

**Introduction and Consent**

The European Commission's Directorate General for Health and Food Safety (DG SANTE) has commissioned ICF, a consultancy, to support its preparation of an impact assessment on revision of Directive 2002/98/EC on safety and quality of human blood and blood components and of Directive 2004/23/EC on safety and quality of human tissues and cells and of their implementing acts.

Details of the Commissions plans for revision of the legislation are available on DG SANTE’s website [here](https://ec.europa.eu/health/blood_tissues_organs/policy/revision_en).

ICF will assess the potential impacts of changes to the blood, tissue and cells (BTC) directives by exploring the different policy options and their effect on stakeholders.

To answer many of the questions in this survey you will need to see details of the new policy options that the Commission has prepared. A document describing the options and the measures they contain is available to download [here](https://icfconsulting.qualtrics.com/WRQualtricsControlPanel/File.php?F=F_2meHWHmcB2ZpZxc). Additional links to this document are provided within the survey itself.

All views expressed in this survey will be anonymised. The data will inform ICF’s report to the Commission and may be used in support of the impact assessment.

If you are unable to use the online questionnaire, please contact us at [BTC@icf.com](mailto:BTC@icf.com) . **If you would like a personalised link that will enable you to part-complete, save and return to your survey response please write to** [**BTC@icf.com**](mailto:BTC@icf.com) **to request one.**

I consent to the use of the data supplied in accordance with the [Data Protection Notice](https://icfconsulting.qualtrics.com/WRQualtricsControlPanel/File.php?F=F_5o5VnwDNt7wfemi)

**Stakeholder Profile**

# About you

Your name and e-mail address:

First name

Pär

Last name

Tellner

We may wish to contact you for further information about a response to this survey. If you are content for us to do so please provide an email address here.

par.tellner@efpia.eu

**I am giving my contribution as a representative of:**

*Select from the first list, then the second*

Manufacturers

Representative organization representaing manufacturers

Please state your sector here if it is not covered by the list above

Operational level of your organisation

X International

X EU/EEA

 National  Regional Local

Organisation Name

EFPIA

Type of organization

 Public

 Not-for-profit Commercial

Organisation size

 Micro (1 to 9 employees)

Small (10 to 49 employees)

 Medium (50 to 249 employees) Large (250 or more)

Country of origin

Please indicate your country of origin, or that in which your organisation is headquartered :



Austria Belgium Bulgaria Croatia Cyprus Czechia Denmark Estonia Finland France

Please specify

Belgium

Countries of operation

In which European countries does your organization operate (or, if you are a representative organization, in which countries are your members located)?

 All EU27

 Austria  Belgium  Bulgaria Croatia  Cyprus

Czechia

Denmark Estonia Finland France Germany Greece Hungary Iceland Ireland Italy Latvia

Liechtenstein Lithuania Luxembourg Malta Netherlands Norway Poland Portugal Romania Slovakia Spain Sweden Switzerland UK

Other

**B1: Impacts resulting from issues of coherence with regulatory framework**

# Section B: Problem definition

This section asks questions on:

Issues at the interface of the EU’s BTC legislation and other EU legislation. The impact of COVID-19 on the BTC sector.

## B1: Issues at the interface of the BTC legislation and other legislation

When BTC substances and products fall in the ‘borderline zone’ between the BTC legislation and other frameworks (e.g. medical devices, medicinal products/ATMP, food legislation) the classification and regulation of the substances can be uncertain.

Please indicate how concerned you are about the issues with regulatory classification on borderline issues on



Comment

Not at all Not very Slightly Very concerned concerned concerned concerned

Innovation

Economic viability of the BTC sector;

Affordability of borderline products/substances for healthcare systems

Patient access to BTC therapies/technologies failing in a ‘borderline zone’ between the BTC legislation and other frameworks (including issues around affordability);

COMMENTS:

* Innovation – ATMP Regulation 1394/2007/EC and Pharmaceuticals Legislation Directive 2009/120/EC, amending Directive 2001/83/EC, defines tissue and cell based products as ATMPs (medicinal products), when human cells and tissues are subject to “substantial manipulation” or are not intended to be used for the same essential function, i.e., “non-homologous use’. The criteria of ‘substantial manipulation’ and ‘non-homologous use’ are clearly defined, and used worldwide for the classification and regulation of human cell/tissue-based medicinal products. Changes to these classification criteria could impact global convergence of ATMP regulations and hamper EU competitiveness in the global development of innovative ATMPs.
* Economic viability & Affordability – Ensuring a stable and predictable regulatory pathway is essential to the viability of any innovative sector. Regulatory classification of ‘borderline products’ should be based on aligned scientific criteria, including definition of cell or tissue product and claimed mechanism of action, and also be independent to concerns on economic viability & affordability
* Patient access to BTC –Issues around patient access including affordability are multi-factorial and complex and should not be addressed by changes to regulatory classification. Regulatory classification should ensure products follow the most appropriate pathway to enable safe and effective therapies with demonstrated positive therapeutic benefit over the potential risks to reach patients for patients.

