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THE REGULATORY APPROACH TO *EX SITU* MANIPULATION OF HUMAN ORGANS*

POSITION PAPER OF THE EUROPEAN COMMITTEE ON ORGANS, TISSUES AND CELLS (CD-P-TO)

Adopted by the European Committee on Organs, Tissues and Cells (CD-P-TO) on 8 October 2026

Organ transplantation is a life-saving and life-enhancing intervention for patients with end-stage organ failure, often representing the only therapeutic option and offering substantial improvements in survival, quality of life and social participation. Transplantation can also contribute to the sustainability of healthcare systems, as exemplified by kidney transplantation which has a lower cost than dialysis.

Organ transplantation has expanded across the member states of the Council of Europe, supported by sustained professional and organisational efforts, a strong commitment to ethical principles and by the development of robust quality and safety standards.[1] Recent data published in the Council or Europe *Newsletter Transplant* confirm the growing scale and importance of organ transplantation, evidenced by more than 44,000 organ transplants having been performed in Council of Europe member states in 2024.[2]

Organ transplantation in Europe is grounded in fundamental principles embedded in the ethical acquis of the Council of Europe, including voluntary and unpaid donation and the non-commercialisation of the human body ("*The human body and its parts shall not, as such, give rise to financial gain*")[3,4]. Organ donation is dependent on public trust in donation and transplantation systems and in the legitimacy of organ allocation, which should be based on transparent, objective and duly justified rules according to medical criteria. Therefore, any regulatory development affecting human organs intended for transplantation should preserve, and not weaken, these ethical foundations.

Important scientific and technological innovations have emerged that involve different forms of interventions on human organs after their recovery and prior to their transplantation, notably through the use of perfusion machines. [5,6] These technologies are widely used to reduce ischaemia-reperfusion injury and facilitate organ assessment. *Ex situ* machine perfusion also provides opportunities for increasingly sophisticated interventions, including targeted repair, conditioning and therapeutic or preventive interventions on organs, some of which remain experimental. Such developments offer real hope to patients awaiting transplantation by potentially increasing organ availability and improving graft function and transplant outcomes. At the same time, this rapidly evolving technological landscape requires a reassessment of the regulatory framework governing organ transplantation to ensure that it enables and fosters innovation while safeguarding the ethical principles and core values inherent to the field.

Ex situ interventions may involve the use of medicinal products, medical devices or substances of human origin applied to an organ outside the body with therapeutic or preventive intent. In some cases, such interventions may appear to fall, at least in part, within the medicines framework, particularly when the use of certain medicinal products may

* For the purposes of this document, "*ex situ manipulation of organs*" refers to any processing or intervention performed on organs outside the human body that goes beyond static or dynamic preservation, including but not limited to genetic or enzymatic modifications.

introduce additional biological risks, such as the genetic or enzymatic modification of the organs. However, whether such interventions should also result in the manipulated human organs being classified, in law or in practice, as a medicinal product requires careful consideration, since doing so could lead to it potentially being considered an industrial or commercial good, raising major conceptual, ethical and policy concerns.[7]

In this position paper, the European Committee on Organs, Tissues and Cells (CD-P-TO) examines the risks associated with the direct or indirect application of the medicines regulatory framework to human organs manipulated *ex situ*. It also presents a series of recommendations that can inform a European model that fosters technological innovation in this field, provides a robust, proportionate framework for the evaluation and oversight of *ex situ* organ manipulation, and upholds the ethical principles underpinning transplantation.

Risks associated with classifying manipulated human organs as medicinal products

In this position paper, the European Committee on Organs, Tissues and Cells (CD-P-TO) examines the risks associated with the direct or indirect application of the medicines regulatory framework to human organs manipulated *ex situ*. It also presents a series of recommendations that can inform a European model that fosters technological innovation in this field, provides a robust, proportionate framework for the evaluation and oversight of *ex situ* organ manipulation, and upholds the ethical principles underpinning transplantation.

1. Ethical conflicts

Regulating, whether directly or indirectly, manipulated human organs as medicinal products may blur the fundamental ethical distinction between a donated human organ and a commercial therapeutic product. Human organs are donated on the basis of altruism, solidarity, the prohibition of financial gain and equity in access. If these principles are perceived to be compromised, public trust and willingness to donate may be adversely affected.

