European Commission

INCEPTION IMPACT ASSESSMENT

TITLE OF THE INITIATIVE	Revision of the Union legislation on blood, tissues and cells
LEAD DG (RESPONSIBLE UNIT)	SANTE B.4 - Medical Products: Quality, Safety and Innovation
LIKELY TYPE OF INITIATIVE	To be determined
INDICATIVE PLANNING	Q4 2021
ADDITIONAL INFORMATION	https://ec.europa.eu/health/blood_tissues_organs/policy/revision_en

The Inception Impact Assessment is provided for information purposes only. It does not prejudge the final decision of the Commission on whether this initiative will be pursued or on its final content. All elements of the initiative described by the Inception impact assessment, including its timing, are subject to change.

A. Context, Problem definition and Subsidiarity Check

Context

This initiative is an element in the EU's ambition to build a stronger European Health Union as announced by the Commission president Ursula von der Leyen in her 2020 state of the Union speech.

The Blood Directive 2002/98/EC and the Tissues and Cells Directive 2004/23/EC (the BTC legislation) have helped ensure the safety of millions of patients undergoing blood transfusion, transplantation and medically assisted reproduction. The legislation sets out **quality and safety requirements** for all steps from donation to human application, unless the donations are used to manufacture medicinal products or medical devices, in which case the legislation only applies to donation, collection and testing.

After more than 16 years in place, the legislation cannot cater for all the new scientific and technical developments that have taken place since. Shortcomings of the legislation have been identified in a 2019 evaluation of the legislation on blood, tissues and cells. The evaluation findings were endorsed by stakeholders and national competent authorities, and welcomed in the Council Working party on health, and in the European Parliament, with some MEPs having called for (Union Act) revising the Blood directive.

The COVID-19 pandemic highlighted some of the shortcomings in particular those impacting on blood transfusions. The strong reliance on third countries for plasma has shown a weakness to be addressed in the Union's ambition for an open strategic autonomy.. This is underlining the need for timely action. A potential revision has therefore been included in the Commission Work Programme 2021.

Problem the initiative aims to tackle

The revision aims to address the following gaps and shortcomings identified in the evaluation:

1. **Patients are not fully protected from avoidable risks:** The EU safety and quality requirements have not kept up to date with frequently changing scientific and epidemiological developments thus potentially exposing patients treated with BTC to avoidable risks. The European Centre for Disease Prevention and Control provides up-to-date but non-binding guidance on safety measures, e.g. to address COVID-19 risks, the Council of Europe provides guidance on quality of BTC and many Member States put more stringent requirements in place. This situation can create legal confusion and unequal levels of safety and quality for patients. In addition, while new therapies have emerged since the BTC legislation was adopted, it is not always clear whether, and if so which, of the BTC Directives apply, leaving these substances unregulated or regulated in divergent ways (e.g., breast milk and faecal microbiota transplants).
2. **Divergent approaches to oversight cause unequal levels of safety and quality and barriers to the exchange of BTC across the EU:** Divergent national interpretations and implementations of the legislation lead to unequal protection and a lack of mutual trust between national authorities. This in turn creates barriers to cross-border exchange and to availability of BTC. These differences reflect the lack of common provisions for verification of effective implementation of inspection, authorisation and vigilance, and inconsistency in the levels of capacities, skills and independence required of inspectors supervising BTC establishments.
3. **Avoidable risks for BTC donors and for children born from donated eggs, sperm or embryos:** Current BTC legislation contains only very limited measures to protect and monitor BTC donors and children born from donated sperm, eggs or embryos. In particular, the requirements to report donor adverse reactions are too limited and provisions for testing egg and sperm donors for genetic conditions are out of date with the technology available. Growing demand by commercial companies (e.g. egg banks for IVF, plasma collectors for medicinal product manufacture) increases the pressure to donate and

consequently the need for robust donor protection measures.

4. **BTC legislation lags behind innovation:** New ways of processing donations in BTC establishments may bring significant benefits. However, these new therapies can also put patients at risk, as current authorisation procedures for new BTC processes do not require evidence that risk is justified by benefits. Moreover, this lack of adequate procedures does not inspire trust and prevent healthcare actors from developing and adopting innovative processes. In addition, there are sometimes difficulties in defining the borderlines for novel BTC with other regulatory frameworks, in particular where medicinal products and medical devices are concerned. This creates administrative burdens and implicit disincentives for BTC establishments, healthcare professionals and academia to innovate. This legal uncertainty issue requires further evidence gathering to allow its extent and consequences to be fully assessed.
5. **EU vulnerable to interruptions in supply of some BTC**: For some essential BTC, the EU is highly dependent on imports to ensure sufficiency. In particular, the EU relies on the United States for an adequate supply of plasma used to manufacture plasma-derived medicines. In the current legislation, sufficiency of supply through voluntary unpaid donation is encouraged, though without concrete measures to protect or increase supply. This approach has not proven adequate to protect EU patients from the risk of shortages or sudden supply disruption. The lack of EU and national monitoring provisions for the supply of BTC makes it difficult to predict EU supply interruptions and to take action to mitigate the risks to patients.

