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RISKS TO SAFETY AND QUALITY IN DONOR SCREENING AND SOHO PREPARATIONS DUE TO POOR IMPLEMENTATION OF THE MDR AND IVDR AND THE RESULTING SHORTAGE OF ESSENTIAL CE-MARKED DEVICES

POSITION PAPER OF THE EUROPEAN COMMITTEE ON ORGAN TRANSPLANTATION OF THE COUNCIL OF EUROPE (CD-P-TO)

Adopted by the European Committee on Organ Transplantation (CD-P-TO) on 10 October 2025 during its 34th plenary meeting in Kalamata, Greece.

- Regulation (EU) 2017/745 (MDR) and Regulation (EU) 2017/746 (IVDR), which apply to medical devices (MDs) and *in vitro* diagnostic medical devices (IVDs) placed on the EU market, were introduced with the objective of establishing a robust and transparent regulatory framework.
- While laudable in intent, implementation has generated unintended consequences for the Substances of Human Origin (SoHO) sector: the time, complexity and cost of conformity assessment under the MDR and IVDR have adversely affected the ability of manufacturers to place niche MDs and IVDs on the market for SoHO applications.
- The aim of this position paper is to highlight the concerns of the SoHO field about the challenges, consequences and potential impact on sufficiency due to these regulations.

Regulatory objectives versus field realities

The Council of Europe Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin[1] (ETS No. 186) lays down in Article 6 the obligation for all professionals involved in organ or tissue transplantation to take all reasonable measures to minimise the risks of transmission of any disease to the recipient and to avoid any action which might affect the suitability of an organ, tissue or cell for implantation. To achieve this, donors must be screened for transmissible infections, which is done,

1. https://rm.coe.int/1680081562.

among other means, through laboratory testing using IVDs. In parallel, SoHO entities and establishments must ensure the overall quality and safety of the collection, processing, storage and distribution of SoHO. MDs and IVDs play a critical role in this process, as their availability, reliability and performance directly impact the application of SoHO preparations. The recently adopted SoHO Regulation (EU) 2024/1938[2] plays a central role in harmonising requirements across EU member states, replacing a fragmented framework with a single, comprehensive set of rules. As EU regulatory decisions, particularly the SoHO Regulation, affect standards beyond EU borders and assign the European Directorate for the Quality of Medicines and HealthCare (EDQM) responsibilities for developing technical standards to support its implementation, it is appropriate for the Council of Europe to issue a position statement.

The MDR and IVDR were introduced in 2017 with the ambition of establishing a robust, transparent, predictable and sustainable regulatory framework for MDs and IVDs, ensuring a high level of safety and health while supporting innovation. However, several years into implementation, these regulations have not fully delivered on their objectives.

While data from notified bodies in May 2025 indicate progress in terms of applications submitted and certificates issued,[3] significant concerns remain. According to the MedTech Europe IVDR & MDR survey,[4] 26% of IVD manufacturers and 29% of MD manufacturers in orphan and niche markets plan to transition fewer than 5% of their devices to compliance under the new regulations. Market contraction is already evident, with devices being discontinued and further withdrawals likely across categories such as infectious disease screening, immunochemistry, histology, cytology and genetic testing, as well as haematology.

This trend is reflected in daily practice, where SoHO entities and establishments frequently face the withdrawal of critical devices such as IVD tests, reagents, consumables and instruments. These devices are vital for safe and effective donor screening, and the collection, processing, storage, distribution and application of SoHO preparations. In the absence of CE-marked alternatives, SoHO entities and establishments are compelled to revert to manual or legacy methods that do not always meet current safety and quality standards, increasing the risk of compromised safety, quality and effectiveness of SoHO preparations and threatening service continuity and patient access.

Key issues arising from MD and IVD regulations affecting the SoHO field

1. IVDs are paramount to ensure the safety of SoHO. IVDs are used to screen SoHO donors for markers of transmissible infections. These tests typically fall under class D in the EU IVDR and are further governed by relevant common specifications (CS). European Union Reference Laboratories (EURLs) verify, through laboratory testing, the performance claimed by manufacturers for applicable class D devices and their compliance with the CS. The results of this mandatory, manufacturer-independent pre-market verification inform notified bodies' decisions on market authorisation. While these requirements are critical for public health, they impose significant financial burdens and can extend time to market.

