



# **Review of the EU medical device regulations – Analysis and recommendations from the Biomedical Alliance in Europe**

***Implementing regulatory science to protect the public health***

**March 2025**



## Executive summary

- Reform of the EU medical device directives was needed, but both the MDR and IVDR have had unintended consequences.
- Issues that concern healthcare professionals include disappearing devices, the absence of special regulatory pathways, insufficient central capacity for managing the EU regulatory system, limited engagement of clinical experts, and insufficient transparency of clinical evidence.
- Summary recommendations from the BioMed Alliance have been published.<sup>1,2</sup>
- This report provides evidence and insights from the experience of healthcare professionals, of the consequences and impact of the EU regulations for medical devices and in vitro diagnostic medical devices. Detailed recommendations are made to address both shared concerns and those particular to each sector.
- The major need is development of a new coordinating management structure. The BioMedical Alliance recommends that a medical devices division should be established within an expanded European Medicines Agency.
- Investment must support the establishment of EU networks of specialist regulators with clinical experience, supported by scientific and medical experts, with the shared capacity to advise and interact with developers, trialists, and manufacturers.
- Transparency, flexibility, and predictability are key.
- These need freely accessible specific standards and guidance for each major device type, within an overarching framework designed on scientific principles.
- Progress towards international regulatory convergence should be accelerated.

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<sup>1</sup> BioMed Alliance position on the MDR review. January 2025. <https://www.biomedeuropa.org/wp-content/uploads/2025/01/MDR-position-summary-jan-25-2.pdf>

<sup>2</sup> BioMed Alliance position on the IVDR review. January 2025. <https://www.biomedeuropa.org/wp-content/uploads/2025/01/IVDR-summary-document-Jan-25-1.pdf>



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## ***About the BioMed Alliance***

The Biomedical Alliance in Europe (BioMed Alliance) is an initiative of 35 leading European medical specialist societies representing researchers and health professionals.

As a registered stakeholder organisation, its expert representatives have advised policy makers and regulators on the implementation of the EU Medical Devices Regulation and the In Vitro Diagnostic Medical Devices Regulation, at the Medical Devices Coordination Group. through the work of its Medical Devices and In Vitro Diagnostics Task Forces, and by active participation in a number of working groups.

The BioMed Alliance was a partner in the EU Horizon 2020 CORE-MD Project [Coordinating Research and Evidence for Medical Devices] from 2021 – 2024, which reviewed methods for evaluating high-risk medical devices in order to translate expert evidence into advice for EU regulators and to recommend an appropriate balance between innovation, safety, and clinical effectiveness.

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## Glossary

CE	Conformité Européenne (European Conformity) (mark)
CEN	European Committee for Standardization (Comité Européen de Normalisation)
CENELEC	European Electrotechnical Committee for Standardization (Comité Européen de Normalisation en Électronique et en Électrotechnique)
CLIA	Clinical Laboratory Improvement Amendments (in USA)
CORE-MD	Coordinating Research and Development for Medical Devices
DG SANTE	Directorate General for Health and Food Safety (of the European Commission)
DNA	Deoxyribonucleic acid
EASD	European Association for the Study of Diabetes
EAU	European Association of Urology
ECDC	European Center for Disease Prevention and Control
EEA	European Economic Area
EFLM	European Federation for Clinical Chemistry and Laboratory Medicine
EFORT	European Federation of National Societies of Orthopaedics and Traumatology
EHA	European Hematology Association
EMA	European Medicines Agency
EMEA	European Medicines Evaluation Agency
EQA	External Quality Assessment (or may be, External Quality Assurance)
EQALM	The European Organisation for External Quality Assurance Providers in Laboratory Medicine
ERN	European Reference Networks
ESC	European Society of Cardiology
ESHG	European Society for Human Genetics
ESPGHAN	European Society for Paediatric Gastroenterology Hepatology and Nutrition
EU	European Union
EUDAMED	European Database on Medical Devices



## Biomedical Alliance in Europe

FDA	Food and Drug Administration (of the USA)
GDPR	General Data Protection Regulation
HTA	Health Technology Assessment
IEC	International Electrotechnical Commission
IFCC	International Federation for Clinical Chemistry and Laboratory Medicine
IH-IVD	In-house developed IVD test (also known as LDT)
IMDRF	International Medical Device Regulators Forum
ISO	International Organization for Standardization
IVD	In vitro diagnostic (medical devices)
IVDD	In vitro diagnostic Medical Device Directive
IVDR	In vitro diagnostic Medical Device Regulation (EU 2017/746)
LDT	Laboratory-Developed Test(s)
MAUDE	Manufacturer and User Facility Device Experience
MD	Medical device(s)
MDCG	Medical Device Coordination Group
MDR	Medical Device Regulation (EU 2017/745)
MDSAP	Medical Device Single Audit Program (of IMDRF)
MRA	Mutual Recognition Agreement
MRD	Minimal residual disease
NANDO	New Approach Notified and Designated Organisations
NBCG-MED	Notified Body Coordination Group
NBOG	Notified Body Operations Group
POCT	Point of care testing
PT	Proficiency testing
RCT	Randomised controlled trial
RfB	Referenzinstitut für Bioanalytik (in Germany)
RUO	Research use only
SMEs	Small and medium-sized enterprises
SSCP	Summary of Safety and Clinical Performance
Team-NB	The European Association of Medical devices Notified Bodies
WHO	World Health Organization



## 1. Introduction

The European Commission is evaluating the implementation of the EU Medical Devices Regulation (MDR)<sup>3</sup> and the In Vitro Diagnostic Medical Devices Regulation (IVDR)<sup>4</sup>, in order to prepare a report for submission to the European Parliament as required by Article 121 of the MDR.

Clinicians in Europe were among those who advocated for reform of the previous EU medical device directives<sup>5</sup> which was initiated by a public consultation in 2009. The laws were passed in 2017 but postponements mean that their complete operation is not envisaged until 2028 (for the MDR) and 2029 (for the IVDR).

Remarkably, this 20-year time-course from conception to delivery means that the EU laws for medical devices are already being reviewed before they have been fully implemented. Key provisions in the Regulations, that were needed to strengthen requirements for clinical evidence about high-risk devices, were endorsed by European medical associations and then supported by their active participation as stakeholders in EU regulatory structures. Despite original good intentions for the legislation, it has become increasingly clear that unintended consequences of the MDR and IVDR threaten the continued availability of essential medical devices and diagnostic tests.

Since welcoming the initial objectives of the Regulations, the medical community represented within the BioMed Alliance has raised awareness of problems related to its delayed full implementation and to the initial limited capacity of Notified Bodies. The BioMed Alliance has presented the experiences of healthcare professionals at meetings of the Medical Device Coordination Group and its Working Groups, in discussions with Commission officials and policy makers, and in statements which are available on its [website](#).

Current concerns include the continued absence of the clinical module of EUDAMED, the high costs of certification, the lack of a dedicated pathway for the evaluation of paediatric and orphan devices, the lack of a single process for an EU-wide derogation, the perception of research and development leaving Europe, limited transparency of

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<sup>3</sup> European Parliament. Regulation (EU) 2017/ 745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/ 83/ EC, Regulation (EC) No 178/ 2002 and Regulation (EC) No 1223/ 2009 and repealing Council Directives 90/ 385/ EEC. <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745>

<sup>4</sup> European Parliament. Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU. <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0746>

<sup>5</sup> Fraser AG, Daubert JC, Van de Werf F, et al; participants. Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform. Report of a policy conference of the European Society of Cardiology. *Eur Heart J*. 2011;32:1673–86. <https://academic.oup.com/eurheartj/article/32/13/1673/507544?login=false>



evidence, limited predictability of conformity assessment decisions, restrictive requirements for In-House IVDs, issues with the recertification of legacy devices, and lack of flexibility for conditional approvals of innovative or ‘breakthrough’ devices for unmet clinical needs. The human resources that were anticipated to be needed within the European Commission to manage the regulatory framework<sup>6</sup> have never been provided.

**Review of the legislation now provides an opportunity to get things right** – but any changes should be planned from a careful analysis of shortcomings, discussions with stakeholders, and an agreement on the essential principles that should underpin our European regulatory system, rather than focussing on expedient short-term fixes for operational problems. Some recommendations proposed by medical professional associations were not enacted but remain relevant. The principle enshrined in primary EU treaties, of common actions to protect the public health, should remain paramount.

## 2. Objectives

The aims of this report from the BioMed Alliance are:

To identify and analyse problems and gaps in the EU regulatory system, from the perspective of practising clinicians and diagnostic specialists, and to present supporting evidence from case studies and scientific investigations;

To define issues common to both Regulations (the MDR and the IVDR), and issues specific to each, that are relevant to their successful implementation;

To propose basic principles that should underpin any regulatory system for medical devices; and

To propose practical solutions that should be introduced to ensure that the MDR and IVDR meet the needs of the public, patients, and healthcare professionals.

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<sup>6</sup> European Commission. Commission Staff Working Document. Impact assessment on the revision of the regulatory framework for medical devices. Brussels, 26.09.2012. SWD/2012/0273 final. <https://eur-lex.europa.eu/legal-content/EN/TXT/DOC/?uri=CELEX:52012SC0273>





### 3. Preparation of this report

#### **BioMed Alliance**

This report has been written by officers and members of the Regulatory Affairs Committee of the BioMed Alliance, its Task Force for Medical Devices, and its Task Force for In Vitro Diagnostic Medical Devices. It has been reviewed, edited, and approved by the Board of the BioMed Alliance.

Member associations of the BioMed Alliance were invited to contribute and comment, and these recommendations were edited to reflect the consensus view.

#### **Supportive evidence**

Members of the BioMed Alliance have brought specific problems arising from the implementation of the medical device regulations to the attention of its Board, Regulatory Affairs Committee, and permanent staff. Details of particular issues that were raised by the individuals concerned, have been included in this report as supporting evidence for particular reforms. Relevant publications in the scientific literature have been summarised and/or referenced.

#### **CORE–MD Project**

The CORE–MD project (Coordinating Research and Evidence for Medical Devices) was funded by the EU Horizon 2020 programme as a Coordination and Support Action (grant 945260) with the primary objective to develop methodological approaches for the improved clinical investigation and evaluation of high-risk medical devices.<sup>7</sup> The insights and key outputs from CORE–MD (conducted from April 2021 to March 2024) have informed recommendations in this document. The deliverables from the project – the final summary report <sup>8</sup>, and individual reports and publications – can be accessed at [[www.core-md.eu](http://www.core-md.eu)].

#### **Relevant publications from member associations of the BioMed Alliance**

##### *Cardiovascular devices - European Society of Cardiology (ESC)*

The ESC organises occasional meetings of its leadership with invited experts and with senior employees of European pharmaceutical and medical technology companies, to discuss topics of common interest. Within the last two years, two meetings have been held to review innovation and regulation relating to medical

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<sup>7</sup> Fraser AG, Nelissen RGHH, Kjærsgaard-Andersen P, Szymański P, Melvin T, Piscoi P; CORE-MD Investigators. Improved clinical investigation and evaluation of high-risk medical devices: the rationale and objectives of CORE-MD (Coordinating Research and Evidence for Medical Devices). *Eur Heart J Qual Care Clin Outcomes*. 2022;8:249–258.