The ethical implications are particularly significant in light of the scarcity of human organs for transplantation. Unlike tissues and cells, the availability of human organs for transplantation remains inherently limited as they cannot regenerate in the human body and are present in very limited amounts. This distinction between organs and tissues/cells is critical.

Ex situ interventions on organs rely on a strictly limited and irreplaceable resource. As such interventions become increasingly integrated into standard transplantation practices, they are likely to affect most organs destined for transplantation. Therefore, if they were to systematically trigger regulation of the organs as medicinal products, this would progressively expose the entire pool of transplantable organs to market-oriented regulatory logic, rather than merely creating a limited category of regulated products.

In this scenario, the distinction between a donation and a medical product would be eroded and, by virtue of being subjected to routine *ex situ* interventions, organs could effectively be perceived as commercial products. This would represent a structural shift from a system grounded in altruistic and non-commercial donation towards one in which market considerations, such as pricing, exclusivity and commercial incentives, play an increasing role. In turn, it could affect how organs are allocated, with access to transplantation potentially being influenced not only by medical need but also by economic factors.

Taken together, these considerations raise fundamental questions as to the sustainability of the current ethical framework governing organ donation and transplantation in Europe, where the non-commercial character of the human body and its parts has long been a core principle.

authority and inspection regime, apply concurrently to the same activities and the same products. The period before 2027 is the appropriate moment to resolve this interface.

The CD-P-TO wishes to signal its readiness to engage constructively with the MDCG and the relevant working groups in developing practical guidance that addresses the concerns raised in this paper. We believe that a collaborative

process, drawing on the operational experience of SoHO entities across Europe, would contribute to guidance that is both legally sound and workable in practice.

The CD-P-TO respectfully invites the European Commission and competent authorities to consider revising MDCG 2023-1 to provide greater clarity on the two scenarios identified above, and to recognise that RUO products used and CE-marked devices used beyond their intended purpose in the SoHO context are appropriately governed by the SoHO Regulation, with oversight consolidated under the designated SoHO competent authority. Such a targeted clarification, requiring no amendment to the MDR or the Commission proposal, would improve legal certainty, reduce unnecessary regulatory duplication, and contribute to a proportionate and coherent regulatory framework for SoHO-related activities across Europe.

2. Difficulties in patient access to transplantation

There is a significant risk of inequity in access if manipulated organs become regulated as medicinal products.[8] High development costs, exclusive market authorisations and premium pricing could result in patient access to transplantation being determined less by clinical need and more by financial resources. That scenario would undermine the core values of equity and solidarity that underpin organ transplantation in Europe, leading to unequal access, especially for patients in regions with fewer financial resources or healthcare options. Such a model could disproportionately favour wealthier healthcare systems or patients, thereby deepening disparities in access to life-saving and life-enhancing treatments. This risk may be exacerbated if *ex situ* interventions become standard practice, such that access to transplantation itself becomes increasingly dependent on access to these technologies.

3. Risks to the sustainability of healthcare systems

A model that channels manipulated organs into the medicinal product framework could substantially increase the costs of transplantation. That outcome could arise not only due to requirements relating to the manufacture of medicines and the regulatory fees applied under that framework, but to costs associated with additional layers of authorisation, licensing and market pricing. Those additional costs are poorly aligned with the current system of donation and transplantation services, which are designed as public-interest healthcare activities. If organ manipulation *ex situ* becomes standard for selected organs or patient groups, the costs could place severe pressure on transplant budgets, potentially compromising the sustainability of transplantation programmes in public healthcare systems across Europe. Diverting funds from other areas of healthcare to compensate for increased organ transplantation costs could undermine the overall effectiveness of public health initiatives.

A European model for regulating *ex situ* manipulation of human organs

The CD-P-TO supports a regulatory approach that ensures the legal and ethical status of human organs for transplantation remains unchanged, even when they undergo *ex situ* manipulation. Consequently, each organ destined for transplantation should retain its status as a human organ, irrespective of any manipulations it undergoes.

