

Wp 4: Summary of European legal and regulatory news relevant for Riset.

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A lively production of new legal measures, norms and guidelines at EU level is presently occurring at EU level in domains relevant for Riset. A number of documents were proposed for public consultation, several EU guidelines appeared, a new Directive in the domain of transplantation was proposed (see below) and several conferences or workshops were held over the last months. We selected two of particular importance for Riset to be summarised below.

1. A proposal of a Directive on standards of quality and safety of human organs intended for transplantation¹ and an Action plan on Organ Donation and Transplantation², adopted on December 8, 2008 by the European Commission.
2. A draft of the Committee for Medicinal Products for Human Use (CHMP): "Biomarkers qualification: guidance to applicants"³. It was open to public consultation until June 30, 2008.

1. Proposal of a Directive on standards of quality and safety of human organs intended for transplantation

On 8 December 2008, the European Commission adopted a proposal of a Directive on standards of quality and safety of human organs intended for transplantation⁴ and an Action plan on Organ Donation and Transplantation⁵. Three challenges are addressed: improving the quality and safety of organs across Europe, increasing organ availability and making transplant systems more efficient and accessible.

Background:

Since 1999, on the legal basis of Article 152 of the European Community (EC) Treaty, as introduced by the Treaty of Amsterdam; the European Parliament and the Council have the possibility to adopt harmonising measures to ensure high standards of safety and quality for organs, substances of human origin, blood and blood derivatives. The Community action should complement national policies to improve public health⁶. Directives have already been adopted for blood in 2003⁷ and for tissues and cells in 2004⁸.

¹ Proposal for a Directive of the European Parliament and of the Council on standards of quality and safety of human organs intended for transplantation, 08/12/08, COM (2008)818 final: http://ec.europa.eu/health/ph_threats/human_substance/oc_organs/docs/organs_directive_en.pdf

² Communication from the Commission, Action plan on Organ Donation and Transplantation (2009-2015) : Strengthened Cooperation between Member States, 08/12/08, COM (2008)819 final: http://ec.europa.eu/health/ph_threats/human_substance/oc_organs/docs/organs_action_en.pdf

³ <http://www.emea.europa.eu/pdfs/human/biomarkers/7289408en.pdf>

⁴ Proposal for a Directive of the European Parliament and of the Council on standards of quality and safety of human organs intended for transplantation, 08/12/08, COM (2008)818 final: http://ec.europa.eu/health/ph_threats/human_substance/oc_organs/docs/organs_directive_en.pdf

⁵ Communication from the Commission, Action plan on Organ Donation and Transplantation (2009-2015) : Strengthened Cooperation between Member States, 08/12/08, COM (2008)819 final: http://ec.europa.eu/health/ph_threats/human_substance/oc_organs/docs/organs_action_en.pdf

⁶ Article 152 (2) of the EC Treaty.

⁷ 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: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:033:0030:0040:EN:PDF>

⁸ 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: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:102:0048:0058:EN:PDF>

In 2003, the European Commission realised a survey on legal requirements related to transplantation in the European Union (EU). It showed important differences in quality and safety requirements within Member States⁹.

On 31 Mai 2007, the European Commission adopted a Communication on organ donation and transplantation¹⁰. It proposed a dual mechanism of action: an Action Plan to enhance active coordination and cooperation between Member States and a legal instrument containing the basic quality and safety principles.

On 8 December 2008, the European Commission adopted a proposal of a Directive on standards of quality and safety of human organs intended for transplantation and an Action plan on Organ Donation and Transplantation.

The Action Plan:

The Commission has identified a list of priority actions grouped under the three challenges: improving the quality and safety of organs across Europe, increasing organ availability and making transplant systems more efficient and accessible.

The action and measures to be taken to achieve the established objectives will be decided by each Member State and included in a national priority actions' programme.

The specific actions proposed are the following:

- **CHALLENGE 1: INCREASING ORGAN AVAILABILITY**

Objective 1: Member states should reach the full potential of deceased donations

Priority Action 1: Promote the role of transplant donor coordinators in every hospital where there is potential for organ donation.

Priority Action 2: Promote quality improvement programmes in every hospital where there is potential for organ donation.

Objective 2: Member states should promote living donation programmes following best practices.