<sup>8</sup> CORE-MD Investigators. Regulatory science for high-risk medical devices in the EU. (2024) [https://www.core-md.eu/wp-content/uploads/2024/03/Booklet-final-conference-001\\_website-version.pdf](https://www.core-md.eu/wp-content/uploads/2024/03/Booklet-final-conference-001_website-version.pdf)



devices; their conclusions are published.<sup>9,10</sup>

### Orthopaedic devices – the European Federation of National Societies of Orthopaedics and Traumatology (EFORT)

EFORT conducted an 'Implant & Patient Safety Initiative' in 2020, from which they published detailed recommendations for the investigation and regulatory approval of new implantable orthopaedic devices.<sup>11</sup> It includes advice on the criteria for claiming equivalence to implants that have already been approved. A detailed account of their methodology for reaching consensus is also available.<sup>12</sup>

### The European Association of Urology (EAU)

The EAU published a commentary that summarised their concerns.<sup>13</sup>

### Paediatric gastroenterology - The European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN)

ESPGHAN conducted a survey on the availability of medical devices for paediatric patients, and published their results in an invited commentary in 2023.<sup>14</sup>

### The European Association for the Study of Diabetes (EASD)

The EASD published a comprehensive statement concerning automated delivery

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<sup>9</sup> Windecker S, Gilard M, Achenbach S, et al. Device innovation in cardiovascular medicine: a report from the European Society of Cardiology Cardiovascular Round Table. *Eur Heart J.* 2024;45:1104–1115.  
<https://academic.oup.com/eurheartj/article/45/13/1104/7609443?login=false>

<sup>10</sup> Windecker S, Fraser AG, Szymanski P, et al. Priorities for medical device regulatory approval: a report from the European Society of Cardiology Cardiovascular Round Table. *Eur Heart J.* 2025 Feb 20:ehaf069.  
<https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehaf069/8026625?login=false>

<sup>11</sup> Overgaard S, Grupp TM, Nelissen RG, et al. Introduction of innovations in joint arthroplasty: recommendations from the 'EFORT implant and patient safety initiative'. *EFORT Open Rev.* 2023;8:509-521.  
<https://pmc.ncbi.nlm.nih.gov/articles/PMC10321045/pdf/EOR-23-0072.pdf>

<sup>12</sup> Grupp TM, Rusch S, Massin P, et al. 1st EFORT European Consensus "Medical & scientific research requirements for the clinical introduction of artificial joint arthroplasty devices": background, delphi methodology & consensus process. *EFORT Open Rev.* 2023;8:499-508.  
<https://eor.bioscientifica.com/view/journals/eor/8/7/EOR-23-0054.xml>

<sup>13</sup> Albisinni S, Rassweiler J, van Poppel H. The future of medical devices in Europe is at stake: concerns over the implementation of the Medical Devices Regulation 2017/745. *Eur Urol.* 2023;83:191-192.  
<https://www.sciencedirect.com/science/article/abs/pii/S0302283822028640?via%3Dihub>

<sup>14</sup> Baumann U, Bronsky J, Dolinšek J, Fewtrell M, Indolfi G, Kolaček S. Impact of new legislation on the availability of paediatric medical devices in the European Union with an emphasis on paediatric gastroenterology, hepatology and nutrition. *JPGN Rep.* 2023;5:2-4.  
<https://onlinelibrary.wiley.com/doi/epdf/10.1002/jpr3.12023>



systems for insulin, that includes recommendations for regulators.<sup>15</sup>

### *The European Federation for Clinical Chemistry and Laboratory Medicine (EFLM)*

The European Regulatory Affairs task force of EFLM has published position papers on the implementation of the IVDR, with specific diagnostic use cases.<sup>16</sup>

A second report demonstrated the utility of applying norms from ISO15189 for the accreditation of processes for quality assurance, that are used to monitor in-house IVD tests<sup>17</sup> – an effective option that seems not to have been considered by the EU regulatory system.

### *The European Hematology Association (EHA)*

The EHA reported on the implications of the IVDR<sup>18</sup>, and then jointly with the European Society for Human Genetics (ESHG) and EFLM it published a survey of practice in European laboratories relating to In-House IVDs (Laboratory-Developed Tests or LDTs).<sup>19</sup>

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<sup>15</sup> Sherr JL, Heinemann L, Fleming GA, et al. Automated insulin delivery: benefits, challenges, and recommendations. A Consensus Report of the Joint Diabetes Technology Working Group of the European Association for the Study of Diabetes and the American Diabetes Association. *Diabetologia*. 2023;66:3-22. <https://link.springer.com/article/10.1007/s00125-022-05744-z>

<sup>16</sup> Cobbaert C, Capoluongo ED, Vanstapel FJLA, et al. Implementation of the new EU IVD regulation - urgent initiatives are needed to avert impending crisis. *Clin Chem Lab Med*. 2022;60:33-43. <https://www.degruyter.com/document/doi/10.1515/cclm-2021-0975/html>

<sup>17</sup> Vanstapel FJLA, Orth M, Streichert T, et al. ISO 15189 is a sufficient instrument to guarantee high-quality manufacture of laboratory developed tests for in-house-use conform requirements of the European In-Vitro-Diagnostics Regulation. *Clin Chem Lab Med*. 2023;61:608-626. <https://www.degruyter.com/document/doi/10.1515/cclm-2023-0045/html>

<sup>18</sup> Lubbers BR, Schilhabel A, Cobbaert CM, et al The New EU Regulation on In Vitro Diagnostic Medical Devices: Implications and Preparatory Actions for Diagnostic Laboratories. *Hemasphere*. 2021;5:e568. [https://journals.lww.com/hemasphere/fulltext/2021/05000/the\\_new\\_eu\\_regulation\\_on\\_in\\_vitro\\_diagnostic\\_2.aspx](https://journals.lww.com/hemasphere/fulltext/2021/05000/the_new_eu_regulation_on_in_vitro_diagnostic_2.aspx)

<sup>19</sup> Dombink I., Lubbers BR, Simulescu, L., et al. (2022). Critical Implications of IVDR for Innovation in Diagnostics: Input From the BioMed Alliance Diagnostics Task Force. *HemaSphere*, 6(6), e724. <https://doi.org/10.1097/HS9.0000000000000724>



## 4. General requirements for a regulatory framework

The evolution of the EU framework for regulating medical devices and *in vitro* diagnostic medical devices should aspire and adhere to certain basic principles and essential characteristics, to ensure that it is evidence-based and fair, and that it supports innovation. Any regulatory system should be centred on the needs of patients. It should implement proportionate, predictable, reproducible, and evidence-based rules that are applicable across the life-cycle evaluation of devices. All those involved in developing, approving and using medical devices, from innovators and regulators to physicians, should adopt ethical practices appropriate to their roles.<sup>20</sup>

**An ideal regulatory system should be:**



### **Transparent –**

All clinical evidence should be publicly shared and easily accessible.<sup>21</sup> This is essential to build trust both in the system and in the use of individual devices.



### **Evidence-based –**

The impact of regulatory requirements on the safety, performance and effectiveness of devices that are approved for clinical use, should be evaluated to determine if the rules and procedures are fit for purpose. Methodologies and principles from ‘regulatory science’ should be applied to determine which regulatory policies are best able to ensure that patients have access to safe and effective devices.



### **Proportionate to risk –**

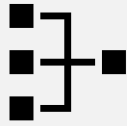
High standards of safety and clinical effectiveness should be assured before new high-risk devices can enter an existing market, but the level of evaluation should be proportionate to the potential risk of a device for patients’ health. Excessively bureaucratic processes to evaluate devices with low risks should be avoided, as they would be disproportionate.

<sup>20</sup> CORE–MD Consortium. An ethics charter for innovation in medical devices. (2024) At [www.core-md.eu](http://www.core-md.eu)

<sup>21</sup> Fraser AG, Butchart EG, Szymański P, et al. The need for transparency of clinical evidence for medical devices in Europe. *Lancet*. 2018;392:521–530. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(18\)31270-4/abstract](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31270-4/abstract)

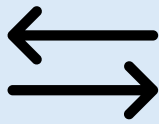


### **Consistent –**



There should be consistency between reviews of different devices within the same type or used for the same clinical indication – so that similar clinical evidence is expected and similar criteria are applied. Predictability requires harmonisation of standards and procedures with the availability of device-specific common technical specifications. Otherwise, all reviews of any particular device type would need to be centralised within a single institution.

### **Flexible –**



Review and approval processes must be responsive to unmet needs e.g. for innovative products for serious diseases or conditions. They must also account for new technological developments and the changing needs of our health systems.

### **Fair –**



Regulations should ensure that particular groups of patients are not disadvantaged, such as people with rare diseases, or infants and children. When no alternatives are available, then it should be possible with expert advice to approve devices for orphan indications and/or for children, with less pre-market evidence being balanced by mandatory post-market clinical studies.

### **Interactive –**



Procedures should be available to allow innovators, developers, manufacturers, and clinical trialists to obtain advice during face-to-face discussions with regulators or with clinical evaluators in notified bodies, on appropriate designs for clinical studies and on relevant requirements for clinical evidence about their device.

### **Efficient –**



A regulatory system needs to be supported by adequate human resources, coordinated structures, and managerial/organisational capacity to ensure that medically appropriate decisions (proportionate regulation) and cost-effective outcomes are delivered in good time (“minimum resources for maximal results”).

**Arguably, while the current EU system meets these requirements to varying extents, it does not meet any of them in full.**



## 5. Concerns and proposals

Each item that is listed below represents a major concern of healthcare professionals about the operation of the EU regulatory system for medical devices, or else identifies a gap where the MDR and/or the IVDR does not provide a standard procedure for fulfilling a necessary function.

Each concern is presented as a statement, followed by a short explanation and/or summary of evidence, and then by proposals how the concern should be resolved.

### Issues that are common to Medical Devices and In Vitro Diagnostic Devices

#### **1 There is a need to establish a standard methodological framework in the EU for the clinical evaluation of high-risk devices.**

The MDR and the IVDR provide a legal framework, but they do not describe standard methodological principles or a common scientific framework for considering the clinical evaluation of high-risk medical devices. This is a fundamental deficiency of the EU system, which cannot be addressed by current regulatory initiatives that focus on updating previous guidance concerning clinical evaluation and on interpreting MDR requirements.

For high-risk, permanently implantable devices, the clinical community expects methodologically rigorous clinical investigations. The absence of regulatory guidance on methodologies for clinical studies, according to the risk class and life-cycle stage of a device, leads to uncertainties about the evidence required or collected or approved, and lack of confidence in the evidence supporting new devices. Registries can monitor the safety and performance of available devices, but they are not implemented systematically within the current regulatory framework.

The clinical evidence threshold that developers are required to meet by the MDR is not defined. They must demonstrate clinical data providing 'sufficient' clinical evidence but because that is not described further, the concept is subjective. The MDR requires 'clinical investigations' for high-risk devices, but leaves it to developers to understand how they should be designed. The General Safety and Performance section of the MDR (Annex I, chapter 1, paragraph 1) expects all medical devices to be safe and effective, but the MDR does not describe if the demonstration of safety and effectiveness should be based upon an assessment of outcomes from patients, or on claims based upon pre-clinical testing such as bench and animal testing. This is because the level of evidence needs to be proportionate to the risks, which will depend on each type of device; hence it becomes the duty of each manufacturer, verified by its notified body, and supervised by its national competent authority. Provision of guidance for clinical evaluation of each type of high-risk device would overcome these challenges.



The manufacturers of legacy devices, which represent the vast majority of available technologies, can supplement their previous clinical evaluations by conducting a high-quality survey of healthcare practitioners (at “Level 4”, the minimum recommended in a hierarchy of evidence listed by MDCG guidance).<sup>22</sup> Surveys are not recognised as contributing to evidence-based medicine, however, as their value is extremely limited.

For lower-risk devices, developers are required to comply with many of the same procedural requirements relating to clinical evaluation and post-market monitoring, but their clinical development strategies are rarely published and may therefore be more variable.

The classification rules for medical devices (into risk classes I, IIa, IIb, and III) are not linked to clinical investigation designs. For example, a coronary stent requires clinical evidence to demonstrate efficacy, whereas an introducer to access the vasculature does not need the same level of pre-market clinical investigation – but both are class III devices, despite clinical evidence expectations that are quite different.

Evaluation of the diagnostic performance of high-risk IVD tests (in classes C and D) is performed routinely, but often outside regulatory processes, at the stage when a new test is being developed within a hospital clinical laboratory or an academic institution. It may then qualify as a “laboratory-developed test” or In House-IVD (IH-IVD) but there is no standard framework in EU guidance on general principles for how such investigations should be performed, before CE- marking, and whether the evidence will be submissible.

There is therefore a need for information and guidance on acceptable methodologies. It should describe when devices require assessment not just of safety and performance, but also of clinical efficacy and/or effectiveness (comparable to methodologies for evaluating drugs). Moving from a standard ‘safety and performance’ approach implies the adoption of a different strategy.

In the absence of clear methodological frameworks, Expert Panels will deliver inconsistent advice, developers will struggle to prepare fundable market strategies, and authorities and notified bodies may apply different requirements to developers at the pre-market and post-access assessment stages. Developers may be faced with the need to conduct multiple, somewhat duplicative clinical studies in order to meet first regulatory and then health technology assessment requirements. This will damage EU competitiveness, lead to research waste, and allow the EU regulatory system to be perceived as inconsistent, arbitrary and hence unattractive to developers of innovative technologies. A single process, or at least shared requirements for evidence of clinical

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<sup>22</sup> MDCG 2020-6. Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC. A guide for manufacturers and notified bodies. April 2020. [https://health.ec.europa.eu/system/files/2020-09/md\\_mdcg\\_2020\\_6\\_guidance\\_sufficient\\_clinical\\_evidence\\_en\\_0.pdf](https://health.ec.europa.eu/system/files/2020-09/md_mdcg_2020_6_guidance_sufficient_clinical_evidence_en_0.pdf)



efficacy, would be better.