2. The challenge is particularly acute for SoHO obtained from deceased donors. There is a lack of deceased-donor test panels at EURL level, a limited number of assays validated for post-mortem blood samples, and persistent

2. Regulation (EU) 2024/1938 on standards of quality and safety for substances of human origin intended for human application. Available at https://eur-lex.europa.eu/eli/reg/2024/1938/oj/eng.

3. European Commission (2025). Study supporting the monitoring of the availability of medical devices on the EU market. Survey results of the 12th NB survey (MDR/IVDR) with data status 31 October 2024. Data included in https://health.ec.europa.eu/document/download/59b9d90e-be42-4895-9f6f-bec35138bb0a_en?filename=md_nb_survey_certifications_applications_en.pdf.

4. MedTech Europe (2024). MedTech Europe IVDR & MDR Survey Results 2024. Available at https://www.medtecheurope.org/wp-content/uploads/2025/01/mte-ivdr-mdr-survey-report-highlights-final.pdf.

difficulty in defining evidence-based time limits for *post-mortem* sampling.[5] Currently, the market for donor screening assays is small and fragmented: only a few manufacturers provide tests for deceased donors, and no single manufacturer covers all required infection markers (e.g. HBV, HCV, HIV, HTLV, *Treponema pallidum*, WNV, Zika virus, CMV) and other critical assays (e.g. HLA typing, chimerism analysis). Emerging infectious threats, such as SARS-CoV-2, further complicate this landscape. Moreover, there is no clarity on which assays will remain available in Europe, creating uncertainty for both testing and contingency planning. These factors risk constraining the safe supply of SoHO for human application and may ultimately reduce donation volumes.

3. Today, most SoHO establishments work together with medical laboratories located in health institutions or blood establishments that typically operate one or two chemistry or immunoassay platforms. Given the limited availability of CE-marked assays on local platforms to screen for transmissible infections in samples from living and deceased donors, laboratories develop in-house IVDs (LDTs). Validation of these LDTs is not always aligned with CS, and clear, appropriate guidance remains unavailable, leaving laboratories without the necessary support and hindering innovative solutions for niche applications, rare diseases and rapid responses to health crises.[6]

4. SoHO is by nature a niche domain, relying heavily on highly specialised MDs that are not produced at large scale. In recent years, SoHO entities and establishments, not only within EU member states but also in Council of Europe member states outside the EU, have increasingly reported the disappearance of essential MD, such as cell separators, sterile containers for the preservation of SoHO preparations (e.g. bone marrow collection bags and cord blood collection bags) and transport, preservation, processing and transplantation media, without any indication of suitable replacements entering the market. The withdrawal of such devices is often linked to high regulatory burden and cost of compliance under the MDR, which disproportionately affect low-volume, niche devices. National Competent Authorities have acknowledged these risks.[7]

5. Due to the widespread withdrawal of devices from the market, many SoHO entities and establishments are left with no choice but to use existing CE-marked devices off-label, rely on research-use-only (RUO) devices, or assemble their own in-house devices. Article 5(5) of the MDR and IVDR allows health institutions to manufacture and use devices internally when no equivalent is available on the market. However, requirements outlined in EU Medical Device Coordination Group (MDCG) documents 2023-1[8] and 2025-5[9] are demanding relative to the resources of most health institutions (e.g. alignment with general safety and performance requirements, justification of unmet needs, quality management, extensive documentation and public declarations). RUO and off-label uses are not explicitly addressed in Article 5(5) and are typically governed by a combination of EU and MDCG provisions, resulting in legal uncertainty. The lack of market alternatives combined with regulatory rigidity places an unsustainable burden on SoHO entities and may compromise continuity of services.

6. Innovation is essential for the advancement of therapies involving SoHO. However, the current EU regulatory environment under the MDR and IVDR has created significant disincentives for innovation within SoHO

5. EDQM (2022) Understanding *post-mortem* blood testing practices for tissue donation. Available at https://freepub.edqm.eu/publications/PUBSD-173/detail.

6. Biomedical Alliance in Europe (2022). Implementation of the new EU regulation for In vitro Diagnostic Medical Devices: a ticking time bomb for the diagnostic sector? Available at https://www.biomedeurope.org/resource/implementation-of-the-ivdr-a-ticking-time-bomb-for-the-diagnostic-sector/.

7. CAMD (2024). Medical device competent authority statement on the status of the EU regulatory system. Available at https://www.camd-europe.eu/wp-content/uploads/2024/07/2024_07_MDCA_Statement-final.pdf.

