for human reproductive cells, e.g. Directive 2006/86/EC, Annex II, D. For ages, human reproductive techniques in Germany have been performed under ambient air without negative side effects. According to 2006/86/EC, Annex II, D, the following applies to human reproductive cells: "Unless otherwise specified in point 4, where

tissues or cells are exposed to the environment during processing, without a subsequent microbial inactivation process, an air quality with particle counts and microbial colony counts equivalent to those of Grade A as defined in the current European Guide to Good Manufacturing Practice (GMP), Annex 1 and Directive 2003/94/EC is required with a background environment appropriate for the processing of the tissue/cell concerned but at least equivalent to GMP Grade D in terms of particles and microbial counts." As a consequence, all laboratories working in assisted reproduction need to upgrade to, e. g. an air conditioning system, even though there is no valid data that the quality and safety of human reproductive cells can be improved by this action. Therefore, human reproductive cells should be excluded from the scope especially of Directives 2004/23/EC, 2006/17/EC and 2006/86/EC, but at least from Directive 2006/86/EC, Annex II, D.