### **Evidence**

An extensive review by CORE–MD demonstrated that regulatory guidance documents almost always recommend only general principles.<sup>23</sup>

In comparison, pharmaceutical products are evaluated according to well-established methodologies, with staged clinical investigations building towards a phase 3 clinical trial designed to demonstrate both safety and efficacy when compared to an appropriate control group. Medical device evaluation, however, is left to the choice of the manufacturer, considering the state-of-the-art (itself is a subjective determination) and typically using observational study designs that are incapable of allowing valid claims of efficacy, effectiveness or clinical performance. The clinical benefit of IVD biomarkers may be insufficiently established, if there has been no trial to assess analytical validity and clinical performance.

### **Recommendations**

- Identify which types of medical devices require clinical trials designed to demonstrate clinical safety *and* efficacy (or effectiveness).
- Identify types of medical devices for which observational clinical investigations are sufficient to establish safety, whether for individual patients or from a public health perspective.
- Develop, publish and implement a scientific methodological framework for the clinical evaluation of high-risk medical devices.
- Apply this methodological framework to specific technology domains, to understand differences between current and expected evidence, and determine when device-specific guidance is needed. An example produced at the request of EU regulators was a report on coronary stents.<sup>24</sup>
- Revise the current definition of ‘state-of-the-art’, so that ‘state-of-the-art’ can be used as a valid comparator for clinical investigations.
- Develop, publish and implement a methodological framework for the clinical evaluation of lower-risk medical devices. This would place greater reliance on observational studies and post-market monitoring for surveillance of safety and clinical outcomes.

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<sup>23</sup> CORE-MD. Report on study design recommendations in guidance documents for high-risk medical devices. A systematic review. Petra Schnell-Inderst, Alan Fraser, Gearóid McGauran, et al. [https://www.core-md.eu/wp-content/uploads/2024/11/CORE-MD\\_D1.6\\_UMIT\\_resubmission\\_v2.5\\_final.pdf](https://www.core-md.eu/wp-content/uploads/2024/11/CORE-MD_D1.6_UMIT_resubmission_v2.5_final.pdf)

<sup>24</sup> Byrne RA, Serruys PW, Baumbach A, et al. Report of a European Society of Cardiology–European Association of Percutaneous Cardiovascular Interventions Task Force on the evaluation of coronary stents in Europe: executive summary. *Eur Heart J*. 2015;36:2608–20. <https://doi.org/10.1093/eurheartj/ehv203>





- Develop, publish and implement a methodological framework appropriate for the clinical evaluation of IVDs, including for In-House IVDs.

### **2 There is an urgent need for common specifications.**

There are almost no EU common technical specifications for medical devices, although their provision is envisaged in recitals and permitted in Article 9 of the MDR. There is a similar statement in Article 9 of the IVDR. The major explanation why there are not more EU standards could be the lack of scientific and medical manpower and of regulatory capacity to coordinate their preparation, whether in the unit in the European Commission and/or offered from the EU national regulatory agencies. Specifications would address the issues raised in the previous paragraph.

#### ***Evidence***

The EU guidance MEDDEV 2.7/1 (revision 4) gave general principles for the clinical evaluation of medical devices, under the previous medical device directives; it had one annex concerning requirements for coronary stents, but that document is seriously outdated. The only other technology-focused specifications relating to medical devices concerns Annex XVI products (devices without a 'medical purpose' such as non-corrective contact lenses).

There are more technical specifications for IVD devices, particularly for class D tests for infectious diseases and blood typing, but the majority of high (individual-risk) IVD devices are in Class C.

#### ***Recommendation***

- A mechanism must be established to identify guidance that is needed, and then to ensure that it is prepared with scientific experts, according to an efficient timetable.

### **3 From a clinical perspective, harmonised standards for medical devices are not an adequate substitute to common specifications.**

In the almost complete absence of EU common specifications, the EU regulatory system relies instead on standards that are prepared by task forces of the International Organisation for Standardization (ISO) and the International Electrotechnical Commission (IEC), and then harmonised to existing EU legal provisions by their European equivalents CEN and CENELEC. Legally in the EU, common specifications cannot be issued if a harmonised standard is already available (see Article 9 MDR).

ISO and IEC standards are produced by task forces composed of individuals nominated by its member organisations, which include national standards bodies, the European Union, and manufacturers. Task forces may include some independent experts but their



names are not published. Scientific and clinical experts cannot be nominated by European medical professional associations and are rarely nominated by the European Commission. Draft proposals are opened for consultation by member organisations but not in a public process. Once published, ISO and IEC standards are available to individual healthcare professionals or patients only on payment<sup>25</sup>, and so they are seldom consulted.

In the EU, demonstration of adherence to the provisions of relevant harmonised standards for a medical device enables its manufacturer to satisfy the requirements for conformity assessment. Nonetheless, ISO standards provide voluntary rather than mandatory guidance. Similarly, compliance is also voluntary with recommendations for the evaluation of medical devices that are developed by task forces of the International Medical Device Regulators Forum (IMDRF). Neither ISO nor IMDRF documents are a satisfactory substitute for EU common technical specifications.

### **Evidence**

The Official Journal of the EU lists harmonised standards for medical devices and in vitro diagnostic medical devices.<sup>26</sup> To date, about 20 ISO standards have been harmonised with the MDR and IVDR.

The ISO constitution requires that task forces, when holding face-to-face discussions, meet in turn in different geographical regions of the world. Participation is expensive. In general, insufficient budgets are allocated for full participation of nominated members from national standards bodies or the European Commission.

### **Recommendations**

- The European Commission and EU national standards bodies must allocate sufficient resources for full participation of their nominated members in ISO and IEC task forces for medical devices.
- A new financial model should be developed, at least for ISO and IEC standards relating to medical devices and relevant to clinical practice, so that they can be consulted by individual healthcare professionals without payment, when they need to understand clinical evidence requirements.
- Mechanisms are needed to ensure that European clinical experts are involved in the development of any medical device standards that will be applied in Europe, both as members of task forces and by being given the opportunity to comment on draft standards during the consultation process.

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<sup>25</sup> This has been challenged by a recent decision of the Court of Justice of the EU, upholding the requirement for harmonised standards to be publicly available; the implications of the judgement are not yet clear. See <https://curia.europa.eu/juris/documents.jsf?num=C-588/21>

<sup>26</sup> [https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:L\\_202400815](https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:L_202400815)



- For IVDs, the relatively widespread validation of relevant ISO standards by diagnostic laboratories during External Quality Assessment and by manufacturers during CE-registration, makes harmonisation between ISO and IVDR a priority, in order to avoid excessive or incoherent regulatory obligations.

#### **4 There is no guarantee of predictability of results for reviews of different devices within the same type or class, when performed by different notified bodies.**

Notified bodies are bound by a duty of confidentiality to their clients and prohibited by the MDR and IVDR from advising a manufacturer before it submits a dossier for conformity assessment of a medical device.

Notified bodies operate as ‘quasi-regulators’ but because they are independent companies rather than an EU agency, they are excluded from the requirements of the EU legislation on freedom of access to information <sup>27</sup> (unlike the European Medicines Agency).

It is difficult for a manufacturer to predict with certainty which if any particular medical device standards its chosen notified body may consider to be relevant, what will be the expectations for an appropriate design of clinical investigations, and what will be judged to constitute sufficient clinical evidence. There is no publicly accessible database that a manufacturer can consult to find out what has been accepted by notified bodies relating to earlier submissions from other manufacturers of similar devices. The manufacturer therefore explains and justifies its choice of study design; the regulations do not enforce use of any particular device standards.

#### **Evidence**

Manufacturers state that unpredictability of clinical requirements is one reason why innovators may now prefer to have their new devices assessed first by non-European researchers and regulatory bodies in other jurisdictions.

#### **Recommendation**

- Specialist communities should be created, composed of reviewers from notified bodies, regulators from competent authorities, and members of EMA Expert Panels, who together are responsible for high-risk devices within particular clinical fields – so that they can share experience, agree on common approaches, and publicly share their decisions.

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<sup>27</sup> Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents. <https://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX%3A32001R1049>



### **5 It should be easier for a manufacturer to consult a notified body for early advice about what clinical evidence will be needed for their device to be approved.**

There are very limited possibilities for consultation with a notified body before submission, that could help a manufacturer to prepare its application for conformity assessment and thereby shorten the length of the time needed for the notified body to complete its review. This is a consequence of the design of the EU regulatory system, which makes the manufacturer responsible for determining how to investigate its device and how to establish that it meets the requirements for a successful conformity assessment. The notified body is responsible for verification of the evidence.

The option of an early “structured dialogue” is now allowed, but what that will entail and how it will differ from consultation which is prohibited by the MDR and IVDR remains unclear. The pilot consultation processes being managed by the EMA need to be open to all.

#### ***Evidence***

The current Team-NB Code of conduct (2024) clarifies that a notified body cannot discuss with a manufacturer its development strategy for a new device.<sup>28</sup> Notified bodies have reported that during the conduct of an average conformity assessment process for a high-risk device, they have to ask the manufacturer to provide more information on an average of 2-3 occasions. That significantly prolongs the duration of the review and increases its inefficiency; it should be avoidable.

#### ***Recommendations***

- Legal amendments should be made to the MDR and IVDR, if necessary, to allow NBs to interact with device manufacturers and researchers before they submit a dossier. Providing advice on types of evidence that are needed is not considered a conflict of interest by other regulatory jurisdictions.
- The procedure for a “structured dialogue” should be agreed and clearly defined. Access should be possible for all innovators, especially from small and medium-sized enterprises (SMEs).
- It should be possible to obtain specific advice from a notified body and/or from specialist regulators in a national agency, before signing a contract or before submitting a dossier for conformity assessment.
- Guidance should differentiate these procedures from the process of obtaining advice from an Expert Panel; ideally, a common mechanism should be developed.

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<sup>28</sup> The European Association Medical Devices – Notified Bodies. Code of conduct for notified bodies under Regulations (EU) 2017/745 and (EU) 2017/746. <https://www.team-nb.org/wp-content/uploads/2024/09/Code-of-Conduct-Team-NB-V5-0-20240916.pdf>



- If there are no EU common specifications relevant to their specialist field, then regulatory communities (as discussed above, in item 4) should provide advice for prospective researchers, manufacturers, and study sponsors, on expected methodologies and clinical evidence.
- Advice that has been given to one manufacturer on clinical evidence requirements and methodologies, should be available (in general terms) to other manufacturers of devices of the same type or designed for the same clinical indication.

### **6 There is no public means of identifying which notified bodies or national regulatory agencies have special expertise for which rare device types.**

Each notified body applies to conduct conformity assessments for specific categories of MDs and IVDs, and the scope codes for which it has been designated are listed in the EU NANDO database.<sup>29</sup> These describe technologies rather than particular clinical types of devices. Listing implies that the notified body has been verified to have access to all the expertise that it needs. The regulations, reinforced by guidance from NBOG<sup>30</sup>, describe the qualifications that reviewers need to have.

Nonetheless, all notified bodies cannot be assumed to have in-depth clinical expertise whether in-house or among their contracted external reviewers, for them to be suitably qualified to undertake conformity assessment of certain very specialised or uncommon high-risk devices. Examples could be a fully implantable artificial heart, a prosthetic limb that is controlled via an electronic interface implanted in contact with the motor cortex, or a diagnostic system that uses a deep neural network.

It should be possible to anticipate when only a very small number of applications may be submitted for approval of highly specialised and complex medical devices. In such instances, an efficient regulatory system would allocate their review to a single expert or to a small dedicated team. That would be the most reliable way to ensure that each review is scientifically sound, high-quality, fair and consistent.

#### ***Evidence***

Many national regulatory agencies of EU member states have limited numbers of medically qualified staff, and some have no full-time medical employees. Probably none has doctors who between them have prior clinical experience across all major medical specialties.

Information is not publicly available about the areas of special expertise of individual notified bodies, about their internal clinical reviewers or external advisers and their previous or current experience of clinical or laboratory practice.