Priority Action 3: Exchange of best practices on living donation programmes among EU Member states: Support registers of living donors.

Objective 3: Increase public awareness of organ donation.

Priority Action 4: Improve the knowledge and communication skills of health professionals and patient support groups on organ transplantation.

Priority Action 5: Facilitate the identification of organ donors across Europe and cross-border donation in Europe.

⁹ "Human Organ Transplantation in Europe: an overview": http://ec.europa.eu/health/ph_threats/human_substance/documents/organ_survey.pdf

¹⁰ Communication from the Commission to the European Parliament and the Council, « Organ Donation and Transplantation: Policy Actions at EU level», 30/05/2007, COM(2007) 275 final : http://ec.europa.eu/health/ph_threats/human_substance/documents/organs_com_en.pdf

- **CHALLENGE 2: ENHANCING THE EFFICIENCY AND ACCESSIBILITY OF TRANSPLANT SYSTEMS**

Objective 4: Support and guide transplant systems to be more efficient and accessible

Priority Action 6: Enhancing the organisational models of organ donation and transplantation in EU Member States.

Priority Action 7: Promote EU-wide agreements on aspects of transplantation medicine.

Priority Action 8: Facilitate the interchange of organs between national authorities.

- **CHALLENGE 3: IMPROVING QUALITY AND SAFETY**

Objective 5: Improve the quality and safety of organ donation and transplantation

Priority Action 9: Evaluation of post-transplant results.

Priority Action 10: Promote a common accreditation system for organ donation/procurement and transplantation programmes.

The proposal for a Directive:

The aim of the proposal is to ensure that the same quality and safety requirements are used for human organs transplantation in the EU.

The proposal has been transmitted to the European Parliament and the Council on 8 December 2008 for adoption according to the codecision procedure provided by Article 251 of the EC Treaty¹¹.

The main elements of the proposal are the following:

- **Scope:**

According to Article 2, it covers human organs that are used for transplantation, during all the phases of the process- donation, procurement, testing, preservation, transport and use – and aims to ensure their quality and safety and hence a high level of protection. And, “where such organs are used for research purposes, this Directive only applies where they are intended for transplantation into the human body”.

However, blood and blood components, human tissues and cells and organs or tissues and cells of animal origin are excluded from the scope of the proposal as they are already covered by Directives 2002/98/EC, 2004/33/EC, 2005/61/EC and 2005/62/EC for blood and blood products and by Directives 2004/23/EC, 2006/17/EC and 2006/86/EC for human tissues and cells.

In this context, one issue will probably give rise to a debate within the European Parliament: it concerns the link between this new proposal and the existing Directive 2004/23/EC on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

The new proposal provides: “An organ donor is also very often a tissue donor. Quality and safety requirements for organs should complement and be linked with the existing Community system for tissues and cells laid down in Directive 2004/23/EC [...]. An unexpected adverse reaction in an organ

¹¹ http://ec.europa.eu/codecision/procedure/index_en.htm

donor or recipient should be traced by the competent authority and reported in the tissue vigilance systems as provided for in that Directive”¹².

The delimitation of this two directives and the interconnection between both reporting systems should be clarified.

- **Ensuring quality and safety for patients at EU level**

As there are significant risks to using organs in therapy, there is a necessity for the application of quality and safety procedures through a well-regulated donation and transplantation system.

The proposal provides for “the creation or designation of a competent authority in each Member State”¹³ ensuring compliance with the requirements of the Directive.

Chapter II sets out:

- A system for the authorisation of programmes of organ procurement and transplantation related notably to the Procurement organisations¹⁴ and the Organ Procurement¹⁵; with a complete list of authorised centres throughout the EU¹⁶.
- common quality and safety standards for the processes of evaluating donors and human organs¹⁷
- “The introduction of national quality programmes to ensure continuous monitoring of performance and improvement and learning”¹⁸.
- A system of traceability system from donation to reception and vice versa is provided by Article 10.
- “Measures to capture serious adverse events related to the procurement, testing and transport of organs, as well as any serious adverse reactions observed during or after transplantation which may be connected to the procurement, testing and transport of the organ in the European Union”¹⁹.

