

EVALUATION AND FITNESS CHECK (FC) ROADMAP			
TITLE OF THE EVALUATION/FC	Evaluation of Union legislation on blood, tissues and cells		
LEAD DG RESPONSIBLE UNIT	SANTE / B4	DATE OF THIS ROADMAP	17/01/2017
TYPE OF EVALUATION	Mixed Ex-Post Evaluation	PLANNED START DATE	Q1 / 2017
		PLANNED COMPLETION DATE	Q4 / 2018
		PLANNING CALENDAR	http://ec.europa.eu/smart-regulation/evaluation/index_en.htm
This indicative roadmap is provided for information purposes only and is subject to change.			

A. Purpose
(A.1) Purpose
<p>The purpose of the evaluation is to provide a comprehensive assessment of the Union legislation on blood and tissues and cells - Directives 2002/98/EC¹ and 2004/23/EC² respectively ('the Main Directives') and their implementing (technical) Directives³ ('the Implementing Directives'), examining their functioning across the EU (the Main Directives and the Implementing Directives are jointly referred to as 'the Directives'). Given the many commonalities between the two main acts, one evaluation will cover both the blood and tissues and cells legal frameworks. In particular the evaluation will assess the extent to which the Main Directives have met their original objectives and whether they remain fit for purpose assessing also the contribution of the Implementing Directives. This assessment will be without prejudice to any need to amend any of the Implementing Directives while the evaluation is still on-going, e.g. in case a new health risk emerges.</p> <p>The evaluation is expected to provide a sound evidence base which will be used to consider the need for any changes to the legislation.</p>
(A.2) Justification
<p>No evaluation of the Main Directives has taken place since their adoption despite a considerable degree of scientific and technological development in the sectors and new risks of transmitting emerging diseases. The sector is also undergoing organisational change including the market entry of private operators (commercial / for profit companies) into a traditionally non-profit oriented sector with mainly public actors..</p> <p>The Commission has published several implementation reports for each sector^{4, 5}, each based on information provided by Member States. The most recent reports were published in April 2016 and point to overall adequate levels of implementation across the EU (also as regards the Implementing Directives). The implementation has ensured that all Member States have functioning authorities in place for the oversight of these sectors, including authorisation, inspection and vigilance activities. However, in line with previous reports, the recent implementation reports also highlight a number of perceived issues and shortcomings put forward by Member States'</p>

¹ Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC. (OJ L 33, 8.2.2003, p.30)

² Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. (OJ L 102, 7.4.2004, p. 48)

³ Directives 2004/33/EC as amended, 2005/61/EC, 2005/62/EC, 2006/17/EC as amended, 2006/86/EC as amended and Directive (EU) 2015/566.

⁴ http://ec.europa.eu/health/blood_tissues_organ/key_documents/index_en.htm#anchor2_more

⁵ http://ec.europa.eu/health/blood_tissues_organ/key_documents/index_en.htm#anchor7_more

authorities and some stakeholders. These suggest the time is now right for a comprehensive evaluation of the legislation, in line with the principles of the Commission's Better Regulation Package⁶.

B. Content and subject of the evaluation

(B.1) Subject area

In the EU, every year 20 million blood donations are handled by 1300 blood establishments, enabling around 26 million transfusions to patients. Around one million tissue and cell donations, including corneas, bone, skin and heart valves for replacement surgery, bone marrow and cord blood for transplantation and reproductive cells for assisted reproduction are handled by over 3000 tissue establishments every year. Several of these substances are exchanged between Member States and the spending on blood, tissues and cells is estimated to be around **€6 billion per year in the EU**, while they allow for healthcare services worth a significant multiple of that amount. Organising bone marrow transplants alone is estimated to be worth another €3 billion each year. These substances are also needed as starting materials for manufacturing medicinal products such as plasma derivatives⁷ and advanced therapy medicinal products (ATMPs⁸). In particular plasma is important for deriving medicinal products estimated to have an annual market value of €4 billion in the EU.