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<sup>29</sup> [https://health.ec.europa.eu/medical-devices-topics-interest/notified-bodies-medical-devices\\_en](https://health.ec.europa.eu/medical-devices-topics-interest/notified-bodies-medical-devices_en)

<sup>30</sup> <https://www.nbog.eu/nbog-documents/>



### **Recommendations**

- A register should be established, maintained, and made accessible for public consultation, to summarise what highly specialist engineering, scientific, or medical expertise can be offered by reviewers within each notified body or by regulators within each national competent authority. These specialists could be members of clinical interest groups (as proposed in item #4).
- For review by the EU of very rare or very innovative medical devices, the principle of pooling of resources and specialisation of regulatory bodies should be accepted, established, and advertised. Specialist regulatory expertise can be matched with the specific needs of manufacturers.
- The clinical advantages of concentrating experience for a specialist field within a limited number of notified bodies, whether by voluntary or legislative measures, should outweigh the principle of allowing open competition between notified bodies. Manufacturers would then be able to identify which notified body will be best qualified to review a particular device for a special application; a corollary will be that the notified body must then accept any request to assess a device of the prescribed type.
- It is recognised that these proposals may require legislation.

### **7 There are no special regulatory pathways in the EU that cater to the specific characteristics of innovative or “breakthrough” devices.**

Most jurisdictions have special programmes to facilitate the early certification of innovative devices. If a new device promises to satisfy an unmet need for a serious, life-threatening or irreversibly debilitating condition, for which no similarly effective treatment exists, then it should be possible for that device to be approved with limited evidence but with conditions.

Satisfactory performance and safety should have been demonstrated in initial studies, while confirmation of longer-term safety and proof of clinical effectiveness can be deferred for mandated and comprehensive post-market surveillance and follow-up clinical studies.

### **Evidence**

There are examples of effective special pathways in other regulatory jurisdictions. They



have been reviewed by recent EU projects including CORE-MD.<sup>31,32</sup>

### **Recommendation**

- The EU should establish a special pathway that will enable breakthrough technologies to undergo an accelerated conformity assessment; if a device is approved by such a route, there should be mandated clinical follow-up during the post-market surveillance phase.
- As a safeguard against bias from the developers of a new device, both the unmet need and the status of the new device as a genuine breakthrough product should be confirmed independently by experts, with advice from patients who may receive the device. This could be a task for Expert Panels.

### **8 There are no special regulatory pathways in the EU that offer pathways to certification that are adapted to the characteristics of orphan and paediatric medical devices.**

Orphan and paediatric devices are needed for small numbers of children and/or patients with rare diseases, or for rare indications in more frequent circumstances. Manufacturers face important regulatory hurdles that hinder the certification of these devices or indications under either the MDR or the IVDR. The comments in this section relate to medical devices, however, since a working group of MDCG is considering how to manage the assessment of orphan and rare IVD tests.

The costs of (re)certification by Notified Bodies form a significant or even critical financial barrier for manufacturers to (re)introduce their devices onto the EU market, when small patient groups offer less return on investment. Excessive invoicing has made the transition from the device directives to the MDR exceptionally costly and in some cases financially prohibitive. There may have been a literal interpretation and (over)application of new requirements, not helped by the very limited opportunities for early dialogue between manufacturers and notified bodies or regulatory agencies.

The European Commission now encourages notified bodies to approve more orphan

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<sup>31</sup> Tarricone R, Banks H, Ciani O, et al. An accelerated access pathway for innovative high-risk medical devices under the new European Union Medical Devices and health technology assessment regulations? Analysis and recommendations. *Expert Rev Med Devices*. 2023;20:259-271.  
[https://www.tandfonline.com/doi/full/10.1080/17434440.2023.2192868?rfr\\_dat=cr\\_pub++0pubmed&url\\_ver=Z39.88-2003&rfr\\_id=ori%3Arid%3Acrossref.org](https://www.tandfonline.com/doi/full/10.1080/17434440.2023.2192868?rfr_dat=cr_pub++0pubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org)

<sup>32</sup> Aranda J, Dobrzynska A, Rosario-Lozano MP, Rejón-Parrilla JC, Epstein D, Blasco-Amaro JA. Regulatory perspectives on post-market evidence generation schemes for high-risk medical devices: a systematic review. *Expert Rev Pharmacoecon Outcomes Res*. 2024 Dec 1:1-15.  
[https://www.tandfonline.com/doi/full/10.1080/14737167.2024.2431234?rfr\\_dat=cr\\_pub++0pubmed&url\\_ver=Z39.88-2003&rfr\\_id=ori%3Arid%3Acrossref.org](https://www.tandfonline.com/doi/full/10.1080/14737167.2024.2431234?rfr_dat=cr_pub++0pubmed&url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org)



medical products, for example by applying conditions to certificates of conformity. Recent MDCG Guidance on the Clinical Evaluation of Orphan Medical Devices<sup>33</sup> is an important step in the right direction, but it has not changed any essential features of the existing regulatory framework. A special pathway is still needed, that can offer more flexibility adapted to the specific needs of orphan and paediatric devices.<sup>34</sup>

### **Evidence**

Orphan devices are especially relevant to the care of children. EU member states respect the United Nations Convention on the Rights of the Child, which refers in Article 24 to “the right of the child to enjoy the highest attainable standard of health”.<sup>35</sup> EU policies should avoid any regulations that would disadvantage sick children.

### **Recommendations**

- An Expert Panel for Orphan and Paediatric Medical Devices should be established.<sup>36</sup> Plans to implement this have been announced.
- The EU should develop special pathways that will enable orphan and paediatric medical devices to be approved if necessary with less pre-market clinical evaluation, as long as that is followed by more post-market studies.
- There should be public funding for registries of orphan medical devices, undertaken by specialist medical professional associations.

## **9 The costs of conformity assessment should be reduced for orphan and paediatric devices, some legacy devices, and some applications by SMEs.**

Notified bodies decide how much to charge for their services. Article 50 of the MDR requires them to publish their standard fees, which may be indicated per person per day. Final total costs will depend on a broad range of factors such as the intensity of the review conducted by the notified body, requests for additional information from the manufacturer, and the number of site audits – which can be difficult to predict.

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<sup>33</sup> Medical Device Coordination Group. Clinical evaluation of orphan medical devices. MDCG 2024–10 (June 2024). [https://health.ec.europa.eu/document/download/daa1fc59-9d2c-4e82-878e-d6fdf12ecd1a\\_en?filename=mdcg\\_2024-10\\_en.pdf](https://health.ec.europa.eu/document/download/daa1fc59-9d2c-4e82-878e-d6fdf12ecd1a_en?filename=mdcg_2024-10_en.pdf)

<sup>34</sup> Melvin T, Kenny D, Gewillig M, Fraser AG. Orphan medical devices and pediatric cardiology – what interventionists in Europe need to know, and what needs to be done. *Pediatr Cardiol*. 2023;44(2):271–279. <https://link.springer.com/article/10.1007/s00246-022-03029-1>

<sup>35</sup> UN General Assembly. Convention on the Rights of the Child. Resolution 25, session 44. Treaty Series. November 20, 1989;1577. [https://treaties.un.org/doc/source/docs/A\\_RES\\_44\\_25-Eng.pdf](https://treaties.un.org/doc/source/docs/A_RES_44_25-Eng.pdf)

<sup>36</sup> Guerlich K, Patro-Golab B, Barnacle A, et al; European Academy of Paediatrics. European expert recommendations on clinical investigation and evaluation of high-risk medical devices for children. *Acta Paediatrica*. 2023;112:2440–2448. <https://www.core-md.eu/wp-content/uploads/2023/08/Acta-Paediatrica-2023.pdf>





A well-functioning market for notified bodies as independent commercial organisations would mean that their fees should differ, but it is unclear if there are significant variations. Total costs for certification may be excessive, particularly for new devices that cater to small groups of patients and thus offer less return on investment for their manufacturer. Costs have been reported to be prohibitive for some smaller SMEs.

High costs seem inappropriate for certain class III but lesser-risk legacy devices that have been certified under the previous medical devices directive and on the market for many years without any clinical issues (such as intravascular catheters and guide wires; or intermediate sizes of orthopaedic implants). Surveys of manufacturers imply that the costs of recertification form a 'significant-to-critical' financial barrier which has contributed to devices being withdrawn from the EU market<sup>37</sup>, while the same devices remain available in other jurisdictions such as the USA or Canada, where the costs of certification can sometimes be ten times lower than in the EU.

### **Evidence**

A survey of manufacturers conducted by Gesundheit Österreich for the European Commission revealed an average cost for certification of €539,859.<sup>38</sup> Since 2021, 46% of the respondents had stopped – or were planning to stop – producing, marketing or supplying some devices on the EU market.

According to Annex VII of the MDR (clause 1.2.8), notified bodies should apply consistent, fair and reasonable conditions, and take account of the interests of SMEs when setting fees.

### **Recommendations**

- The full costs of certification should be more transparent. A single web source should give the standard fees per notified body, and compare examples of indicative costs for the different stages of review.
- Notified bodies should be encouraged to reduce their charges by avoiding any duplication of their procedures (such as repeated assessment of a sterilisation protocol separately for each size in a range of a product, when it is common to them all).
- More affordable pathways to regulatory approval, with reduced costs, should be available for devices that are needed rarely, since they can provide only a small return on investment, and for devices that have been developed by SMEs which demonstrate that they would otherwise need financial support to remain viable.

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<sup>37</sup> See Biomedical Alliance press release of 27 June 2023:

[https://www.biomedeuropa.org/images/news/2023/Letter\\_Kyriakides\\_Med\\_Devices\\_signed\\_270627.pdf](https://www.biomedeuropa.org/images/news/2023/Letter_Kyriakides_Med_Devices_signed_270627.pdf)

<sup>38</sup> [https://health.ec.europa.eu/study-supporting-monitoring-availability-medical-devices-eu-market\\_en](https://health.ec.europa.eu/study-supporting-monitoring-availability-medical-devices-eu-market_en)



- Implementation of national and EU-wide derogations should be facilitated for devices that are essential for clinical care but which are about to disappear from the market because they are no longer profitable (see article 59 of the MDR).<sup>39</sup>
- Even at this late stage in the transition to the new regulations, the option of providing certificates with conditions should be explored for essential legacy devices that have been on the market without issues for many years.

### **10 There is a need for additional regulatory capacity within DG SANTE.**

A well-functioning regulatory system relies on effective governance and is dependent on the availability of relevant expertise.

The small team in the Medical Devices Unit (D3) of the Directorate General for Health and Food Safety (DG SANTE) of the European Commission has been very active in supporting the implementation of the MDR and IVDR, but it is hugely overworked and has very limited capacity for new initiatives. There are too few officials with clinical and scientific expertise, either within the European Commission or within the competent authorities at national level.

#### **Evidence**

In 2012 the Impact Assessment for the recast of the medical device directives and the in vitro diagnostic device directive estimated – for the option that was eventually chosen – that 53 full-time equivalent staff would be needed in the European Commission in order to provide effective management of the future regulatory framework.<sup>40</sup>

That has never happened. A moratorium on expansion in the number of staff within the European Commission limited recruitment to the Medical Devices Unit in DG SANTE to internal transfers or to the temporary secondment of staff from national regulatory authorities. The number of policy officers *and* support staff is approximately 23.

#### **Recommendation**

- Additional expert staff must be appointed, and external recruitment for suitably qualified experts should be permitted. There should be a substantial expansion of staff, either in DG SANTE or in a new coordinating centre (see below, section 6).

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<sup>39</sup> Melvin T, Dooms MM, Koletzko B et al. Orphan and paediatric medical devices in Europe: recommendations to support their availability for on-label and off-label clinical indications. Expert Review of Medical Devices 2024;21: 893–901. <https://doi.org/10.1080/17434440.2024.2404257>

<sup>40</sup> Commission Staff Working Document. Impact Assessment on the Revision of the Regulatory Framework for Medical Devices, accompanying the documents Proposals for Regulations of the European Parliament and of the Council on medical devices, and amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and on in vitro diagnostic medical devices. SWD/2012/0273 final. [https://eur-lex.europa.eu/resource.html?uri=cellar:487acc33-213b-4fdf-bdbb-8840209a8807.0001.04/DOC\\_1&format=PDF](https://eur-lex.europa.eu/resource.html?uri=cellar:487acc33-213b-4fdf-bdbb-8840209a8807.0001.04/DOC_1&format=PDF)



### **11 There is no mechanism for identifying who can represent EU regulators, for external collaborations within a specialist medical field.**

The EU espouses global regulatory convergence and is an active member of the IMDRF but it has been unable to participate fully in some of its activities such as the Medical Device Single Audit Programme (MDSAP)<sup>41</sup>, due to the decentralised and fragmentary structure of the EU regulatory system. Some mutual recognition agreements (MRAs) have been established at a high level between the European Commission and other IMDRF members.