The uncertainty issue on legal borderlines for innovative BTC results from the fact that certain substances/products are susceptible to being classified either as BTC or as other therapeutics, in particular medicinal products. This can only be addressed fully when also considering how the legislation applicable to medicinal products is currently delivering. The impact assessment will collect further information on the nature and extent of the problem. A comprehensive solution for this challenge would only be delivered in the future, jointly through this initiative and the pharmaceutical strategy.

COVID-19 pandemic has emphasised these challenges. The legislative provisions on donor selection and testing could not be updated rapidly enough and voluntary compliance with ECDC guidance was relied on to achieve a common level of donor and recipient protection from the risks of COVID-19 infection. Outcome data needed to be collected and assessed for the authorisation of a new plasma-based therapy to treat critical COVID-patients and monitoring of critical supply and demand was challenged by a lack of reliable donation and use data.

Basis for EU intervention (legal basis and subsidiarity check)

The BTC legislation is based on Article 168(4)(a) of the Treaty on the Functioning of the European Union (TFEU). As a shared competence with the Member States, and in line with the principle of subsidiarity, this Treaty Article gives the EU a mandate to set out measures establishing high standards of quality and safety for BTC while allowing Member States to maintain or introduce more stringent protective measures. Member States remain responsible for decisions of an ethical nature, such as allowing the donation of certain BTC or deciding who may access certain BTC therapies, and for the implementation of the voluntary unpaid donation (VUD) principle.

Ever-evolving disease threats, such as Zika or hepatitis E, which can be transmitted through BTC, constitute cross-border threats to public health. Increasing cross-border exchanges of BTC necessitate ever-closer cooperation between a number of health professional groups and authorities to ensure that BTC remain traceable from the donor to the recipient and vice versa. The evaluation confirmed the benefits of setting quality and safety standards for BTC at EU level although pointed to a need for a more responsive approach to changing risks.

The COVID-19 pandemic highlighted the risks for supply interruptions, the need for adequate donor and recipient protection and for adequate authorisations of health innovation through blood transfusion. By providing a framework for such cooperation, based on a common set of rules, EU-level measures are best placed to address such issues effectively. Establishing rules at an EU level could bring significant efficiencies for Member States, avoiding the need for multiple exercises in risk, benefit and cost analysis.

B. Objectives and Policy options

The overall objectives of this initiative are to ensure a high level of health protection for EU citizens. The EU legal framework should therefore:

1. **Ensure safety and quality** for patients treated with BTC therapies, for donors and for children born from in vitro fertilization, and enforcement of safety and quality requirements.
2. **Optimize access to, and avoid shortages of BTC therapies.**
3. Ensure the framework is **future-proof and facilitates the development of innovative BTC therapies**.

The baseline for this assessment will be the continuation of the current legislative framework without changes. Under the current directives, technical criteria for safety and quality are defined through implementing legislation at EU level, and would continue to be updated at intervals, as in the past. The identified problems will continue

and may even exacerbate.

Three options will be assessed in the impact assessment. The key differences between them concern (1) by whom and in which detail technical requirements are defined and kept up to date in order to ensure safety and quality, and (2) how these requirements are enforced through oversight by competent authorities at national level and by controls and audits by EU experts.

The options have been designed taking into account Member States' competences in this area. This concerns in particular organisational and ethical considerations[1], the implementation of the voluntary unpaid donation (VUD) principle, and the Member States' prerogatives in intervening to control the supply of BTC on their territory.

Policy option 1: Strengthened quality and safety requirements defined by blood and tissue establishments with strengthened national inspection, EU audits and classification advice

This option would strengthen safety of recipients, donors and offspring through a system of self-regulation by establishing general safety and quality principles at EU level, complemented by technical rules and specifications to be set and regularly updated by BTC establishments. Establishments will be required to base their own specific rules on documented risk assessment and scientific evidence, and to update them whenever the need arises.

The EU principles will respect Member States' competence, in particular with regard to implementing the VUD principle and ethical aspects such as donor anonymity, access to pre-implantation genetic screening tests, etc.