- **Ensuring the protection of donors and recipients**

Chapter III of the proposed Directive contains a set of measures to protect the rights and health of donors and recipients. They concern:

- The voluntary and unpaid donations of human organs²⁰
- The consent and authorisation requirements prior to procurement²¹
- The protection of the living donor²²
- The protection of personal data, confidentiality and security of processing²³
- The anonymisation of donors and recipients²⁴

- **Facilitating cooperation between Member States and cross-border exchanges**

¹² See Whereas 13 and Article 11 (3) of the Proposal.

¹³ Article 18 of the Proposal

¹⁴ Article 5 of the Proposal.

¹⁵ Article 6 of the Proposal

¹⁶ Article 9 of the Proposal

¹⁷ Article 7 of the Proposal.

¹⁸ Article 4 of the Proposal.

¹⁹ Article 11 of the Proposal.

²⁰ Article 13 of the Proposal.

²¹ Article 14 of the Proposal.

²² Article 15 of the Proposal.

²³ Article 16 of the Proposal.

²⁴ Article 17 of the Proposal.

The proposal takes into account the freedom of movements of citizens and the need to enhance the cross-border exchange of organs within the EU given that it is necessary to have a large donor pool to cover the needs of all the patients on the waiting lists and to match donor and recipient.

In this way, Chapters IV and V contain disposals related to:

- Registers and reports concerning procurement organisations and transplantation centres²⁵
- Exchange of information²⁶
- Exchange of organs with third countries²⁷
- European organ exchange organisations²⁸.

2. Draft of the Committee for Medicinal Products for Human Use (CHMP): “Biomarkers qualification: guidance to applicants”.

On April 24th, 2008, EMEA published a draft of the Committee for Medicinal Products for Human Use (CHMP): “Biomarkers qualification: guidance to applicants”²⁹. It was open to public consultation until June 30th, 2008. The final version post-analysis of the Commentaries is not yet available.

It sets up an EMEA qualification process which addresses innovative drug development tools and methods and “focus on the use of Biomarkers developed by consortia, networks, public/private partnerships, learned societies, pharmaceutical industry for a specific intended use in pharmaceuticals R&D”³⁰.

This scientific pathway leads to two main types of CHMP Advice on innovative methods or drug developments tools:

- An EMEA **Scientific Advice** on future protocols and methods for further development towards qualification is provided. It concerns data which are not matured and results in a confidential document.
- An EMEA and FDA **Qualification Advice** on the acceptability of the proposed biomarker for a specific use. It results in a public document and there is an EU public consultation prior to the Qualification advice.

Moreover, a specialised group, named “**Qualification team**” is appointed by the CHMP on a case by case basis. It is in charge, on behalf of the CHMP, to perform the scientific and technical preparatory work.

The procedure for the **Biomarkers Qualification** is the following³¹:

- Day -30: letter of intent to request a qualification procedure
- Day 0: Appointment of the Coordinator and the Qualification Team
- Day 5-15: Preparatory meeting
- Day 15-90: Evaluation of data and discussion with the Applicants and draft report
- Day 90-120: Scientific Advice Working Party (SAWP) review

²⁵ Article 19 of the Proposal.

²⁶ Article 20 of the Proposal.

²⁷ Article 21 of the Proposal.

²⁸ Article 22 of the Proposal.

²⁹ <http://www.emea.europa.eu/pdfs/human/biomarkers/7289408en.pdf>

³⁰ Scope of the “Biomarkers qualification: guidance to applicants”.

³¹ For more details, see Figure 1 of the draft.

- Day 130: CHMP adoption of **Scientific Advice** and discussion of **Qualification Advice**
- Day 160-220: Public consultation only for **Qualification Advice**
- Day 220: Adoption of the final CHMP **Qualification Advice**

NB: On July 3, 2008, EMEA has made publicly available the “final report on the pilot joint EMEA/FDA VXDS experience on qualification of nephrotoxicity biomarkers”³².

As Riset has focused a large part of its research work on biomarkers for tolerance, this guideline is a paramount importance to follow for future developments and official recognition of the biomarkers identified. Such developments are of relevance for Riset participants and all those who are following the legal and regulatory framework regarding transplantation and its accompanying treatments at EU level.

³² <http://www.emea.europa.eu/pdfs/human/biomarkers/25088508en.pdf>