Practical collaborations yielding concrete results will depend on building confidence between specialist regulators who are responsible within their own jurisdictions for overseeing medical devices within focussed fields of clinical activity. There is currently no system whereby a specialist regulator from a national regulatory authority (or a notified body) could be delegated responsibility to speak on behalf of the EU as its identifiable ‘point of contact’ (see paragraph 6, above). It is likely that there may be some smaller medical specialties that are not represented by any regulator in any of the national agencies of EU member states – whereas, for example, the US FDA has employed more than 120 physicians full-time, across all medical fields.

#### **Evidence**

An example of a gap in the provision of essential medical technologies is that there are no devices approved in any jurisdiction worldwide, and limited options for using devices off-label, to perform dialysis in infants and children with renal failure.<sup>42,43</sup> Concerted action is needed, but who would represent the EU as its ‘renal device regulator’?

#### **Recommendation**

- The EU needs to identify and coordinate its specialist regulators – from among those employed by the regulatory authorities of member states and/or the notified bodies (or failing that, with support from members of Expert Panels or European specialist medical associations). Individuals should be appointed with authority to give advice about standards of clinical evidence applicable to devices for a particular clinical indication. The same individuals could represent the EU as members of task forces writing international standards or guidelines.

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<sup>41</sup> This refers to the involvement of regulatory agencies. It is recognised that EU notified bodies have been contracted to conduct reviews for the MDSAP.

<sup>42</sup> Ranchin B, Schmitt CP, Warady B, et al. Devices for long-term hemodialysis in small children – a plea for action. *Kidney Int.* 2023;103(6):1038–1040. [https://www.kidney-international.org/article/S0085-2538\(23\)00185-0/abstract](https://www.kidney-international.org/article/S0085-2538(23)00185-0/abstract)

<sup>43</sup> Ranchin B, Schmitt CP, Warady BA, et al. Technical requirements and devices available for long-term hemodialysis in children – mind the gap! *Pediatr Nephrol.* 2024;39(9):2579–2591. <https://link.springer.com/article/10.1007/s00467-023-06233-0>



### **12 Access for conformity assessment should be readily available.**

There is currently no system to ensure that a manufacturer will be able to access a notified body, when it wishes to present evidence for review of a medical device. Large medical technology companies have well-established links with ‘their’ notified bodies, but some small companies have found it difficult to have their application taken on by any notified body. It should not be possible for them all to refuse.

#### ***Evidence***

Reduced availability of notified bodies, related to delays in their re-designation and to fewer organisations being notified to review devices under the MDR and IVDR compared with those under the previous directives, initially constrained their capacity.

A group of Belgian hospitals acting on behalf of a consortium of clinical cardiologists approached 15 notified bodies, all of which declined to review their application.<sup>44</sup>

#### ***Recommendation***

- Every manufacturer which wishes to place a device on the European market should be guaranteed access to a notified body for review of its dossier submitted for conformity assessment. A manufacturer should not have to apply in turn to multiple notified bodies; if necessary, it should be possible for the national competent authority to direct a notified body to process an application.

### **13 There is no single reporting mechanism for healthcare professionals in the EU, for example to report suspected serious incidents or concerns about specific devices.**

Article 87(10) of the MDR states that the EU member states “shall take appropriate measures [...] to encourage healthcare professionals, users and patients to report to the competent authorities suspected serious incidents”. Individuals with concerns or questions should contact their national regulatory agency.

Regulation (EU) 2024/1860 (Article 10A) has introduced the requirement for any medical device manufacturer “to inform the competent authority of the Member State where it or its authorised representative is established, as well as the [...] health institutions and healthcare professionals to whom it directly supplies the device” at least 6 months in advance of any anticipated interruption or discontinuation of a device “where it is reasonably foreseeable that such interruption or discontinuation could result in serious harm or a risk of serious harm to patients or public health in one or more Member States”.<sup>45</sup> This provision is important and must not be diluted – particularly if a device

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<sup>44</sup> Personal communication, Professor Hein Heidbuchel, University of Antwerp.

<sup>45</sup> Regulation (EU) 2024/1860 of the European Parliament and of the Council of 13 June 2024 amending Regulations (EU) 2017/745 and (EU) 2017/746 as regards a gradual roll-out of Eudamed, the obligation to



that is going to be withdrawn is the ‘last-in-class’ for a clinical or diagnostic indication, meaning that no alternative will be available.

The proposal, however, is that manufacturers should tell their national regulator. It is unclear how “health institutions and healthcare professionals” across the EU will be informed. It is uncertain which criteria a manufacturer will apply to determine if its decision to discontinue a device will lead to “serious harm or a risk of serious harm to patients or public health”.

All these functions could be managed more efficiently, and probably with more impact, if there was a single reporting point (or portal) for clinicians and patients in the EU.

The planned early-warning system will be effective only if practising clinicians are consulted as soon as possible. Otherwise, they may learn that a device is no longer available, once it is too late for them plan alternative approaches. Also, clinicians may know about off-label applications of the device that otherwise would be ignored, and they can advise regulators if any derogations should be considered (see point 9 above).

### **Evidence**

Problems from the discontinuation of high-risk devices have particularly affected paediatric cardiological practice. For example, the supply of Rashkind balloon catheters for emergency atrial septostomy in newborn infants with transposition of the great arteries became tenuous, with potentially life-threatening consequences.

### **Recommendations**

- An active mechanism must be established to ensure that when a manufacturer reports to its national regulator that it is going to withdraw a device, the information is shared not only with other regulators across EU member states but also with the clinical community (perhaps via European medical associations), with patients, and with purchasers.
- Guidance should be prepared on steps to be taken after withdrawal of a device has been announced, including options that could mitigate shortages and measures to reduce any clinical impact.
- Healthcare professionals and providers should have access to a single mechanism and point of contact where they can report shortages or non-availability of devices that are needed for patient care, and where they can raise key concerns about safety, or notify regulators about adverse incidents that have occurred with the devices that they use.

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inform in case of interruption or discontinuation of supply, and transitional provisions for certain in vitro diagnostic medical devices. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32024R1860>



### **14 Regulatory duplication must be avoided.**

Since the MDR and IVDR were approved in 2017, several important EU cross-sectoral initiatives have also impacted the medical device sector – in particular, the General Data Protection Regulation (EU 2016/679, applicable from from 25<sup>th</sup> May 2018) and the Artificial Intelligence Act (EU 2024/1689, from 1<sup>st</sup> August 2024).

Other new laws with notable implications for the medical device regulatory framework are the Health Technology Assessment (HTA) Regulation (EU) 2021/2282, in application since 12<sup>th</sup> January 2025, and the European Health Data Space Regulation that was approved by the European Parliament in 2024 and adopted by the Council of the EU in January 2025.

The Clinical Trial Regulation (EU) 536/2014 that came into force on 31<sup>st</sup> January 2022, and the proposals for a regulation and directive to reform EU pharmaceutical governance, do not apply to medical devices but there are substantial areas of overlap. More concordance would be logical, especially if the European Medicines Agency (EMA) is given additional responsibilities relating to medical devices (see section 6 of this document).

#### ***Evidence***

It is likely that clinical evidence that is evaluated by a notified body during a conformity assessment will also be reviewed during the assessment introduced by the HTA Regulation, which came into force in January 2025; at least the evidence on clinical efficacy should be common, while HTA authorities may also require some studies of relative clinical effectiveness in real-world contexts of use. Secondly, there is a process whereby a pharmaceutical company can obtain advice jointly from the EMA and HTA authorities, before it designs clinical studies which will satisfy the requirements of both. An equivalent possibility for devices was envisaged by the MDR but has not been implemented. Sharing these activities could hasten access to the market for an approved device. Horizon scanning could be a third joint activity.

There may now be conflicting requirements in EU laws. For example, the MDR states that a manufacturer must conduct post-market surveillance of its device, perhaps using a registry, and IMDRF guidance recommends that at least 95% of patients should be included<sup>46</sup> – but the GDPR gives patients the right to refuse to have their data collected. Which requirement would have precedence? A second example could be that the AI Act mandates that the use of a machine learning algorithm should be explained and recorded, with patients being informed – but for AI-enabled high-risk medical devices, that would already be done according to the MDR. There is a need for legal clarity, and

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<sup>46</sup> International Medical Device Regulators Forum. Principles of international system of registries linked to other data sources and tools. IMDRF/REGISTRY WG/N33FINAL:2016.

<https://www.imdrf.org/sites/default/files/2024-07/imdrf-tech-160930-principles-system-registries.pdf>



simple rules, concerning such relationships between EU regulations.

### **Recommendations**

- If implementation of the AI Act, and of the EU Health Data Space Regulation, includes drafting of tertiary legislation and/or the development of guidance relevant to diagnostic and therapeutic technologies, then it will be important for healthcare professionals to be involved in each process. The opportunity could be taken to address any persisting doubts about conflicting recommendations.
- EU requirements for the management of clinical studies of medical devices should be simple and clear, as proposed by the Coalition for Reducing Bureaucracy in Clinical Trials<sup>47</sup>, and confirmed in the principles of the Good Clinical Trials Collaborative adopted by the World Health Organization.<sup>48</sup>

### **15 Investment is needed to support engagement by clinical experts.**

As recognised stakeholders, the BioMed Alliance and some specialist European medical associations (including ESC, EFORT, ESHG, EHA and EFLM) attend open sessions of the Medical Device Coordination Group (MDCG). Nominated expert representatives participate when invited in working groups and task forces, providing feedback and contributing to guidance documents.

These opportunities are welcomed, but it is challenging for volunteers to contribute to all the consultations with stakeholders, considering that deadlines are often short. Medical experts have clinical duties that may be set many weeks in advance.

### **Evidence**

Dates for EU committees for medical devices and in vitro diagnostic devices have often been confirmed or changed with only a few weeks of notice. One explanation has been that there is great pressure on the facilities of the EU conference centre in the European quarter in Brussels. Many meetings are now run successfully on-line, but attendance in person can be more informative and valuable.

### **Recommendations**

- Dates for face-to-face meetings, and selection of the times for open sessions with stakeholders, should be set well in advance (> 2 – 3 months) and not changed.
- Travel costs for clinicians, patients, and civil society representatives who attend and contribute to the MDCG should be reimbursed by the European Commission.

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<sup>47</sup> The Coalition for Reducing Bureaucracy in Clinical Trials.

<https://bureaucracyincls.eu/#:~:text=The%20Coalition%20for%20Reducing%20Bureaucracy%20in%20Clinical%20Trials&text=The%20statement%20calls%20for%20urgent,and%2C%20crucially%2C%20patient%20safety>

<sup>48</sup> World Health Organization. Guidance for best practices for clinical trials. Geneva: World Health Organization; 2024 <https://iris.who.int/bitstream/handle/10665/378782/9789240097711-eng.pdf>



## Concerns relating particularly to Medical Devices

### **16 There is still insufficient transparency of the clinical evidence for medical devices.**

Providing more information was an important objective for the regulatory reforms of 2017 (for example, see Recital 43 of the MDR) but to date there is still insufficient transparency of clinical evidence.

Transparency is essential for healthcare professionals to ensure that they can take informed and evidence-based decisions for patient care. It is vital that clinicians have easy access to all clinical evidence for medical technologies and not only to the Summaries of Safety and Clinical Performance (SSCPs). Patients also need access to the evidence supporting any devices that are recommended for their care, if they wish to read it; individual preferences will vary but all patients should be able to obtain full details before they give informed consent.

#### ***Evidence***

Systematic reviews that were undertaken by the CORE–MD consortium included 641 studies of high-risk medical devices that together had enrolled more than 1.9 million patients. No randomised controlled trial (RCT), and only 9% of all studies of any design, had been published for 71 high-risk cardiovascular devices before their dates of CE-marking.<sup>49</sup> No clinical study of any design was publicly available for 30 selected orthopaedic implants, before their dates of CE-marking<sup>50</sup>, and even up to 20 years later there had been no scientific publications for 25% of those devices.

Concerning devices for diabetes care included in the third review, 17% of studies had been published by the date of CE-marking.<sup>51</sup>

It was planned that EUDAMED would enable the public as well as healthcare professionals to be adequately informed about all devices placed on the market, and that it would provide information on their clinical investigations. EUDAMED will have a key role but its implementation has faced severe delays. It is essential that the clinical module is fully implemented as soon as possible.