Three possible causes of these borderline problems are identified below. Please indicate the importance of each cause, on a scale where 10 = very important and 1 = not important

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 10 (very important) | 9 | 8 | 7 | 6 | 5 | 4 | 3 | 2 | 1 (not important) |
| There are differences in interpretation of definitions which define the borderlines  e.g. substantial manipulation, same surgical procedure |  |  |  |  |  |  |  |  |  |  |
| There are weaknesses in the collaboration between the authorities that regulate BTC, medical devices, medicinal products and other frameworks |  |  |  |  |  |  |  |  |  |  |
| There is no mechanism that decides whether a Member State should apply the BTC framework or another framework to a particular BTC. |  |  |  |  |  |  |  |  |  |  |

Possible impacts of borderline/regulatory issues are identified here. Please indicate the importance of each impact, on a scale where 10 = very important and 1 = not important

10 (very

important) 9 8 7 6 5 4 3 2

1 (not important)

Barrier to cross-border exchange

Reduced economic sustainability of the sector

Reduced affordability of BTC substances

Increased costs to the processor/manufacturer

Less innovation in the BTC sector

What other impacts do these borderline problems create?

 Answer

‘Borderline problems/issues’ are not sufficiently defined to provide meaningful comment on impacts.It is difficult to answer the “borderline” questions without a definition and examples of borderline cases. In the current legislation, the definition of what is an ATMP and when BTC becomes ATMP is clear. In order to achieve greater clarity on the scope of the BTC and ATMP legislation, clear differentiation should be implemented in the revision of the BTC legislation, by excluding products falling into the current definition of an ATMP and defining the meaning of “innovative BTC” by providing examples of innovative BTC which are only minimally manipulated and for “homologous use” to distinguish them from products that should be regulated as ATMPs.

Don't know

What kind of collaboration between the regulators of BTC, medical devices, medicinal products and other frameworks would be most effective?

 Answer

Agreement between regulators on interpretation of the scientific concepts that should be applied consistent with current legal definitions in making classification decisions may reduce inconsistencies and potential for disagreements.

This should be accompanied by a hierarchy of classification that considers potential risk for patients. Medicinal products & ATMPs are more complex than BTCs and the product experts (CHMP/CAT) should have the final say.

There should be a mechanism for regulators to consult with each other during advice procedures.

Don't know

What impacts do these borderline concerns have on innovation in BTC therapies and technologies?

 Answer

To comment on impact, ‘borderline concerns’ need to be clearly described. The ATMP regulation has provided a predictable regulatory pathway for innovation of new therapies based on BTC. The current regulation provides clear definition to delineate between ATMP and BTC.

Streamlining areas where there is lack of harmonisation in implementation of the current BTC framework in Member States is welcome. The revision of the BTC legislation offers an opportunity to harmonize differences in implementation of national standards for donation, procurement and testing of cells/blood-derived treatments that create additional burden for developers and can delay products reaching patients.

Don't know

What impact do these borderline concerns have on innovation by public sector actors?

 Answer

Don't know

To what extent do you agree with the following statements?

The current donation, procurement and testing requirements of BTC legislation for starting materials of autologous therapies/technologies...



(1)

Comment

Strongly agree

Agree

Neither agree nor disagree

Disagree Strongly Don't

disagree know

Increase the cost (and therefore affordability) of therapies/technologies



(2)

Comment

Strongly agree

Agree

Neither agree nor disagree

Disagree Strongly Don't

disagree know

Extend the timeline to access therapies/technologies

Increase exposure of/to inefficacious/unsafe products

Reduce the quality of these therapies/technologies

Reduce the efficacy of the therapies/technologies

Comment (1): Current EU requirements for autologous donations are more stringent creating additional operational costs vs other regional.

Comment (2): Differences and divergences in national implementation of requirements can create operational challenges that slow set up of supply chains across countries.

**B2: Impact of COVID-19 on the BTC sector**

## B2: Impact of COVID-19 on the BTC sector

What were the impacts of the pandemic on...

...the safety and quality of BTC substances?

 Answer

Don't know / no response

...sufficiency of supply?

 Answer

Don't know / no response

...oversight of BTC activities?

 Answer

Don't know / no response

What did we learn about the resilience and functioning of the BTC sector during the COVID pandemic?

 Answer

Don't know / no response

What actions have you taken to increase safety and quality of substances, and supply sufficiency during the pandemic and what has been the effect?

 Answer

None/no response

If COVID-19 has revealed weaknesses in the EU legislation’s ability to support pandemic response what were they?

*Tick all that are relevant*

Lack of provisions requiring contingency/emergency planning

 Lack of provision for continuous monitoring of the supply situation  Lack of provision for export bans

 Lack of proportionate approach to quick assessment of novel therapies (CCP)

 Lack of a legally binding requirement that ECDC donor selection and Covid testing guidance be followed

 Other (please specify)

 Don't know None of these

What will be the permanent effects of the COVID-19 pandemic on the BTC sector?