Blood, blood components, tissues and cells all come from the same source – **donations from human beings** - either during life or after death. Following the collection of blood or blood components or the procurement of tissues and / or cells from donors they are subject to a number of intermediate steps such as testing, processing, preservation, storage and distribution prior to their use in transfusion (blood) or other types of human application (tissues and cells).

While the basic principles and certain procedures and techniques in the sectors have been well-established over a number of years, these fields are also subject to **considerable scientific and technological development** resulting in the availability of new techniques for testing, processing and preservation, to name but a few. Some of these developments raise questions on whether the original legislation remains suitable for the regulation of safety and quality.

Given their source (human donors), their recipients and the intermediate steps involved, there are inherent risks for public health – for the (living) donors themselves and recipients of such substances. Risks are related to a number of factors such as infectious diseases transmitted from the donor, from cross-contamination during processing, environmental contamination during processing or storage, or poor quality due to inadequate preservation or testing. Indeed, a **key driver for the adoption of the Main Directives was the public outcry following thousands of transmissions of HIV in the early 1980's**, and some years later even more of hepatitis C, to recipients of blood transfusion and plasma derived medicinal products. Over forty transmissions of Creutzfeldt Jacob disease by transplantation of highly processed dura mater (a tissue that lines the skull) and documented HIV transmissions by transplanted bone underlined the need for equivalent high levels of quality and safety for human tissues and cells across the EU.

In order to mitigate such risks and **ensure high levels of public health protection**, quality and safety standards are necessary for all stages of the process from donation leading up to transfusion or human application of blood and tissues and cells. However, when blood, tissues and cells are further used in the manufacturing of medicinal products or medical devices, the protection of public health is ensured by the combined application of the Directives (applicable to donation, procurement and testing of blood, tissues and cells used as starting materials) and the medicinal products/medical device legal framework.

A number of the risks for quality and safety in the blood and tissues and cells fields are common to all Member States. The Directives were introduced in order to lay down **common (minimum) quality and safety standards at Union level**, which also aimed to facilitate increased exchange of these substances between EU Member States, while leaving the regulation of clinical application and (ethical) decisions, for example on donor consent systems and access to treatment, at Member State level. The EU minimum standards are designed to apply to the various activities in the chain from donation leading to transfusion / human application as well as to the various actors / establishments responsible for each step in the chain. In order to ensure these quality and safety standards are adhered to, the Directives foresee an oversight function for Member State competent authorities which must implement licensing and inspection schemes as well as national vigilance and reporting

⁶ https://ec.europa.eu/priorities/democratic-change/better-regulation_en

⁷ Plasma derivatives are proteins filtered out of human plasma. The main proteins are immunoglobulins and clotting factors which have functions in the body's immune and bleeding systems.

⁸ Advanced Therapy Medicinal Products are gene therapy, somatic cell therapy or tissue engineered medicinal products, manufactured from human tissues and cells with an intention to be placed on the market

systems. These common standards facilitate increasing exchange of substances across borders. While there are some specific differences between blood and tissues and cells necessitating separate legislation, given the many commonalities, a parallel approach is taken to their regulation. Oversight of establishments by competent authorities through authorisation and inspection schemes, vigilance and traceability schemes, reporting and record-keeping requirements, as well as specific quality and safety rules for each activity thus form the main pillars of both sets of legislation.

While the types of risk to be addressed today, compared with 14 years ago, remain largely the same, their source and specific nature has changed over time. Notably, for instance, the increased movement of people around the world, combined with global warming, has promoted the spread of existing and new infectious agents, presenting new challenges for the prevention of their transmission by transfusion, transplantation and assisted reproduction. In parallel, technological advances present opportunities for more sensitive tests to be performed on donors, for microbial inactivation steps to be introduced during processing and for greater utilisation through improved preservation methodologies. These advances bring benefits but also potential risks associated with increased levels of complexity. They also bring new models and approaches to the organisation of donation and supply by the organisations involved, including increased exchanges of substances between countries within the EU and with third countries. Greater exchange activities have led to the need for a common oversight culture for blood, tissues and cells within the EU, with joint work between authorities and their inspectorates an increasingly important requirement.