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<sup>49</sup> Siontis GC, Coles B, Häner JD, et al; CORE-MD investigators. Quality and transparency of evidence for implantable cardiovascular medical devices assessed by the CORE-MD Consortium. *Eur Heart J.* 2024;45:161–77. <https://doi.org/10.1093/eurheartj/ehad567>

<sup>50</sup> Lübbecke A, Combescure C, Barea C, et al. Clinical investigations to evaluate high-risk orthopaedic devices: a systematic review of the peer-reviewed medical literature. *EFORT Open Reviews.* 2023;8:781–791. <https://eor.bioscientifica.com/view/journals/eor/8/11/EOR-23-0024.xml>

<sup>51</sup> Bano A, Künzler J, Wehrli F, Kastrati L, et al, on behalf of CORE-MD investigators. Clinical evidence for high-risk CE-marked medical devices for glucose management: a systematic review and meta-analysis. *Diabetes Obes Metab.* 2024;26:4753–4766. <https://dom-pubs.pericles-prod.literatumonline.com/doi/10.1111/dom.15849>





### **Recommendations**

- Notified bodies should be given authority to insist that manufacturers publish the clinical studies that were submitted for approval of their devices, for example in an open-access archive if not yet in the peer-reviewed literature, no later than when they start to market their devices. Manufacturers have an ethical responsibility to make all clinical results publicly available.
- Until EUDAMED is fully functional, access to all SSCPs should be possible through a single portal. It should not be necessary for individual enquirers to have to ask any manufacturer to provide its SSCP.
- Healthcare professionals should have access to the EUDAMED database of reported concerns about high-risk devices (i.e. anonymised incident reports, which are available in other regulatory jurisdictions e.g. the MAUDE database maintained by the FDA); as well as the alerts, recalls, and field safety notices that are already public documents and which provide different information.<sup>52</sup>
- The CORE–MD project has developed a search tool to support post-market surveillance by automatically collecting and aggregating notices about medical device alerts and recalls from the websites of EU and non-EU regulators.<sup>53,54</sup> Sustainable funding should be found for the maintenance of this useful resource.

### **17 There is insufficient clinical evidence before approval for many high-risk devices.**

Even when evidence from clinical studies is published, it is often suboptimal in quality.

#### **Evidence**

The proportions of all studies reviewed by the CORE–MD consortium that were RCTs were 19% for cardiovascular devices<sup>46</sup>, 9% for orthopaedic implants<sup>47</sup>, and 29% for devices used for diabetes mellitus.<sup>48</sup> No RCT had been published at any time, for 30% of the cardiovascular devices.<sup>46</sup> The proportion of studies undertaken to assess medical

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<sup>52</sup> Hoogervorst LA, Ren Y, Melvin T, et al. Safety notices and registry outlier data measure different aspects of safety and performance of total knee implants: a comparative study of safety notices and register outliers. *Acta Orthop.* 2024;95:667-676. <https://actaorthop.org/actao/article/view/42361>

<sup>53</sup> Ren Y, Bertoldi M, Fraser AG, Caiani EG. Validation of CORE-MD PMS support tool: a novel strategy for aggregating information from notices of failures to support medical devices' post-market surveillance. *Ther Innov Regul Sci.* 2023;57(3):589–602. <https://www.core-md.eu/wp-content/uploads/2023/01/s43441-022-00493-y-jan-23-Enrico-Caiani-1.pdf>

<sup>54</sup> Ren Y, Caiani EG. Leveraging natural language processing to aggregate field safety notices of medical devices across the EU. *NPJ Digit Med.* 2024;7(1):352. <https://www.nature.com/articles/s41746-024-01337-9>



devices in children that were RCTs was 29%.<sup>55</sup>

### **Recommendations**

- Guidance on methodologies for clinical evaluation of high-risk medical devices should stress the need for more RCTs when feasible, as they provide the highest level of evidence. Ideally, a new device should be tested against others for the same indication.<sup>56</sup>
- A score has been developed by the CORE–MD consortium that estimates the clinical risks of using a medical device that employs an artificial intelligence or machine learning algorithm.<sup>57</sup> The score can now be developed and trialled and, if implemented, it could guide (and raise) the level of clinical evidence that should be established for AI-enabled devices before they are CE-marked.
- CORE–MD also developed an index for assessing the quality and regulatory utility of medical device registries, to provide reliable clinical information during post-market surveillance and clinical follow-up.<sup>58</sup> It could be used by EU regulatory bodies to improve the quality of clinical data collected after market access.

### **18 There is often an excessive duration of the conformity assessment process.**

There continues to be a long average duration of the EU regulatory process for many devices, from submission to approval and issue of a certificate of conformity. This increases costs, and it may delay access for patients and their physicians to effective therapies.

The certificate of conformity issued by notified bodies is valid for a maximum of 5 years, but that may be extended for another 5 years upon the manufacturer's application. For some legacy devices, a longer duration could be applied at no risk to patients. For high-risk implantable devices with late risks, however, that would be inappropriate (e.g. orthopaedic implants; heart valves).

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<sup>55</sup> Guerlich K, Patro-Golab B, Dworakowski P, et al. Evidence from clinical trials on high-risk medical devices in children: a scoping review. *Pediatric Research*. 2024;95:615–624. <https://www.nature.com/articles/s41390-023-02819-4>

<sup>56</sup> CORE–MD consortium. Recommendations for a hierarchy of clinical evidence for high-risk medical devices. [https://www.core-md.eu/wp-content/uploads/2024/11/CORE-MD\\_D4.3\\_ESC\\_v2.1\\_edited\\_clean.pdf](https://www.core-md.eu/wp-content/uploads/2024/11/CORE-MD_D4.3_ESC_v2.1_edited_clean.pdf)

<sup>57</sup> Rademakers FE, Biasin E, Bruining N, et al. CORE-MD clinical risk score for regulatory evaluation of artificial intelligence-based medical device software. *NPJ Digit Med*. 2025;8(1):90. <https://www.nature.com/articles/s41746-025-01459-8>

<sup>58</sup> Hoogervorst LA, Nelissen RGHH, Melvin T, et al. Development of a minimum dataset to assess the quality and analysis of registry data for post-market surveillance of medical devices. 2025 [submitted for publication; project report available via [www.core-me.eu](http://www.core-me.eu)].



### **Evidence**

The survey among manufacturers conducted by Gesundheit Österreich (see point 9 above) indicated that the time taken for approval of the quality management system and for the award of a certificate of conformity for a medical device, exceeded 13 months at more than 77% of all notified bodies.

### **Recommendation**

- Medical professional associations (or the Expert Panels) could advise EU regulators which established types of devices used in their clinical practice can be considered to be safe, with such low risks that a longer duration of validity could be awarded for their certificates – thereby lessening the impact of long reviews.

## **19 The Expert Panels can contribute more.**

The main role of the Expert Panels has been to consider and advise on the quality of assessments performed by the notified bodies, but most of the experts will not previously have seen any notified body assessment. They should have access, if required before they can provide an expert opinion, to the totality of clinical evidence presented in the Clinical Evaluation Report rather than the ‘Clinical Evaluation Assessment Report’ that they currently see.

There is imprecision of the criteria for referring dossiers to Expert Panels, and limited transparency of screening decisions by scrutiny panels. There is little feedback from notified bodies to Expert Panels on actions taken on receipt of their recommendations.

### **Evidence**

The number of reviews performed by the Expert Panels has been less than expected. There have been instances where their recommendations were not adopted by the notified bodies concerned. Pilot consultations have been useful.

### **Recommendations**

- Expert panels should be provided with methodological frameworks for the appropriate clinical investigation of devices, by their device class, and they should have the authority to comment on the clinical evidence when appropriate, and not only on the conclusions or the quality of notified body assessments.
- The pilot project for Expert Panels to provide early advice should now be expanded and made permanent, so that they can support more manufacturers in the early stages of their route to conformity assessment.
- Expert Panels could provide independent opinions on whether devices should be designated either as an orphan device, or as an innovative breakthrough device – thereby acting as unbiased gatekeepers for access to special regulatory pathways.



- For some rare types of devices, it may be difficult to identify clinical experts who have no relationships with industry. Disclosures and potential conflicts of interest should then be managed transparently; such individuals could advise, without making decisions.

### **20 Reprocessing of medical devices.**

Some medical devices designated as ‘single-use’ can be reprocessed safely and used again. Article 17 of the MDR allows the reprocessing of devices when it is permitted by national law. According to information provided to the European Commission, 18 EU and EEA countries do not permit any reprocessing of medical devices; 10 countries do permit it but maintain different options and apply different restrictions or prohibitions.<sup>59</sup>

An institution or company that reprocesses a device becomes the legally designated manufacturer of the device, with all the responsibilities which that entails. This makes it difficult for a hospital clinical service to obtain regulatory approval for reprocessing.

#### ***Evidence***

Clinical electrophysiologists in Belgium found it almost impossible to find a notified body that would agree to review their application for approval of reprocessed ablation catheters, which can be safely reused.

#### ***Recommendation***

- A more harmonised approach is needed to the reprocessing of devices, with the possibility of approval at an EU rather than a national level.

### **Concerns relating particularly to In Vitro Diagnostic Medical Devices**

#### **21 There needs to be sufficient regulatory capacity and expertise to classify and evaluate all in vitro devices.**

The IVDR classifies devices into four groups, with respect to personal and public risk:

- **Class A** has the lowest individual and the lowest public risk;
- **Class B** moderate personal risk and/or low public health risk;
- **Class C** high personal risk and/or moderate public health risk; and
- **Class D** both high personal and high public health risk.

IVDs consist of IVD devices (instrumentation and software) and IVD tests (‘wet lab’), which are fundamentally different; the generic term does not discriminate between

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<sup>59</sup> See European Commission, ‘National rules on reprocessing of single-use devices’ at [https://health.ec.europa.eu/medical-devices-topics-interest/reprocessing-medical-devices/national-rules-reprocessing-single-use-devices\\_en](https://health.ec.europa.eu/medical-devices-topics-interest/reprocessing-medical-devices/national-rules-reprocessing-single-use-devices_en)



these constituents. All instrumentation hardware used to run tests of the various risk classes is considered class A (Annex VIII, Rule 5). The overall classification may vary depending on the clinical context in which the device is to be used.

Classes B, C, and D, as well as sterile class A devices now require certification from a notified body. This represents an increase in the percentage of tests requiring evaluation by notified bodies, compared with the IVD directive, rising from 7% to 84%.<sup>60</sup> The same survey reported that the percentage of self-certifiable tests reduced from 93.1% under the previous IVD directive to 15.9% applying the IVDR risk categories. Capacity in the notified bodies to undertake all these reviews is increasing.

Many applicants (particularly SMEs) are new to this process, however, with little prior experience of regulatory submissions. There are few common assessment standards under which the individual NBs are required to operate, potentially leading to unequal criteria being applied. It may be impossible even for all Class D devices to be certified under the IVDR by the end of the transition period.

### **Evidence**

The risk classification of IVDs is based on potential harms to the individual subject and/or to the public, but individual risk may be seen as dynamic.

A majority of IVD devices used for analyses in laboratory diagnostic medicine are considered Class B (Annex VIII; Rule 6) yet their non-availability could constitute a high risk to health (e.g. measurement of potassium in the blood, which if very abnormal can be a cause of cardiac arrest).

“Devices intended for self-testing” are typically considered class C devices, by Rule 4(a). The skills of the operator of the device determines its correct use, and incorrect test results may generate a high personal risk to patients. In contrast, Rule 4(b) defines IVD devices that are located outside a professional medical laboratory, for example in a doctor’s office or on an ITU, as point-of-care-testing (POCT). Based on Rule 6, a class B device could be up-graded based on Rule 3(k) or it could be put into class C by analogy with the Rule 4(a) concerning home-testing devices.

Regarding class B IVDs, the overall requirements appear to be unnecessarily strict, compared to higher-risk devices (in classes C and D). The regulatory requirements place a disproportionate burden for technical documentation, performance evaluation and post-market surveillance. Increased costs for compliance of (lower volume) specialty IVD devices may reduce the overall availability of Class B devices since manufacturers (often SMEs) may withdraw them from the market. Any disappearance of

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<sup>60</sup> van Drongelen A, de Bruijn A, Pennings J, van der Maaden T. The impact of the new European IVD-classification rules on the notified body involvement; a study on the IVDs registered in the Netherlands. Rijksinstituut voor Volksgezondheid en Milieu, RIVM Letter Report 2018-0082. <https://rivm.openrepository.com/bitstream/handle/10029/622381/2018-0082.pdf?sequence=1&isAllowed=y>



IVDs from the market particularly impacts the availability of IVD devices used for small groups of patients, or in the context of rare metabolic, malignant or genetic diseases – with an ultimate impact on clinical decision-making at the bedside.