 Answer

Don't know

**Section C: The future if there is no reform of EU law on BTC.**

## Section C: The future if there is no reform of EU law on BTC.

The following questions consider how the situation in Europe will develop if the EU’s BTC legislation is not reformed.

The European Commission has identified five problems with the current situation. In each case, how will the situation change over the next 10 years if there is no change to EU legislation on BTC?

Much

better Better No change Worse

Much

worse Don’t know

BTC legislation lags behind innovation.

Patients are not fully protected from avoidable risks

The EU is vulnerable to interruptions in some BTC supplies

There are barriers to the exchange of BTC within the European Union and variation in the protection given to citizens due to differences in oversight practices

BTC donors and for children born from donated eggs, sperm or embryos are exposed to avoidable risks.

How will the following change over the next ten years if the EU’s BTC legislation is not reformed?



Comment

Large Slight No Slight Large Don't increase increase change decrease decrease know

Use of BTC as starting materials for manufacturers of medicinal products or medical devices

Demand for assisted reproductive therapies

Use of genetic tests for BTC donors

Use of BTC for transplantation and transfusion

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Large increase | Slight increase | No change | Slight decrease | Large decrease | Comment  Don't know |
|  |  |  |  |  |  |  |
| Differences in regulation at national level |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
| Availability of data on BTC supplies |  | | | | | |

How will BTC technologies and applications evolve over the next ten years?

 Answer

BTC are starting materials for many advanced therapy medicinal products, such as cell & gene therapies, which will transform the treatment of many serious diseases. There are over 1000+ ATMP clinical trials underway worldwide including 200+ trials for cell therapies (EFPIA Pipeline Review 2021 Update, Feb 2021). There needs to be a very clear line where the BTC regulations end and where the ATMP regulation begins. Development could be hindered if interpretation of this changes over time.

As medicinal products, ATMPs are developed to very high quality and safety standards required by ATMP regulation. If the BTC regulation creates a framework for cell therapies to bypass ATMP regulation, it will undermine the development of ATMPs in Europe and put patient lives at risk.

BTC technologies must be allowed to evolve, but the regulation should not create an alternative path for cell-based medicinal products to be offered to patients without the rigorous scientific review that medicinal products are currently subjected to in the ATMP regulation.

Don't know

What will be the social (health) impacts of these changes?

 Answer

Don't know

What changes do you expect to see in the structure of your part of the BTC sector over the next decade (the number, average size, etc. of establishments )?

 Answer

Don't know

Considering only the type of activities relevant to your organisation, what change would you expect to see in the overall use of BTC therapies and therapies derived from BTC over the next 10 years (assuming no change to EU legislation).

 Answer

As described above the ATMP sector including those utilizing BTC is expected to continue growing with increasing number of patients being treated driving an increase in transport of BTC within EU and across regions for ATMP manufacture. The number of BTC establishments is also expected to grow globally to serve the demand for source material for ATMPs.

If there is no change to the current lack of harmonisation and lack of global regulatory convergence on requirements for BTC intended for ATMP manufacture the attractiveness of EU to develop and manufacture ATMP may continue to lose pace, compared to other regions globally.

Don't know

**OBJECTIVE 1: Increase patient protection from all avoidable risks.**

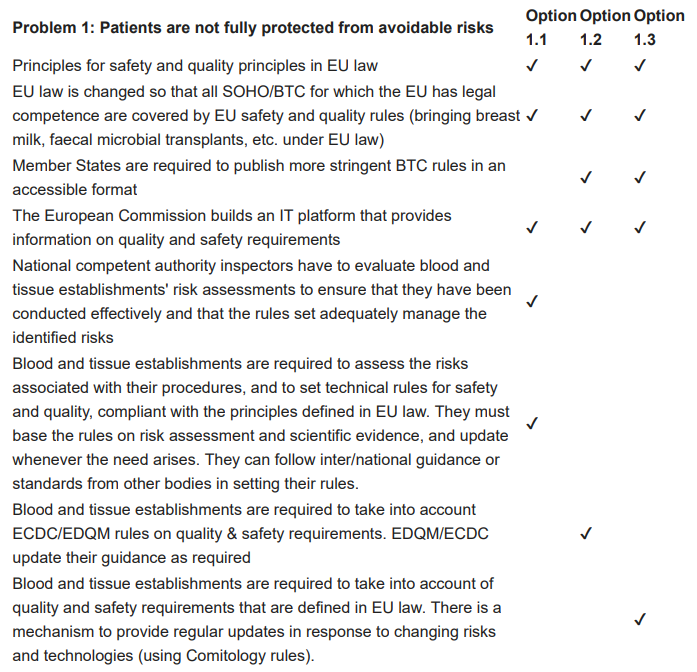
# Section D: Implications of potential future changes to EU legislation on BTC

This section asks about the impacts of possible changes to EU legislation on BTC. There are five sets of proposals. Each tackles one of five problems identified during the evaluation of the BTC legislation. Information on each of options set is provided at the start of each section.