Substantially strengthened oversight principles will be laid down in the legislation, addressing independence of inspectors, conflicts of interest, and competency requirements for staff in authorities. Competent authorities will perform risk-based scheduling of inspections to optimise control of compliance with safety and quality requirements.

The Commission will perform controls in Member States, including audits of national systems of inspection, authorisation and vigilance. The Commission will develop common guidance and training activities on oversight in Member States. Better oversight is expected to significantly improve mutual trust between Member States and possibilities to exchange BTC between countries, and hence optimise access and use of BTC for patients.

To improve access to and sufficiency of BTC, mandatory EU monitoring and notification of sufficiency data and measures for emergency supply responses will be introduced (Reporting of donations, distribution, import, export and use by BTC establishments to national authorities and to the Commission, as well as rapid notifications in cases of serious impending shortage). The revised legal provisions will strengthen Member States ability to intervene to control and adjust supply, as necessary, under their national competence, and allow evidence-based support action at EU level.

To accommodate innovative BTC therapies, the scope of the BTC legislation will be clarified to include novel substances of human origin currently used but not regulated at the EU level.

For major changes in the steps of collection, processing and use of BTC, competent authorities will 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. An EU level mechanism will be set up to advising Member States on whether the BTC framework, or other frameworks (in particular medical devices and medicinal products), should be applied for particular novel BTC.

Policy option 2: EU-level safety and quality requirements defined by European Expert Bodies and strengthened national inspection, EU audits and classification advice

Safety of donors, recipients and offspring will be strenghtened through a ***system of co-regulation***. As under option 1, general safety and quality principles will be established at EU level, but with the obligation for establishments to take into account technical rules and specifications that will be defined and updated by authoritative bodies such as the European Centre for Disease Prevention and Control (ECDC) and the Council of Europe's European Directorate for the Quality of Medicines & HealthCare (EDQM). These principles and rules will respect Member States competences, in particular regarding VUD and ethical aspects.

The approach will be complemented by similar measures as under option 1 for strengthening oversight, including risk-based inspections by national authorities and EU level audits of national control systems. In addition a framework for joint compliance inspections (by two or more Member States), where appropriate, will be introduced.

New measures relating to ensuring sufficiency and supporting innovation, once shown to be safe and beneficial for patients, will be as in Option 1.

[1] e.g. decisions to authorise different technologies in assisted reproduction, or donor consent decisions.

Policy option 3: EU-level safety and quality requirements laid down in the BTC legislation with improved national inspections systems and classification advice

Not only will safety of donors, recipients and offspring be strengthened through general safety and quality principles established at EU level, as under options 1 and 2, but the EU BTC legislation will also define common binding technical rules and specifications for their implementation, along with a mechanism for regular updates to respond to changing risks and technologies under Comitology rules. These principles and rules will respect Member States competences, in particular regarding VUD and ethical aspects.

The approach will be complemented by similar oversight measures as in option 2 except that no controls system audits by the Commission will be proposed.

New measures relating to ensuring sufficiency and supporting innovation, once shown to be safe and beneficial for patients, will be as in Options 1 and 2.

Combining policy options: It would also be possible to formulate approaches to safety and quality rules based on a more granular approach, where the level of rule definition is aligned with the type of substance in question. So for example, the Commission might propose binding technical rules and specifications for some substances (as under option 3), but only in those areas where no such rules or specifications are defined by a well-recognised scientific expert body (as under option 2).

In addition, the Commission can consider further support for voluntary Member State cooperation.

C. Preliminary Assessment of Expected Impacts

Likely economic impacts

The likely economic impacts will be assessed taking into account the different players involved in the collection, delivery and use of BTC and the products derived from them.

- Organisations in charge of collection, testing, processing, storage and distribution of BTC products (healthcare services, hospital departments and non-governmental organisations involved in collection and delivery in the BTC sector such as the Red Cross).
- Organisations conducting research based on BTC technologies.
- Private establishments collecting plasma for medicinal product manufacturing and other standard processes (e.g. bone banking, the supply of sperm for routine assisted reproduction treatments, the banking of umbilical cord blood for family use)
- Industries in the medicinal product sector manufacturing products regulated under other EU legal frameworks but dependent on supply of BTC
- Industries in the medical device sector, supplying and regulating necessary devices and test kits to the BTC sector
- Organisations delivering and financing health care and health systems who apply and fund BTC-related activities and therapies

BTC donations should be used for optimal patient benefit, while enabling the **sustainability of health services** organising the service chain from collection, testing, processing, storage and distribution to recipient follow-up, whether they are public or private. Substances of human origin are not to be considered commodities.