During the COVID-19 pandemic, the new diagnostic challenge was met within weeks solely by a group of international specialty laboratories who rapidly developed and provided appropriate IVD devices for viral testing, as IH-IVD assays.<sup>61</sup> This collaboration and distribution of an IH-IVD would not be allowed under the IVDR.

### **Recommendations**

- There is a need for the European Commission to provide more actions towards safeguarding the availability of Class D devices.
- Differential management should be considered for class C and class B IVDs, since only the former are of high individual risk to patients and/or public health, while the latter represent half of all IVDs. Reduction of regulatory complexity for the latter would allow concentration of resources for the assessment of class C and D IVDs, with little or no significant risk to patients or society.

## **22 There is insufficient recognition of established laboratory quality control procedures.**

There has been insufficient recognition by EU regulators of existing laboratory quality management procedures, such as external quality assessment (EQA) strategies for comprehensive monitoring of diagnostic performance. These schemes are well-established by medical professional associations and professional bodies and have been in routine use for decades. They either assess the entire diagnostic workflow in laboratories, including medical interpretation, or they compare analytical performance between laboratories by proficiency testing (PT).<sup>62</sup>

These quality management tools were active before the IVDR but they were not integrated into the regulatory framework. It appears that when the IVDR was drafted, there was insufficient understanding of the current status of European “CLIA-equivalent” laboratories, most (but not all) of which have ISO 15189 certification.

### **Evidence**

According to IVDR Articles 5.5b and c, diagnostic laboratories are required to comply with the harmonised ISO standard EN ISO 15189 regarding analytical quality and

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<sup>61</sup> Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill.* 2020;25(3):2000045. <https://doi.org/10.2807/1560-7917.es.2020.25.3.2000045>

<sup>62</sup> World Health Organization. Laboratory quality management system: handbook. 1 January 2011. Chapter 10: Assessment – external quality assessment. <https://extranet.who.int/lqsi/sites/default/files/attachedfiles/LQMS%2010.%20Assessment%20-%20EQA.pdf>



competence in medical laboratories, or with applicable national conditions. European medical laboratories in various IVD disciplines operate under tight quality regulations, with mandatory adherence.

For independent assessment of laboratory performance and monitoring of diagnostic quality, participation in External Quality Assurance (EQA) programs is usually required. For-profit or not-for-profit EQA providers operate within the EU and beyond. The European umbrella organisation EQALM currently lists 49 full or associated member organisations providing EQA programs.<sup>63</sup> These are often associated with national scientific laboratory societies; for example, the German Reference Institute for Bioanalytics<sup>64</sup>, itself an EN ISO/IEC 17043 accredited conformity assessment body, currently offers 61 different EQA programs covering more than 840 IVD tests across fields such as haematology, clinical chemistry, microbiology and virology, molecular diagnostics, endocrinology, immunology, and pharmacology.<sup>65</sup> Laboratories can subscribe to these schemes, and participate as required by the national guidelines issued by the German Medical Association.

Proficiency testing provides the most comprehensive means for a laboratory to probe and document the quality of its analytical operations. There are EQA formats primarily to assess analytical quality (validity and imprecision) and others to assess medical interpretative skills of findings obtained during the EQA. As subscribing laboratories participate at regular intervals, longitudinal data accumulate for each individual IVD device. This reveals where the laboratory stands in comparison to other participants using the same IVD device or to laboratories using equivalent IVD devices from a different manufacturer. These data are used for laboratory surveillance, but they could be extended or adapted for the surveillance of devices and tests.

EQA organisations provide an EU-wide network for continuous proficiency testing (PT), that allows laboratories to document:

- their own performance for individual diagnostic biomarkers, in comparison with other laboratories using the same or other IVD devices,
- early warning for systematic problems associated with devices and lab operations,
- objective evidential data of quality, and
- areas for improvement and training needs.

Laboratories that fail the EQA test are directly supported to improve their analytical performance. Furthermore, EQA programs provide the best comparability between laboratories using the same IVD device. Different IVD devices for the same biomarker

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<sup>63</sup> See list of European organisations providing EQA at <https://eqalm.org/eqalm/members>

<sup>64</sup> More information available at [www.rfb.bio](http://www.rfb.bio)

<sup>65</sup> See example of program at <https://www.rfb.bio/pdf/2025/RfB-Programmheft-2025-en.pdf>



can be compared on a regular basis, which could support national competent authorities who undertake market surveillance of IVDs.

The importance of EQA and PT has been acknowledged by the WHO, the European Center for Disease Prevention and Control (ECDC)<sup>66</sup>, the European and the International Federation for Clinical Chemistry and Laboratory Medicine (EFLM and IFCC)<sup>67</sup> and many others. In 2023 the IFCC task force on Global Laboratory Quality (TF-GLQ) reported that 21 out of 26 European laboratory societies (EFLM members) who responded to a survey, run national EQA programs, and 23 participate in nationally or internationally organised EQA programs. These cover all major analytical methodologies and diagnostic areas of laboratory medicine. There is evidence that participation in EQA improves the results from IVD devices.

### **Recommendations**

- Regulators should consider using the external quality assessment structures already in place in Europe to support quality monitoring of IVD devices.
- Guidance for IVDs should be prepared to allow aspects of EQA to be extended from evaluation of the users to surveillance of the tests/devices with regard to analytical precision and performance. Retrieval and harmonisation of Europe-wide EQA data could be organized through networking organizations like EQALM. Since provisions made in EN ISO 15189:2022 mandate appropriate internal and external quality assessments for accreditation (chapter 7.3.7.3), dissemination of ISO 15189 accreditation of laboratories throughout the EU will support this.
- The need for proving clinical relevance beyond satisfactory test performance has not been adequately demonstrated for many IVDs; appropriate generic methodologies need to be developed.

### **23 No special provisions have been made for legacy IVD tests.**

The EU regulatory system now requires procedures for the approval and certification of routine laboratory diagnostic tests (legacy IVD tests), which from a clinical perspective is inappropriate since the tests are standard and well-established assays that have excellent diagnostic performance and for which there are no concerns. Stricter compliance requirements for clinical evidence, performance evaluation and post-market surveillance, are unnecessary.

Without addressing the challenges surrounding legacy devices, as a result of implementation of the IVDR, there is a risk that certain standard assays and diagnostic tests will be withdrawn – leading to significant impacts on clinical care and health.

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<sup>66</sup> see ECDC <https://www.ecdc.europa.eu/sites/default/files/documents/EQA-strategy-2018.pdf>

<sup>67</sup> see IFCC TF-GLQ: <https://doi.org/10.1515/cclm-2023-0057>





### **Evidence**

Most legacy devices fall into the risk category class B. They represent 80-95% of the total number of analytical tests routinely performed in the average clinical diagnostic laboratory. These IVD devices are under continuous PT control, both internally and externally and according to national legislation or accreditation rules.

In the medical laboratory, legacy IVD devices are high-throughput tests kept available on consolidated analyser platforms and carried out in a highly automated fashion using closed-loop reagent packs. There is little or no possibility for the technical operator to interfere with the machine's procedures. Depending on the size of a laboratory, several hundred thousand analyses may be performed annually for the most common individual biomarkers (e.g. haemoglobin, potassium, total protein, creatinine, and many others). Dedicated batch-specific calibrators are provided by the IVD manufacturer, with calibrations used automatically or triggered by the technical staff should recalibration be necessary. Repeated calibrations are validated using dedicated control specimens containing defined and verified biomarker concentrations. Only then are clinical specimens investigated.

Long-standing collaborations coordinated by national and international societies have led to the adoption of metrological standards, reference methods and materials, which have improved the analytical traceability of biomarkers. Results from an IVD device are tested using IFCC reference methods, Système Internationale (SI) units of measurement, and certified reference materials (CRM). Results are characterized and distributed by official bodies, national metrological institutes, or commercial sources<sup>68</sup> as the basis for demonstrating analytical validity and safety.

Well-established and highly reliable IVD devices based on these standards are offered by all major diagnostic companies. These legacy devices are typically inexpensive, so they tend to generate less revenue for the manufacturer. Requiring recertification of legacy tests places an analytical and administrative burden on the diagnostics industry, that may risk interruptions and discontinuations of IVD devices that are essential for medical diagnoses in the majority of patients.

### **Recommendations**

- EU regulators should enable notified bodies to grant certificates with conditions for legacy devices, without requiring them to undergo a full conformity assessment ('grandfathering'). The IVD Expert Panel could provide advice on

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<sup>68</sup> For sources of CRM see:

- <https://crm.jrc.ec.europa.eu/>;
- [https://www.sigmaaldrich.com/DE/en/products/analytical-chemistry/reference-materials/certified-reference-materials?srsId=AfmBOoq3\\_Aeti0y6647nOzB\\_75mtiTSNrJEzw8\\_3RHRXcscIvK41M9VS;](https://www.sigmaaldrich.com/DE/en/products/analytical-chemistry/reference-materials/certified-reference-materials?srsId=AfmBOoq3_Aeti0y6647nOzB_75mtiTSNrJEzw8_3RHRXcscIvK41M9VS;)
- <https://www.lgcstandards.com/GB/en>



specific cases. Alternative regulatory pathways are needed for legacy devices with excellent diagnostic performance and no concerns.

### **24 No special provisions have been made for orphan IVD tests.**

The increase in personalised medicine has led to an increased need for orphan IVDs, but the costs of certification or recertification are challenging. Orphan IVDs are produced for small numbers of patients, so manufacturers will have a limited return on investment. Without a special regulatory pathway, there is a risk that patients will lose access to essential diagnostic tests that guide or even determine their treatment. Orphan IVDs include tests for a wide range of inherited genetic disorders, and also biomarkers for cancer.

#### ***Evidence***

Cancer is the second most common cause of deaths in Europe, with about 1.3 million annually, while more than 3 million individuals per year are newly diagnosed. Improved biological therapies and demographic trends will increase the number of patients living with cancer who need to be monitored using therapy-associated diagnostics.<sup>69</sup> The molecular make-up, genetic defects, and paths towards tumour progression and metastasis, differ for individual cancers and for their heterogeneous subclones, so IVD testing will be challenging if it is to be effective.

The fastest growing area in cancer diagnostics is the detection and characterization of DNA and other nucleic acids shed from dying tumour cells into the patient's blood (called "Liquid Profiling" or "Liquid Biopsy"). Diagnostic liquid profiling is becoming a standard-of-care within Europe, as it is capable of answering three major questions in oncology:

- 1) Is there minimal residual disease (MRD) after therapy?
- 2) Is there an imminent tumour relapse, due to newly acquired resistance to therapy?  
and
- 3) Can alternative druggable targets be identified that would allow adaptation of therapeutic regimens?

Most IVD devices for liquid profiling either measure tumour-specific mutations that were identified in the primary tumour tissue (tumour-informed), or they use massive parallel DNA sequencing on the patient's blood (untargeted). The former strategy is limited to detecting pre-defined mutations for which the particular IVD test is designed, while the massive parallel sequencing approach can identify all mutated sequences in body fluids. Tumour-informed tests are approximately 10- to 20-fold more sensitive than

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<sup>69</sup> see European Parliament: <https://www.europarl.europa.eu/topics/en/article/20200131STO71517/>



sequencing, so they can detect occult tumours earlier, whereas untargeted approaches provide far more molecular information.

This emerging field of cancer diagnostics is characterized by the development of analytical technologies, but with the potential need to adapt a given IVD device to detect tumour-specific genetic defects in each patient. This may generate an unforeseeable number of new IH-IVDs, mostly used to detect rare sub-populations of each category of cancer. They will qualify as orphan IVDs.

### **Recommendations**

- A special regulatory pathway should be created to facilitate the conformity assessment of rare, niche, or orphan IVDs.
- Pre/early certification access models should be developed (equivalent to conditional approval), preferably in collaboration with academic diagnostic experts, the IVD Expert Panel, EU Reference Laboratories, the European Rare Disease networks (ERN), and EU regulators.
- Validation should be focussed on the analytical methods underlying the IVD device, rather than its specific molecular targets. Otherwise, every single molecular deviation would need its own validation, which would be impossible.