The quality and safety framework laid down in the Directives and outlined above, and its adequacy in relation to the current risks and challenges facing these sectors, will be the main subject of this evaluation.

(B.2) Original objectives of the intervention

General objective

The main objective of the Directives was to ensure a high level of human health protection through setting safety and quality standards for blood, tissues and cells for implementation by those providing these services and those overseeing them on behalf of citizens.

Specific objectives

In broad terms, the legislation aimed:

- To ensure availability of safe blood tissues and cells for EU citizens that need them;
- To provide citizens with transparent systems that would enhance public confidence, whether citizens are engaged as potential donors or recipients;
- Define clear lines of accountability for ensuring safety and quality both at service provider and health authority levels.

The specific objectives led to legislation that specifically aimed at achieving the following operational objectives:

1. To define technical safety and quality requirements for all stages of the chain from donor to recipient;
2. To ensure effective regulatory oversight of the blood, tissues and cells sectors
3. To achieve a degree of harmonisation of safety and quality at Union level and facilitate EU-wide exchanges;
4. Establish a high level of legal certainty at Union level, i.e., to clarify how does the legislation on blood, tissues and cells relate to other Union legislation;
5. To achieve Union sufficiency through the encouragement of voluntary and unpaid donation and a strong public sector.

(B.3) How the objectives were to be achieved

To achieve operational objective 1, the intention was to define legally binding minimum requirements for professionals that would address issues such as donor selection, testing, processing, storage and distribution and for blood establishments that would have to meet organisational provisions for personnel, quality management etc. These provisions would be adapted in line with scientific, technological and epidemiological changes, so that the public can support and trust in safety and quality in all steps from donation to application.

To achieve operational objectives 2 and 3, the legislation included provisions for the establishment of national competent authorities for each sector, working in an effective network across the Union. The authorities were tasked to establish programmes of inspection, authorisation and vigilance that would increase confidence and trust in safety and quality of blood, tissues and cells, including those circulating between Member States and those imported from outside the Union. The Commission would support the network through the organisation of

meetings, the collection and publication of data and the provision of shared platforms for information exchanges (rapid alerts). This was to help ensure that risks are mitigated and unsafe activities are prevented.

Specific objective 4 was to be achieved through providing a clear legal scope and definitions of the blood, tissues and cells to be regulated by these sets of legislation.

To achieve operational objective 5, the legislation requires Member States to encourage voluntary and unpaid donation and the achievement of sufficiency through this type of donation. This aimed to increase public support and willingness to donate and reduce dependence on supply from 3rd countries.

The achievement of all 5 objectives would be supported via actions funded by the Public Health Programme.

C. Scope of the evaluation/FC

(C.1) Topics covered

This evaluation will primarily cover Directives 2002/98/EC and 2004/23/EC and their Implementing Directives **in all EU Member States from the date of their entry into force until now**. For those Member States which joined the Union after the entry into force of the Directives, the evaluation will cover the period from their date of accession. The evaluation will focus on the main pillars of the legislation as outlined above, as well as looking at whether the intended objectives of the legislation, as outlined above, have been achieved.

Aspects which fall within the competence of Member States, such as clinical application and ethical decisions, are not covered by this evaluation.

The frameworks governing medicinal products, in particular advanced therapy medicinal products (ATMPs), or medical devices are excluded from the scope of this evaluation. However, the evaluation will cover the coherence of the blood and tissues and cells legislation with other relevant Union legislation. In the light of the significant and increasing import or exchange of a number of human substances, particularly blood-forming stem cells, plasma, bone and reproductive cells with third countries, the evaluation will also consider coherence with relevant regulatory frameworks for blood and tissues and cells outside the EU, particularly in terms of equivalence of safety and quality of substances imported into the EU.