Please review the descriptions of the options that are being considered before answering the questions.

## Problem 1: Patients are not fully protected from avoidable risks.

To protect patients from avoidable risks eight measures are being considered. They are grouped into three options, as described in [**this**](https://icfconsulting.qualtrics.com/WRQualtricsControlPanel/File.php?F=F_2meHWHmcB2ZpZxc) document and summarized in the table below. We recommend that you read Annex 1 of this document before answering the questions below



In considering your answer to each question, compare each proposed option to a scenario in which the EU’s BTC legislation is not reformed, and consider the expected development of the problem/issue over the next 10 years.

To what extent will **each policy option** solve the problem that safety and quality rules applied by blood and tissue establishments do not reflect the best scientific and technical knowledge in the BTC sectors?

Policy Option 1-1:

Policy Option 1-2:

Policy Option 1-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



To what extent will each policy option solve the problem that consistent safety and quality rules are not applied within and across Member States?

Policy Option 1-1:

Policy Option 1-2:

Policy Option 1-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



To what extent will each policy option solve the problem that some BTC applications fall outside the scope of the EU’s safety and quality rules?

Policy Option 1-1:

Policy Option 1-2:

Policy Option 1-3:

**5 Fully**

**solve 4 3 2**



**1 No Impact**



**Don't Know/No answer**



To what extent do the options address the problem of unequal protection of patients, within and across Member States?

Policy Option 1-1:

Policy Option 1-2:

Policy Option 1-3:

5 High

impact 4 3 2



1 Not confident at all



Don't Know/No answer



How confident are you that each option will result in stronger protection of patients treated with BTC than would be seen if EU law on BTC is not reformed?

Policy Option 1-1:

Policy Option 1-2:

Policy Option 1-3:

5 High

confident 4



3

Somewhat

confident 2



1 Not confident at all



Don't Know/No answer



To what extent will each option improve the EU’s ability to react/respond appropriately to new epidemiological developments by changing donor selection and testing measures?

Policy Option 1-1:

Policy Option 1-2:

Policy Option 1-3:

**5 To a great**

**extent 4**



**3**

**Somewhat 2 1 Not at all**



**Don't Know/No answer**



How feasible is the implementation of each of the proposed measures and what do you see as the main issues to be addressed when implementing them?

*(on a scale where 5 = implementation is very feasible to 1 = implementation is not feasible)*



Feasibility of implementation

5 4 3 2 1 Don't

know

Implementation issues (if any)

Blood and tissue establishments are required to comply with quality and safety technical requirements defined in EU law. There is a mechanism to provide regular updates in response to changing risks and technologies.

Blood and tissue establishments are required to take into account ECDC/EDQM technical rules on quality & safety requirements.

EDQM/ECDC update guidance as required

Blood and tissue establishments are required to assess the risks associated with their donor selection and other procedures, and set technical rules for safety and quality compliant with the principles defined in EU law. They must base the rules on risk assessment and scientific evidence, and update when necessary. They can follow inter/national guidance or standards from other bodies in setting their rules.

Member States are required to publish in an accessible format, any more stringent national rules, i.e. rules which go beyond EU rules or referenced guidance..

High level principles relating to safety and quality are adopted into EU law

The scope of the BTC Directives is extended to include all SOHO/BTC for which the EU has legal competence (bringing breast milk, faecal microbial transplants, etc. subject to EU law)

**OBJECTIVE 2: Strengthen and harmonise oversight among Member States to ens**

## Problem 2: Divergent approaches to oversight cause unequal citizen protection and barriers to the exchange of BTC across EU.

To strengthen and harmonise oversight among Member States six measures are being considered. They are grouped as a single option, as described in [**this**](https://icfconsulting.qualtrics.com/WRQualtricsControlPanel/File.php?F=F_2meHWHmcB2ZpZxc) document and summarized below. We recommend you read Annex 2 of this document before answering the questions below.

**Problem 2: Divergent approaches to oversight cause unequal citizen protection and barriers to the exchange of BTC across EU**

**Option 2.1**

EU law incorporates oversight principles for the NCA and for staff ✔

EU law requires competent authorities to base their inspection regimes on a risk-based ✔

approach

The European Commission will develop and maintain common guidance on oversight ✔ Commission audits of national control systems, accompanied by MS experts ✔ EU law is amended to implement a legal framework for Joint Member State inspections ✔

of blood and tissue establishments

The European Commission will develop the relevant component of the IT platform for ✔

oversight

In considering your answer to each question, compare each proposed option to a scenario in which the EU’s BTC legislation is not reformed (the baseline), and consider the expected development of the problem/issue over the next 10 years.