Rather than focusing on the organs themselves, the emphasis of the regulatory framework should be on the *ex situ* procedures and technologies involved, including the use of medicinal products to treat the organs. Thus, a distinction should be drawn between deployment of such products and technologies, which should remain subject to the applicable regulatory frameworks, and authorisation of organ processing itself, which should be subject to requirements proportionate to the degree of intervention and the risks introduced by the manipulation process.

The use of such products and technologies should not alter the legal and ethical status of the donated organ itself. Consequently, medicinal products that are specifically developed for organ manipulation and use of which is inextricably linked to organs themselves should be manufactured in accordance with legislation governing medicinal products and remain subject to the applicable requirements relating to quality, safety and efficacy under the supervision of the relevant national authorities. However, their use should be subject to **an authorisation for organ manipulation rather than a marketing authorisation**, as otherwise organs could indirectly become subject to market-based mechanisms. This approach would allow technological innovation, guarantee the quality, efficacy and safety of manipulated human

organs in accordance with scientific standards, while also respecting the ethical framework governing organ donation and transplantation. It would also preserve the distinction between prohibited financial gain derived from the human body and remuneration for legitimate transplantation-related services, including the recovery of justified costs, and investment in research, development and innovation.[9]

The CD-P-TO proposes the following measures for member states of the Council of Europe and relevant European regulatory bodies:

1. **Integration of ex situ manipulated organs into regular organ donation programmes** – The donation of organs that might be subject to *ex situ* manipulations should be formalised within official, publicly managed programmes overseen by donor co-ordinators or organ procurement organisations. The evaluation and selection of donors must be based on scientific and ethical criteria established and approved by the authorities responsible for organ donation and transplantation.

2. **Distinction between ownership of organs and of technologies for organ manipulation** – There must be a clear distinction between ownership of an organ itself and ownership of the technologies used to manipulate it. As a donated substance of human origin, each human organ must remain a non-commercial public resource and must not become subject to proprietary ownership, whereas the technologies applied to it (e.g. perfusion systems, medicinal products) can be subject to intellectual property rules. Companies developing or providing such technologies should be viewed as service providers that deliver technical interventions on the organs without acquiring any proprietary rights over those organs or altering their non-commercial status.

3. **Distinction between assessment and authorisation** – The process of assessment (where pharmaceutical standards may apply) should be differentiated from that of authorisation. A robust system should be developed to assess the quality, safety and efficacy of an organ manipulated *ex situ* prior to authorising its clinical use, with a view to avoiding serious risks for patients, healthcare professionals and the environment. The type of assessment should be proportionate to the nature and level of risk introduced by the intervention. Although both assessment and authorisation necessitate existing collaboration between medicine and transplant authorities, the authorisation process should remain under the purview of transplant authorities, thereby ensuring that clinical needs and ethical considerations are central to decision-making processes.

4. **Specific authorisation for organ processing** – Medicinal products specifically developed for organ processing and whose use is inextricably linked to human organs should be subject to an authorisation for organ processing rather than a marketing authorisation; otherwise, processed human organs could indirectly become subject to market-based mechanisms. This process should operate without prejudice to the applicable requirements of pharmaceutical legislation relating to manufacturing authorisations, good manufacturing practice, quality, safety and regulatory oversight.

5. **Incorporation of organs manipulated *ex situ* into the organ allocation system** – Manipulated organs should be incorporated into the existing organ allocation system, where eligible patients are registered on official waiting lists, with organ distribution guided solely by clinical criteria and medical need, rather than market dynamics or financial considerations. Providers of technologies, devices, substances or services used for *ex situ* manipulation should have no role in recipient selection, organ allocation, prioritisation or clinical decision-making. Preserving this model is essential to ensure equitable access to transplantation.

6. **Safeguarding the transplant framework and non-commercialisation** – Regardless of any *ex situ* interventions or indications, human organs must remain regulated under the transplantation framework. They should not be commodified and treated as commercial products. This is essential to maintain the ethical integrity of the current organ donation and transplantation systems.

The CD-P-TO emphasises that regulatory policies in this field must foster responsible innovation to ensure that technological advances, such as *ex situ* manipulation of organs, serve the ultimate goal of increasing access to transplantation and improving patient outcomes. However, these innovations must not result in donated human organs becoming market commodities. Instead, regulatory frameworks should focus on supporting progress in biomedical innovations for human organs.

References

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