(C.2) Issues to be examined

This evaluation will seek to provide answers to **a number of high-level questions** outlined below grouped under the following **five specific assessment criteria**:

- **Relevance:**

1. To what extent is the legislation and its original objectives still valid and meeting current regulatory needs? In particular to what extent is the legislation:
 - a. Sufficiently adapted to, adaptable to, and up-to-date with scientific, technical and epidemiological developments / innovation?
 - b. Adapted to other changes in the sector such as commercialisation and internationalisation?
 - c. Are there any gaps in terms of substances of human origin or activities that are not regulated by the Directives?

- **Effectiveness:**

2. To what extent has the legislation increased the quality and safety of blood and tissues and cells and achieved a high level of human health protection?
3. Has the legislation led to any unintended effects (positive or negative)?
4. What, if any, have been the barriers preventing effective implementation of the legislation?
5. Are the rules on oversight sufficient to address the increased internationalisation?
6. What, if any, are the challenges to maintaining compliance with the legislation?
7. To what extent, if any, has the legislation impacted on patient access to blood, tissues and cells.

- **Efficiency:**

8. How cost-effective has the application of the quality and safety requirements in the legislation been for operators (have the benefits outweighed the costs)?
9. Are there particular administrative or other burdens for specific groups of operators, including downstream users of blood, tissues and cells as starting materials for medicinal products?
10. To what extent has the legislation resulted in cost implications for hospitals/patients using/receiving blood, tissues and cells?

	<p>11. To which extent does the oversight required by regulatory bodies pose a burden to public authorities (has the burden been proportionate to achieving the original oversight objectives of the legislation?)?</p> <ul style="list-style-type: none"> • Coherence: <p>12. To what extent is the legislation on blood and tissues and cells consistent and coherent within its own provisions? To what extent is the legislation coherent and consistent with other relevant Union legislation? Are the requirements of the Directives suitable when blood, tissues and cells are used as starting materials for the manufacture of medicinal products/medical devices? To what extent is the legislation coherent with other relevant international / third country approaches to the regulation of the quality and safety of blood and tissues and cells?</p> • EU Added Value: <p>13. To what extent has the legislative framework at EU level added value to the regulation of blood and tissues and cells across the EU-28 in a manner that could not have been achieved by measures taken at national or global level?</p> <p>14. To what extent do stricter national measures pose an obstacle to exchange of supplies between Member States?</p>
(C.3) Other tasks	
An external study will be commissioned to support the evaluation.	

D. Evidence base
(D.1) Evidence from monitoring
<p>Commission Reports on overall implementation and the implementation of the principle of voluntary and unpaid donation are available on the Commission's public health website and will provide key inputs into the evaluation. The most recent reports, for example, highlight some areas of concern including issues such as unclear scope, incomplete or missing definitions for key terms, lacking provisions for the independence and expertise of competent authorities, high administrative workload for inspections, challenging overlap/coordination with related areas, inadequate donor protection, need for better procedures for authorisation of new preparation processes, including no definition of quality criteria and requirements for clinical patient outcome monitoring.</p> <p>Annual summary activity reports on the use of the rapid alert platforms and reporting of serious adverse events and reactions are also available on the same website and will be taken into account.</p>
(D.2) Previous evaluations and other reports
<p>The Directives have not been subject to any previous formal evaluations or impact assessments. The following documents have been prepared recently and could be used as part of the evidence base:</p> <ul style="list-style-type: none"> • Two recent studies⁹¹⁰ of the sectors have focused on their economic landscape, highlighting increasing commercialisation and international exchange. These studies are available on the Commission's public health website; • In addition, in 2015 two Eurobarometer reports were published, outlining the European public's attitude to blood and tissue and cells donation and transfusion / application. They highlight overall confidence in the systems, but low levels of awareness on the possibilities of tissue and cell donation. These can be compared with previous Eurobarometer reports on the same fields and used in the overall analysis; • Summary minutes from meetings of an Expert Group consisting of representatives of Member State competent authorities (CASoHO), including an increasing number of questions regarding scope and interpretation of the legislation in view of innovative therapies and changing technologies; • Summary minutes from meetings with stakeholders published on the Commission's website; • Reports and final deliverables from EU-funded actions (projects, tenders, and Joint Actions) in the blood and tissues and cells fields, mapping and addressing national differences in ensuring safety and quality. • In addition, parallel work developed by the Council of Europe and the World Health Organisation can be taken into account. Whilst not of scientific nature, the contractor might also look at the 2012 Own-Initiative Report of the European Parliament on the voluntary and unpaid donation of tissues and cells.
(D.3) Evidence from assessing the implementation and application of legislation (complaints, infringement