Thus, instead of analysing markets, the impact assessment will look rather into structures of cooperation between these actors, to identify effective models for improving donor protection and patient benefit.[2] It is also expected that all three policy options will allow to increase the efficiency of these cooperative mechanisms. For example as some current exclusion criteria are no longer justified by science, updated donor eligibility criteria would reduce donation wastage.

Compared to the baseline, all three policy options are expected to impact favourably on **innovation** in the sector. Many innovative processing and treatment approaches are led by the public and non-profit professionals in the

[2] Such structures of cooperation also cover social and simplification aspects.

BTC establishments or their collaborators in public academic centres. A streamlined and more robust authorisation process will reduce burden for these innovators by helping to provide clearer and more harmonised indications on the safety and quality framework to be applied for novel BTC. This will thus contribute to removing barriers for the development and use of innovative therapies based on BTC, benefiting to patients. Sharing this innovation within networks of (public/non-profit and private) health providers and academia, typical of the sector, will further increase access to such innovative therapies.

In addition, including requirements for establishing the efficacy/effectiveness of certain substances of human origin in the authorisation process will ensure that innovation delivered to patients will come with real added value. This will not only avoid use of unnecessary therapies, but also contribute to the **sustainability of public health budgets**.

Finally, greater harmonisation and clear rules should **help health industries** interacting with the BTC sector, often as a supplier or a user of BTC as a starting material. Where appropriate, this impact assessment will also consider the work under the pharmaceutical strategy and under the new regulations on medical devices and in-vitro diagnostics, in order to seek for synergies to achieve innovation, sustainability, accessibility and autonomy.

It is important to note that none of the policy options foresee provisions to substantially change the principles of voluntary unpaid donation; neither to benefit nor disadvantage different private or public actors that currently collect BTC. The revised legislation is expected to clarify certain definitions and concepts and Member States would continue to define detailed rules on donor reimbursement or compensation and the conditions for the operation of the private sector.

Likely social impacts

All 3 policy options will improve the quality and safety of BTC across the EU by updating technical requirements for donor testing and eligibility, in line with current standards and risks, and ensuring that the provisions remain up to date.

In the case when decisions on safety and quality rules and specifications are left to blood and tissue establishments (option 1), it is likely that they will be adapted rapidly as risks change but that they will come to diverge even more than they do today, thus increasing in**equalities in the safety** of patients and in the quality of treatments.

The initiative will also increase the **health protection** of certain population groups including BTC donors, children born from assisted reproduction and patients treated with currently unregulated BTC. Greater BTC exchange and access through increased inter-Member State trust in oversight will be an important benefit for patients. New and clear requirements to demonstrate the safety and effectiveness of novel processes introduced by BE/TEs, and improved clarity at the borderlines with other frameworks, will improve **access** to innovative therapies and also prevent patients from being misled by those offering treatments without proven clinical benefit. **Critical interruptions or shortages** of BTC will be mitigated by supply monitoring and improved contingency planning.

Likely environmental impacts

None of the policy options identified is expected to produce significant impacts, positive or negative, on the environment.

Likely impacts on fundamental rights

None of the policy options identified is expected to produce significant impact on human rights. Ethical aspects, including those relating to assisted reproduction would remain under Member State competence.

Likely impacts on simplification and/or administrative burden

Policy options 1 and 2 include options with significant elements of simplification. The most important is the possible removal from legislation of many technical provisions, which will allow faster updating of standards (as they are subject to frequent change). Policy options 1 and 2 also bring the potential to merge the basic acts into a single instrument to regulate the high-level principles applicable for all BTC.

Despite the overall simplification, there are some elements that imply additional reporting.

- It is likely that some **updated requirements**, such as for donor testing, will bring additional costs. The follow up of children born from sperm, egg and embryo donation will be an additional requirement for establishments in the assisted reproduction sector that will imply costs. These elements can also have an indirect impact on the related device, diagnostics and pharma industries.
- Additionally, possibly extending the scope of the BTC legislation to include other substances of human origin would increase the **oversight** workload. This will be mitigated by a risk-based inspection scheduling to increase oversight efficiency.
- For all BTC establishments involved in developing innovative BTC processes, the collection of some **additional clinical outcome** data to demonstrate safety and effectiveness will add cost, though many are

already doing this on a voluntary basis or to meet Member State requirements.

- **Mandatory EU monitoring** and notification of **sufficiency** data and measures for emergency supply responses will bring administrative burden for competent authorities; however the extent of this is limited as much of the information required is collected currently for different purposes.