How confident are you that competent authority inspections will be performed objectively and competently (i) if there is no change to EU law and (ii) if Option 2-1 is adopted?

No change to EU law Policy Option 2-1:

5 Fully

confident 4 3 2



1 Not confident



To what extent will the measures solve the problem of lack of trust/confidence among EU Member States?

5 Fully

solve 4 3 2

1 No Impact

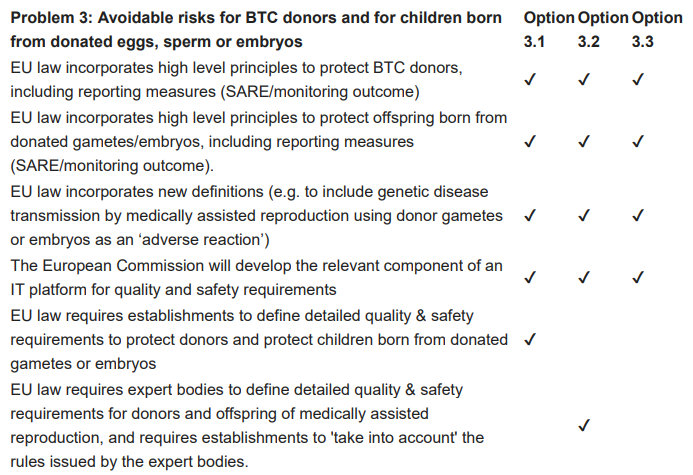
Don't Know/No answer

**OBJECTIVE 3 - Increase protection of BTC donors, and children born from do**

## Problem 3 - Avoidable risks for BTC donors and for children born from donated eggs, sperm or embryos

To increase protection of BTC donors and children born from donated sperm, eggs or embryos from specific risks, seven measures are being considered. They are grouped into three options, as described in [**this**](https://icfconsulting.qualtrics.com/WRQualtricsControlPanel/File.php?F=F_2meHWHmcB2ZpZxc) document and summarized in the table below. We recommend that you read Annex 3 of this document to answer the questions below



**Problem 3: Avoidable risks for BTC donors and for children born Option Option Option**

**from donated eggs, sperm or embryos**

EU law incorporates quality and safety requirements for donors and offspring of medically assisted reproduction, and a mechanism to update these as needed

**3.1**

**3.2**

**3.3**

✔

In considering your answer to each question, compare each proposed option to a scenario in which the EU’s BTC legislation is not reformed, and consider the expected development of the problem/issue over the next 10 years.

To what extent will each policy option solve the problem that **donors** are not fully protected from avoidable risks?

Policy Option 3-1:

Policy Option 3-2:

Policy Option 3-3:

5 Fully

solve 4 3 2



1 No impact



Don't Know/No answer



To what extent will each option solve the problem that children born as a result of medically assisted reproduction (MAR) are not fully protected from avoidable risks?

Policy Option 3-1:

Policy Option 3-2:

Policy Option 3-3:

5 Fully

solve 4 3 2



1 No impact



Don't Know/No answer



To what extent will each policy option help resolve the problem that comprehensive, prompt reporting of adverse reactions or events does not always occur?

Policy Option 3-1:

Policy Option 3-2:

Policy Option 3-3:

5 Fully

solve 4 3 2



1 No impact



Don't Know/No answer



To what extent will each policy option resolve the problem of quality and safety requirements relating to children born as a result of medically assisted reproduction not reflecting the best available technical expertise?

Policy Option 3-1:

Policy Option 3-2:

Policy Option 3-3:

5 Fully

solve 4 3 2



1 No impact



Don't Know/No answer



To what extent will each option improve protection of the fundamental rights of children?

Policy Option 3-1:

Policy Option 3-2:

Policy Option 3-3:

5

Substantially

improve 4 3 2



1 No impact



Don't Know/No answer



How feasible is implementation of each of the proposed measures and what do you see as the main issues to be addressed when implementing them?

*(on a scale where 5 = implementation is very feasible to 1 = implementation is not feasible)*



Feasibility of implementation

5 4 3 2 1 Don't

know

Implementation issues (if any)

EU law requires expert bodies to define detailed quality & safety requirements for donors and offspring from medically assisted reproduction, and require establishments to 'take into account' the rules issued by the expert bodies

Principles for donor safety are added to EU law

Blood and tissue establishments are required to define detailed quality & safety requirements to protect donors and protect children born from donated gametes or embryos

EU law incorporates new definitions (e.g. defining genetic disease transmission by medically assisted reproduction using donor gametes or embryos as an ‘adverse reaction’)

EU law includes high level principles to protect children born from donated gametes/embryos to ensure that such children do not have genetic conditions reasonably avoidable through selection and testing; and that genetic conditions in such children are reported and appropriate follow-up actions taken.