8. MDCG 2023-1 (2023). Guidance on the health institution exemption under Article 5(5) of Regulation (EU) 2017/745 and Regulation (EU) 2017/746. Available at https://health.ec.europa.eu/system/files/2023-01/mdcg_2023-1_en.pdf.

9. MDCG 2025-5 (2025). Questions & Answers regarding performance studies of *in vitro* diagnostic medical devices under regulation (EU) 2017/746. Available at https://health.ec.europa.eu/latest-updates/mdcg-2025-5-questions-answers-regarding-performance-studies-vitro-diagnostic-medical-devices-under-2025-06-18_en.

establishments, healthcare institutions and academic research settings, sectors that are traditionally at the forefront of developing novel solutions for niche applications such as SoHO therapies. The heightened regulatory complexity, increased costs and prolonged approval timelines have led to a marked decline in enthusiasm among clinicians and researchers to engage in translational research. Ethical approval processes for clinical investigations and performance studies involving MDs or IVDs have become so complex under the MDR/IVDR framework[8, 10] that they often exceed the duration of the research itself, discouraging early-stage innovation altogether. The situation is further complicated by the unclear expectations regarding clinical evidence. This lack of transparency and harmonisation significantly increases the risk and cost of innovation.

Recommendations

The CD-P-TO believes that a further postponement of the implementation of the EU IVDR and MDR will not prevent many CE-marked IVDs and MDs from disappearing from the niche market. SoHO entities and establishments (health institutions) will be obliged to fill the gap, even though they lack the necessary resources. Therefore, the CD-P-TO proposes the following recommendations:

1. The European Commission should consider a dedicated, proportionate regulatory pathway for MDs and IVDs used in niche fields such as SoHO. This could include simplified conformity assessment procedures, reduced documentation requirements and targeted exemptions for low-risk, low-volume devices that are critical for public health but not commercially viable under current rules.

2. The European Commission and national Competent Authorities should explicitly limit Article 5(5.g) requirements to the highest-risk categories of in-house manufactured class III MDs and class D IVDs, as originally intended by the regulations. In practice, several member states have extended these requirements to lower-risk categories, resulting in a disproportionate regulatory burden, particularly for SoHO establishments and health institutions operating in niche areas such as SoHO.

3. The European Commission and the MDCG should revise MDCG guidance documents applicable for in-house devices extensively in close co-operation with the stakeholders representing health institutions. The requirements outlined in MDCG 2023-1 and 2025-5 should better reflect the operational reality of health institutions. Specifically, the guidance should:

    - allow for tiered compliance based on low-volume production, number of patients treated within the health institutions and risk assessment;
    - introduce a simplified and proportionate pathway for the ethical approval of clinical investigation and performance studies involving in-house MDs and IVDs developed within academic and health institutions;
    - provide clearer criteria for the "no equivalent device on the market" condition;
    - recognise the public health value of in-house innovation in the absence of commercial equivalents.

4. The European Commission and the MDCG should urgently provide clear, harmonised guidance on the use of off-label and RUO devices in the context of in-house manufacturing. Neither off-label use nor the use of RUO devices is explicitly covered by Article 5(5) of the MDR or IVDR, which applies only to devices that are manufactured and used in-house by health institutions. In the case of off-label or RUO use, there is no manufacturing activity as defined in the regulations. As a result, these practices fall into a regulatory grey zone, leaving institutions exposed to legal uncertainty and potential non-compliance.

10. MDCG 2021-6 rev. 1 (2023). Regulation (EU) 2017/745 – Questions & Answers regarding clinical investigation. Available at https://health.ec.europa.eu/system/files/2023-12/mdcg_2021-6_en.pdf.

5. In collaboration with National Competent Authorities and stakeholders, the European Commission or a relevant designated expert body could establish and maintain a dynamic list of essential MDs and IVDs used in SoHO applications. Devices on this list could benefit from accelerated review, extended transition periods or conditional exemptions to prevent supply disruptions.

6. The European Commission, in collaboration with the EDQM, and National Competent Authorities should develop a harmonised guidance document on emergency preparedness and response for MDs and IVDs used in SoHO-related and other niche applications.

7. To safeguard the reliability and quality of in-house niche IVD testing, especially in response to the emerging infectious threats, the EDQM should expand its existing Proficiency Testing Scheme (PTS). This expansion should include critical niche applications such as deceased-donor blood screening and diagnostics for rare or tropical diseases, where current PTS coverage are limited or absent. Strengthening these programmes would enhance the EU's preparedness and resilience while ensuring high diagnostic standards in areas that are essential but lack commercial incentives.