For all three options, additional resources will be needed by competent authorities to comply with more robust oversight measures and the monitoring of sufficiency of supply. Some additional resources by national authorities may also be needed to assess the safety and effectiveness of novel BTC processing methods introduced by BTC establishments; these costs could be reduced by the use of common collaborative tools at EU level to avoid the need for repeated assessments of the same processes. Supportive IT-platforms can allow for increased administrative efficiency.

In **Policy Option 1,** defining and updating the technical rules and specifications will be the responsibility of blood and tissue establishments; therefore, they will bear the related costs. The setting up of EU audits of national control systems would require additional resources.

In **Policy Options 2 and 3**, the defining and updating the technical rules and specifications will be done centrally, in option 2 by authoritative bodies such as ECDC and EDQM and in option 3 by the Commission. In this latter case the Commission will need additional resources in terms of expert and scientific advice as option 3 implies the frequent updating of the EU BTC legislations.

D. Evidence Base, Data collection and Better Regulation Instruments

Impact assessment

An impact assessment will be carried out to support the preparation of this initiative and to provide a robust evidence base for the contents of the legal proposal(s). The impact assessment process is expected to run until Q4 2021 (timing might however be delayed or impacted by COVID-19 related activities)

The impact assessment will quantify, as far as possible, the costs and benefits of the changes described in the options presented above.

Evidence base and data collection

The following information and data sources will be used in this impact assessment process:

- There is a well-established EU level cooperation among competent authorities and establishments. Current processes and data collected will provide valuable inputs for defining the necessary resources and impacts for the policy options;
- The BTC evaluation report will be a key source of evidence used;
- The BTC evaluation evidence base including the external study, results of the online stakeholder consultation, stakeholder consultation and dissemination events, bilateral and multilateral meetings with stakeholders and commission reports on the implementation of the BTC legislation;
- The results of a new stakeholder consultation conducted as part of the impact assessment (see below);
- At least one study will be commissioned to support the impact assessment process. It will be used to source additional evidence on the costs and benefits of the different policy options outlined. In particular, it will provide data on expected economic, social and administrative impacts.
- Information and data collected during the first months of the COVID-19 pandemic will be assessed in particular on challenges raised and the actions needed to address them. The way in which the policy options would have provided improved mechanisms to better manage pandemic will serve as a test case for assessing and comparing the options in the context of potential future crises.

Consultation of citizens and stakeholders

A thorough stakeholder consultation process will be carried out with the aim of complementing the information already provided by stakeholders during the evaluation process and gathering views on the policy options outlined in this document, as further developed during the impact assessment process. It is expected that this will provide useful input in particular in relation to the problem definition, possible policy options and their likely impacts. The consultation will include public and targeted consultation.

Stakeholder consultation will consist of the following:

- A 12-week public consultation with a likely starting date in Q4 2020. This consultation will address general questions to citizens and specific questions to interest groups. It will include some questions relating to borderline issues with other legislation (medical products and medical devices) in order to collect additional evidence on the nature and extent of the problems and on possible ways forward, particularly for BTC and BTC based products prepared in hospitals. The public consultation will be published on Commission's 'Have Your Say' web portal.
- Targeted consultation of relevant interest groups will also be carried out through bilateral / multilateral

meetings.

The stakeholders identified during the evaluation process remain relevant for this consultation. A particularity of the BTC sector is the very strong professional community and institutional network – including the public and private establishments - and a limited role of traditional industrial actors.

Stakeholders include:

- Member State competent authorities for BTC;
- Member State Ministries of Health and other relevant regulatory bodies;
- Professionals working in BTC donation and supply and their professional associations;
- Healthcare professionals using BTC in their clinical practice and their professional associations; ;
- Donors and their associations;
- Patients and their associations;
- Manufacturers of medicinal products / medical devices that use BTC as starting materials; or manufacturing and supplying devices necessary and test kits to the BTC sector
- Upstream / downstream service and equipment suppliers and users;
- Other EU and national authorities, including authorities for medicinal products and medical devices, and agencies such as the European Medicines Agency and the European Centre for Disease Control;
- Relevant international organisations such as the Council of Europe and the World Health Organisation;
- Ethics bodies;
- Third country regulators and professionals;
- Research organisations/associations and academia;
- Any interested citizen.

A synopsis report, summarising the results of all consultation activities will be published on the consultation page once all consultation activities are closed.

Will an Implementation plan be established?

As required by the current BTC legislation, all Member States have put in place implementation structures including the establishment of national competent authorities. A network of those authorities has also been set up in the form of a Commission Expert Group that will continue to meet regularly to discuss implementation issues. It therefore does not appear that there will be a need for an implementation plan for this initiative. However, this will be considered further during the impact assessment and in the light of the final choice of legal proposal.