EU law incorporates quality & safety requirements for donors and offspring from medically assisted reproduction are built into EU law, with a mechanism incorporated to update these as needed

**OBJECTIVE 4: Facilitate innovation of safe BTC therapies (= removing barri**

## Problem 4: BTC legislation lags behind innovation

To facilitate innovation of safe BTC therapies 12 measures are being considered. They are grouped into three options, as described in [**this**](https://icfconsulting.qualtrics.com/WRQualtricsControlPanel/File.php?F=F_2meHWHmcB2ZpZxc) document and summarized below. We recommend you read section Annex 4 of this document before answering the questions below.

**Problem 4: BTC legislation lags behind innovation legislation lags behind innovation**

The “same surgical procedure” exclusion for point of care preparations is refined/removed.

An EU level advisory mechanism is established to recommend/advise MS on when/what BTC requirements should be applied in part or in full A mechanism is introduced to prompt regulators of 'adjacent' legal frameworks (SOHO/Pharma/Medical Devices) to better coordinate their rules, especially in respect of substances that are regulated under more than one legal framework.

An EU level advisory mechanism will advise where other frameworks (in particular medical devices and medicinal products) might be applied for particular novel BTC. Implementation might involve exchange/mutual consultation with advisory bodies for MP (EMA innovation task force, EMA CAT) and MD frameworks (Borderlines and Classification Working Party).

EU law sets principles for authorisation procedure (good practice for

**Option Option Option**

✔ ✔ ✔

|  |  |  |
| --- | --- | --- |
| **4.1** | **4.2** | **4.3** |
| ✔ | ✔ | ✔ |
| ✔ | ✔ | ✔ |
| ✔ | ✔ | ✔ |

authorisation procedures including validation of facilities, equipment and ✔ ✔ ✔

processing and clinical data requirement according to level of risk and

novelty) to demonstrate safety and efficacy in patients.

EU law requires that, for major changes in the steps of collection, processing and use of BTC, competent authorities have to grant prior

authorisation based on data demonstrating safety and benefit for patients that justifies any risks associated with treatment with BTC prepared in innovative ways.

✔ ✔ ✔

EU law sets rules for implementing a clinical trial for BTC (if high level of ✔ ✔ ✔

risks)

The European Commission will develop an exchange (IT) platform for competent authorities to exchange info regarding (novel) process

authorisations (the platform would be used for (voluntary) acceptance of ✔ ✔ ✔

authorisations among MS). This includes clinical evidence collected by clinicians with the support of learned societies.

EU law requires establishments to conduct risk assessments on novel processes. These are evaluated by the competent authority inspectors. EU law requires establishments to design the risk assessments on

✔ ✔ ✔

novel processes. Establishments could follow inter/national or standards ✔

from other bodies.

EU law requires establishments to conduct risk assessments on novel

processes in compliance with technical guidance from expert bodies as ✔

referred to in EU legislation.

EU law requires establishments to conduct risk assessments on novel ✔

processes in compliance with technical rules set in EU legislation

In considering your answer to each question, compare each proposed option to a scenario in which the EU’s BTC legislation is not reformed, and consider the expected development of the problem/issue over the next 10 years.

To what extent will each option provide a strengthened preparation process authorisation system that is outcome based?

Policy Option 4-1:

Policy Option 4-2:

Policy Option 4-3:

5 Fully 4 3 2 1 Not at all



Don't Know/No answer



To what extent will each option solve the problem that preparation process authorisation procedures for novel BTC applications are not fully harmonised across the EU?

Policy Option 4-1:

Policy Option 4-2:

Policy Option 4-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



To what extent will the BTC classification/ clarification mechanism solve the problem of legal uncertainty for borderline BTC applications?

5 Fully

solve 4 3 2

1 No Impact

Don't Know/No answer

Policy Option 4-1:

Policy Option 4-2:

Policy Option 4-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



To what extent will the coordination mechanism proposed to address interfaces between BTC, pharma and medical devices solve improve coherence of technical rules, and oversight (traceability, vigiliance, ...) when a BTC becomes a starting material to manufacture pharmaceutical products and medical devices

Policy Option 4-1:

Policy Option 4-2:

Policy Option 4-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



To what extent will each option address the challenges faced by public sector entities wanting to develop innovative BTC therapies and technologies?

Policy Option 4-1:

Policy Option 4-2:

Policy Option 4-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



To what extent will each option improve patients’ access to novel therapies?

Policy Option 4-1:

Policy Option 4-2:

Policy Option 4-3:

**5 Fully**

**solve 4 3 2**



**1 No Impact**



**Don't Know/No answer**



To what extent will the options facilitate innovation in the BTC sector?

Policy Option 4-1:

Policy Option 4-2:

Policy Option 4-3:

5 To a great

extent 4



3

Somewhat 2 Very little 1 Not at all



Don't Know/No answer



How feasible is implementation of each of the proposed measures and what do you see as the main issues to be addressed when implementing them?

*(on a scale where 5 = implementation is very feasible to 1 = implementation is not feasible)*



(1)

(2)

(3)

Feasibility of implementation

Implementation issues (if any)

5 4 3 2 1

Don't know

EU law requires establishments to design the risk assessments on novel processes following inter/national or standards from other bodies.