⁹ http://ec.europa.eu/health/blood_tissues_organ/docs/economiclandscapes_humantissuescells_en.pdf

¹⁰ http://ec.europa.eu/health/blood_tissues_organ/docs/20150408_cc_report_en.pdf

procedures)
Information on the transposition of the Directives into the national law of the Member States has been summarised in the Reports on implementation while cases which have been subject to formal infringement proceedings are in the public domain and should also be taken into account. The latter addressed such issues as incomplete transposition of the Directives, e.g. vis-à-vis reproductive tissues and cells and relevant Court cases related to the application of the Directives, including judgements on the correct legal framework (blood or medicinal products) to be applied for a particular product and on the application of a blood donor deferral criteria, e.g. for men having sex with men. A number of further issues and complaints have been brought forward regarding issues such as implementation of the principle of voluntary and unpaid donation in the blood sector, direct distribution of tissues and cells (eg sperm) to recipients, potentially insufficient oversight over the ART sector, testing requirements for partner donations, and divergences in national inspection approaches.
(D.4) Consultation
<p>Stakeholder consultation will consist of three parts:</p> <ul style="list-style-type: none"> • A 12-week open public consultation which is due to start in Q2 2017. The consultation will address general questions to the public and specific questions to targeted stakeholders; • A targeted consultation of relevant stakeholders will also be carried out through bilateral meetings (including those which have already taken place), meetings of the CASoHO Expert Group (consisting of representatives of Member State competent authorities), group meetings with key stakeholders and Member State competent authorities' representatives; • A stakeholder event following the open public consultation period. This event will be used to present the findings of the open public consultation and to plug any remaining information gaps. <p>Key stakeholder groups have been identified as follows and in no particular order:</p> <ul style="list-style-type: none"> • Member State competent authorities for blood, tissues and cells; • Member State Ministries of Health and other relevant regulatory bodies; • Professionals working in blood, tissue and cell donation and transfusion their professional associations; • Healthcare professionals using blood, tissues and cells in their clinical practice; • Blood and tissue establishments and procurement organisations and their professional associations; • Upstream / downstream service and equipment suppliers and users; • Donors and their associations; • Patients and their associations; • Manufacturers of medicinal products / medical devices that use blood, tissues and cells as starting materials; • 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 and academia; • Any interested citizen. <p>The launch of the open public stakeholder consultation related to this initiative will be announced in the consultation planning which can be found at: http://ec.europa.eu/yourvoice/consultations/docs/planned-consultations_en.pdf.</p> <p>Information on the stakeholder event will be made available prior to the event on the Commission's public health website.</p>
(D.5) Further evidence to be gathered
The external contractor referred to in (C.3) above will produce a study based on the documents and reports provided, the relevant published literature, documents developed by other bodies (like the European Parliament, the Council of Europe or the World Health Organisations) and possibly the results of the public and targeted consultation. Where information gaps remain, the contractor will be expected to find additional sources of information.

E. Other relevant information/ remarks
<i>[e.g. comments on scope, further detail on communication activities or validation exercises]</i>