EU law requires application of clinical trials legislation for BTC if there is a high level of risk.

An EU level advisory mechanism is established to recommend/advise MS on when/what BTC requirements should be applied in part or in full

Comment:

(1)

(2) Measure will ensure high level of patient protection but should be careful not create a parallel pathway for products that should be regulated under another framework where these requirements are already existing, e.g. medicinal product framework. Parallel / duplicative pathways only increase uncertainties for developers

(3) The mechanism needs to be agile and not procedurally burdensome. Developers need timely answers to such questions and often cannot wait months for an answer

|  |  |  |
| --- | --- | --- |
|  | Feasibility of implementation  5 4 3 2 1 Don't  know | Implementation issues (if any) |
| EU law requires establishments to conduct risk assessments on novel processes in compliance with technical guidance from expert bodies as referred to in EU legislation.  EU law requires establishments to conduct risk assessments on novel processes in compliance with technical rules set in EU legislation  An new EU advisory mechanism is established to advise where other frameworks (e.g. medical devices and medicinal products) might be applied for particular novel BTC.  EU law obligates establishments to conduct risk assessments on novel processes. These are evaluated by the competent authority inspectors.  EU law includes principles for authorisation procedure to demonstrate safety and efficacy in patients (e.g. validation of facilities, equipment and processing and clinical data requirement according to level of risk and novelty).  “Same surgical procedure” exclusion for point of care preparations is refined/removed.  EU law required that, for major changes in the steps of collection, processing and use of BTC, competent authorities have to grant prior authorisation based on data demonstrating safety and benefit for patients that justifies any risks associated with treatment with BTC prepared in innovative ways  A new mechanism is introduced to prompt regulators of 'adjacent' legal frameworks (SOHO / Pharma / Medical Devices) to coordinate their rules, especially for substances regulated under more than one legal framework. |  | *(1)* |
| *(2)*  *(3)*  *(4)*  *(5)*  *(6)*  *(7)*  *(8)* |

*Comments:*

1. *Expert bodies need to ensure coherence and alignment with other regulatory frameworks when setting technical standards and take account of international convergence efforts*
2. *EU legislation would more easily ensure there is a common set of technical standards being applied but legislative process is often not nimble enough to adapt to advances in science and technology so could still become outdated quickly*
3. *This could lead to further complexity in borderline issues if committees have divergent views; need to clearly delineate and respect scope and remit of authorities to advise on when the relevant framework applies*
4. *Fragmentation / lack of harmonisation can still occur if common standards are not interpreted and implemented in the same way across competent authorities*

*(5) In order to ensure an efficient, coherent, and holistic system procedures duplication should be minimized by leveraging existing infrastructure and procedures perhaps in adjacent frameworks for the purposes of BTC*

*(6) Situations where urgent care is needed should be accommodated while retaining oversight*

*(7) Increased coordination between regulators in different legal frameworks is encouraged but should respect the scope of each authority in the context of the final product; a product should not be regulated under more than one legal framework but transition points and scope of authority should be clearly outline to avoid any overlaps that further complicate the system*

*(8) Prior authorization needs to be based on a common set of criteria across all member states to avoid fragmentation and inconsistencies in decision making; it will need to be defined what constitutes a major change*

**OBJECTIVE 5 - Avoid shortages of critical BTC therapies**

## Problem 5 - EU vulnerable to interruptions in some BTC supply

The measures planned to avoid shortages of BTC therapies are grouped into three options, as described in [**this**](https://icfconsulting.qualtrics.com/WRQualtricsControlPanel/File.php?F=F_2meHWHmcB2ZpZxc) document and summarized in the table below. We recommend that you read Annex 5 of this document before answering the questions below. The schedule of ‘critical’ BTC is given in Annex 6

**Option Option Option**

**Problem 5: EU vulnerable to interruptions in some BTC supply**

|  |  |  |
| --- | --- | --- |
| **5.1** | **5.2** | **5.3** |
| ✔ | ✔ | ✔ |
| ✔ | ✔ | ✔ |
| ✔ | ✔ | ✔ |
| ✔ | ✔ | ✔ |

EU law is amended to impose mandatory monitoring obligations on blood and tissue establishments for critical BTC

EU law is amended to require mandatory notification of sufficiency data for certain critical BTC in case of shortage/drop in supply (rapid notifications)

EU law is amended to require mandatory emergency plans, for certain critical BTC

The European Commission will develop the relevant component of the IT platform for exchange of information on supply and activity

EU law is amended to strengthen MS ability to intervene to control and

adjust supply, as necessary, under their national competence, and allow ✔ ✔ ✔

evidence-based support action at EU level.

EU law is amended to obligate BE/TEs to develop monitoring and

notification systems and contingency plans. These will be reviewed for ✔

adequacy by the authority during inspection.

EU law is amended with references to guidance from expert bodies for

rules on sufficiency data reporting (incl monitoring and notifications) and ✔

on emergency preparedness/contingency.

EU law is amended to include rules on sufficiency data reporting (incl ✔

monitoring and notifications) and on emergency preparedness

In considering your answer to each question, compare each proposed option to a scenario in which the EU’s BTC legislation is not reformed, and consider the expected development of the problem/issue over the next 10 years.

To what extent will each policy option solve the problem of decision-makers needing information with which to identify and manage risks to supply for critical BTC applications?

Policy Option 5-1:

Policy Option 5-2:

Policy Option 5-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



To what extent will the options increase the collection of critical BTC in the EU?

Policy Option 5-1:

Policy Option 5-2:

Policy Option 5-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



To what extent will the following options solve the problem of lack of resilience and preparedness for future outbreaks and emergencies?

Policy Option 5-1:

Policy Option 5-2:

Policy Option 5-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



To what extent do the options address the problem that stakeholders and authorities lack up-to- date information on supply of critical BTC for crisis management purposes?

Policy Option 5-1:

Policy Option 5-2:

Policy Option 5-3:

5 Fully

solve 4 3 2



1 No Impact



Don't Know/No answer



What impact will the proposed options have on the risk of interruptions of supply and shortages relating to vis-à-vis third countries, and the EU’s dependency on plasma imported from the USA?

*Please elaborate your response.*

5- High Impact

4

3 - Moderate impact 2

1 - Low impact **Don't know**

Please explain your response

A distinction should be made between establishments processing ‘critical BTC’ intended for therapeutic use vs onward manufacture of ATMPs and medicinal products. Some ATMP manufacturers are required to hold a tissue establishment license to import and store BTC materials solely intended for ATMP manufacture. Proposed policy options risk creating additional unnecessary and burdensome reporting requirements for these actors, if not exempt from new BTC requirements, that duplicate existing shortage reporting requirements in pharmaceutical legislation

To what extent would the foreseen measures to monitor supply (including donations, exchanges between EU Member States, imports and exports, shortages) reduce the risk of critical shortages and help build strategic independence?

5 To a great

extent 4

3

Somewhat 2 Very little 1 Not at all

Don't know/No answer

How confident are you that this option will provide sufficiency data that are comparable across the EU?

**5 Very**

**confident 4**

**3**

**Somewhat**

**confident 2**

**1 Not confident at all**

**Don't Know/No answer**

To what extent will each option improve the EU’s preparedness for future crises and public health emergencies?

Policy Option 5-1:

Policy Option 5-2:

Policy Option 5-3:

5 To a great

extent 4



3

Somewhat 2 Very little 1 Not at all



Don't Know/No answer



How feasible is implementation of the proposed measures and what do you see as the main issues to be addressed when implementing them?

*(on a scale where 5 = implementation is very feasible to 1 = implementation is not feasible)*



(1)

(2)

(3)

(4)

Feasibility of implementation

5 4 3 2 1 Don't

know

Implementation issues (if any)

EU law is amended to strengthen MS ability to intervene to control and adjust supply, as necessary, under their national competence, and allow evidence-based support action at EU level.

EU law is amended with references to guidance from expert bodies for rules on sufficiency data reporting (incl monitoring and notifications) and on emergency preparedness/contingency

EU law is amended to impose mandatory monitoring obligations on blood and tissue establishments for critical BTC

EU law is amended to obligate BE/TEs to develop monitoring and notification systems and contingency plans. These will be reviewed for adequacy by the authority during inspection

|  |  |  |
| --- | --- | --- |
|  | Feasibility of implementation  5 4 3 2 1 Don't  know | Implementation issues (if any) |
| EU law is amended to require mandatory notification of sufficiency data for certain critical BTC in case of shortage/drop in supply (rapid notifications)  EU law is amended to include detailed technical rules on sufficiency data reporting (incl monitoring and notifications) and on emergency preparedness  EU law is amended to require mandatory emergency plans, for certain critical BTC |  | (5) |
| (6)  (7) |

(1)

(2)

(3) A distinction should be made between tissue establishments processing ‘critical BTC’ intended for therapeutic use vs onward manufacture of ATMPs and medicinal products. Some ATMP manufacturers are required to hold a tissue establishment license to import and store BTC materials solely intended for ATMP manufacture. Additional reporting requirements should not apply in this case as it would create additional unnecessary burden and duplicate reporting requirements already existing in pharmaceutical legislation for reporting of shortages.

(4)

1. See comment above. For ATMP manufacturers who hold tissue establishment licenses this would be additional burden and duplicative to pharmaceutical requirements
2. See comment above. A distinction should be made for ATMP manufacturers who only hold TE licenses for import and storage of BTC material intended for onward ATMP manufacture

(7)

**See more**

Thank you for your answers. Do you have time to answer question about the impacts of another of the proposed policy options?

 Yes  No

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