### **25 Procedures for removing outdated tests should be implemented.**

There is no standard process for removing outdated IVD tests from the market. This is not the responsibility of the European Commission, but it could perhaps be a task for national authorities which oversee the delivery of health care, or a responsibility of the notified body to suspend a certificate. Such “diagnostic pruning” could also result from good prescribing guidelines developed by relevant medical experts.

### **Evidence**

The advent since the 1990s of troponins as specific biomarkers of myocardial damage has transformed the diagnosis of acute coronary syndromes and myocardial infarction. Previously, less specific markers were used, including the MB isoenzyme of creatine kinase (CK-MB). Troponins have exquisite sensitivity, but CK-MB is still available – unnecessarily.

A 2010 French national Cancer Institute program on judicious prescribing in haematological cancers classified tests into those that were “indispensable, when clinically appropriate; state of the art; under evaluation within clinical trials; and



obsolete”<sup>70</sup>. Such categorisation lends itself to regular updating, and could be linked to clinical guidelines developed by European specialist societies.

### **Recommendation**

- There should be a framework for removing obsolete IVD devices from the market.

### **26 There is no special pathway for the approval of in-house developed tests.**

The IVDR provides limited flexibility for in-house developed tests (IH-IVD; also referred to as Lab-developed tests or LDTs, which is the term preferred in the USA).

IH-IVDs allow appropriate diagnostic testing to be performed for a patient when there are no suitable CE-certified commercial devices. IH-IVDs can correspond to modified CE-certified tests, RUO devices (research use only) used for diagnostics following validation by the IH-IVD user, or an IVD device developed by the user to accommodate the needs of smaller patient cohorts – in order to improve evidence-based diagnostics of rare and/or complex diseases, such as orphan diseases or cancer. IH-IVD are validated in specialty (often academic) laboratories which have developed analytical excellence in a specific diagnostic field due to long-standing research interests. Most IH-IVD devices are based on genetics tests, but they may also be used for immunochemical detection of biomarkers by specific antibodies, where their detection and quantification are often influenced by the ‘matrix composition’ of the specimen (e.g. whole blood, serum, plasma, other bodily fluid).

The previous EU Directive on In Vitro Diagnostic Medical Devices (IVDD) (98/79/EC) required a third-party (notified body) assessment for only a small number of IVDs, and allowed self-certification without NB assessment for the vast majority of IVDs. It did not regulate in-house IVDs (“devices manufactured and used only within the same health institution”, see article 1.5 IVDD).

The IVDR exempts IH-IVDs from most requirements that apply to CE-marked devices, but these are replaced by specific provisions outlined in article 5.5. Those discourage test development, whether to compensate for shortages in the availability of commercial tests or to provide innovative diagnostic tests, because of administrative obligations and uncertainty regarding sustainability.

More specifically, Article 5.5d mandates that health institutions justify their use of an IH-IVD even when an equivalent CE-marked device is not available or does not meet the needs of a target patient group. Key terms such as “equivalent” and “patient-specific needs” are not defined, which limits the basis upon which laboratories can develop an optimal mix of CE-IVDs and IH-IVDs.

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<sup>70</sup> Macintyre E. Les guides de juste prescription du Réseau de biologie innovatrice en onco-hématologie (RuBIH, programme STIC 2004-9. *Hématologie* 2010;16:102. <https://doi.org/10.1684/hma.2010.0491>



### **Evidence**

A study by the central laboratory of a large academic health care provider evaluated the IVD devices used to generate 11.5 million test results per year <sup>71</sup> :

- Only 42% of 922 tests in use were carried out using CE-certified IVD devices.
- 537 (58%) of the 922 laboratory tests were IH-IVDs (or LDT), of which more than 70% had no alternatives on the market, particularly in specialty testing areas like flow cytometry, special chemistry, and molecular diagnostics.

In the USA, the FDA is permitted to practise “enforcement discretion” for LDTs, albeit under increasingly restricted circumstances following a ruling in May 2024.<sup>72</sup>

Lack of flexibility in the EU can be demonstrated by a current example concerning companion diagnostics for the anti-cancer drug Elacestrant (Oserdu, Menarini) used for a highly specific therapy of Her/2negative, Estrogen receptor (*ESR1*)-positive metastatic breast cancer in postmenopausal patients who have failed one round of previous endocrine therapy including a CDK4/6 inhibitor. To stratify these women for therapy, activating *ESR1* receptor mutations need first to be identified. The decision requires the specific identification of *ESR1* mutations in the blood by Liquid Biopsy (and not by molecular histopathology). Such tests, which impact the use of drugs for individual patients, are known as theranostic or actionable markers. At the time of market approval of Elacestrant, no CE-certified test was available, which forced medical laboratories to establish them as IH-IVDs. In addition, and as mandated by Article 5(5)a (“...devices are not transferred to another legal entity”), availability to *ESR1* testing was restricted to each individual laboratory, with probable variations in performance specifications and potential consequences for biospecimen tourism, delay in diagnostic turn-around-time, data and biomaterial safety issues, and a risk of incorrect results due to preanalytical quality issues.

As a consequence, the German RfB has included *ESR1* mutation detection in the blood into an EQA program in August 2024, confirming the ability of the medical diagnostic community to react to the challenge, and also the value of the EQA circuit – all without reference to the IVDR. Similar examples exist for many cancer biomarkers, such as leukaemia and lymphoma, whereby not-for-profit EQA providers encourage and evaluate optimised, standardised diagnostic practices.<sup>73</sup> Similar strategies should be

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<sup>71</sup> Vermeersch P, Van Aelst T, Dequeker EMC. The new IVD Regulation 2017/746: a case study at a large university hospital laboratory in Belgium demonstrates the need for clarification on the degrees of freedom laboratories have to use lab-developed tests to improve patient care. *Clin Chem Lab Med*. 2020;59:101-106. <https://doi.org/10.1515/cclm-2020-0804>

<sup>72</sup> See details in <https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests>

<sup>73</sup> Alary AS, Maute C, Kosmider O, et al. Improvement of standardization of molecular analyses in hematology: The 10-year GBMHHM French Experience. *Hemasphere*. 2021 Nov 17;5(12):e658.



supported within the EU regulatory framework for IVDs.

Every hospital laboratory will adapt CE-marked IVDs in certain circumstances, particularly with paediatric samples (low volumes) and non-blood samples (e.g. cerebrospinal fluid (CSF); or urine). All academic hospital labs will use IH-IVDs, with the proportion varying by specialty.

A survey of European laboratories published in 2022 by the Biomedical Alliance showed that the most frequently performed tests were CE-marked IVDs (50%), but about 25% of tests were IH-IVD, and 25% were modified CE-IVD/RUO. IH-IVD use was most frequent in genetics, pharmacology and microbiology.<sup>19</sup>

### **Recommendations**

- Additional support and provisions are necessary to help laboratories comply with regulatory requirements when using IH-IVDs. The responsibility for interpretation and execution of an IH-IVD test should be assigned to ISO15189-accredited members of professional societies and their working groups, since they have a clear understanding of evidence-based laboratory medicine (EBLM).
- Article 5.5 of the IVDR should be amended. Conditions (d) to (i) for in-house exemptions and also (a), should be removed. Failure to do this will increase healthcare costs and jeopardize ability to design personalized laboratory tests (necessary for precision medicine) and to adapt to shifting test needs (as happened with the repurposing of instruments for Covid-19 testing).
- Conditions (b) and (c) of Article 5.5 should be retained.
- A policy that is equivalent to “enforcement discretion” could be applied for laboratories which have demonstrated a clear application of regulatory requirements, which have sufficient annual activity to assure appropriate experience, and which participate satisfactorily in relevant EQA and surveillance of regional/national/European activity within their field of reference. This non-exhaustive description of what might be considered ‘reference laboratories’ (subject to periodic review of their reference status) should be considered for rare tests (whether CE-IVD or IH-IVD), thereby protecting regulatory capacity for surveillance of higher-throughput tests. The clearest example of such a category is the blood transfusion reference laboratories, which have been highly regulated for decades and which work with ascending degrees of centralisation of rare blood cell typing.

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[https://journals.lww.com/hemasphere/fulltext/2021/12000/improvement\\_of\\_standardization\\_of\\_molecular.6.aspx](https://journals.lww.com/hemasphere/fulltext/2021/12000/improvement_of_standardization_of_molecular.6.aspx)



### **27 Incentives are needed to promote academic development of new tests.**

Article 5.5(d) in the IVDR may discourage academic laboratories from continuing to develop and implement new tests, since they have to justify that no equivalent device is available. Once a commercial alternative has been marketed and its non-inferiority has been documented, production of a test that was developed in an academic institution or hospital should be discontinued, unless otherwise justified. A lower cost of testing is considered insufficient justification, which may lead to spiralling diagnostic budgets. Inadvertently, the IVDR may have provided disincentives for competition, and the risk of monopoly providers.

Since IH-IVD are not admitted to the market and are allowed to be used only within the confines of the health organisation, it can be expected that new specimens will be sent from other institutions for diagnostic testing. Such traffic within the EU would be costly, but more importantly could pose problems such as the safety of data, potential biomaterial safety issues (for class C and D devices), delayed or disrupted diagnostic procedures, and unclear influences of preanalytical nature due to biomolecular decay.

#### ***Evidence***

There is no indication that laboratories will be capable of mustering constant market surveillance to defend their IH-IVD (prior to EUDAMED being fully established).

A major problem is the requirement to show equivalency of IH-IVD with commercial tests once they are available. This puts the burden of proof squarely on the laboratories, and it will be impossible to prove equivalency without extensive studies. It would be necessary to show that the local study is comparable to studies used by industry to put their new tests on the market. Even the establishment of a new IH-IVD that is required because a commercial device on the market is unsuitable for clinical diagnostic purposes, would require the laboratory to show equivalency or lack thereof. Hospital laboratories do not have staff, resources or budget to meet this obligation. IH-IVD devices may be abandoned quickly because there is usually no economic benefit for the local laboratory from continuing to perform the test.

Diagnostic laboratories also face challenges due to the increased administrative burden and requirements of the IVDR, especially for smaller laboratories with limited resources. The need to invest in continuous education and training for staff, to keep up with new processes, will bring additional costs. Laboratories may find it difficult to interpret, implement and comply with the IVDR, especially if they do not receive adequate guidance from regulatory authorities.

#### ***Recommendation***

- IH-IVD categories should be evaluated by the reviewers of ISO 15189 accreditation bodies. Appropriate EQA should be provided so that hospitals can specify their methods and demonstrate delivery of reproducible results.



- Certification under ISO 15189 should suffice with respect to activity as specified in Article 5.5(b) and 5.5(c).
- Recognition of reference laboratories and networks for IH-IVDs and rare tests will ensure progressive harmonisation of practices and standardisation of results.
- EU medical device regulators should participate in the development and review of the ISO 5649 standard on IH-IVDs. Once finalised, this document will support regulatory surveillance of IH-IVD activity.

### **28 General regulatory guidance is needed for IVDs.**

There are EU guidance documents for some class D tests, but there is persisting uncertainty about general requirements for many IVDs – such as how to demonstrate clinical relevance beyond analytical precision and performance studies. This is linked to the need to identify appropriate HTA of IVDs, in addition to technical efficacy and diagnostic accuracy (which are both required for market authorisation). It requires evidence of clinical performance (also included in the IVDR), when results have a positive impact on treatment and on health outcomes, at both individual patient and societal levels.

#### ***Evidence***

Gaps that are perceived in existing EU guidance for IVDs include:

- How to implement quality assurance systems into post-market surveillance.
- How to assess IH-IVD performance.
- How to fix the imbalance between hospital laboratories and manufacturers regarding proof of equivalency.
- How to remove obsolete IVDs through scientific test evaluation.

#### ***Recommendations***

- The IVD Working Group of MDCG should produce guidance on the interface between regulatory market approval (including how to establish clinical utility) and HTA assessment.
- More specialised Expert Panels should be established, in place of the present single IVD panel. As a minimum, these would include clinical chemistry, genetic testing, infectious diseases, and cell/tissue-based methodologies. Their remit can be extended.





## 6. Functions of a new regulatory support structure

**There is a clear need for a new body to manage the EU regulatory system.**

Notified Bodies have gained responsibilities, functions and workload under the MDR and IVDR, but they are private companies which are designated by the same Authorities that oversee their performance. Cooperation and coordination are foreseen through the Notified Body Coordination Group (NBCG-MED), but they do not go far enough to address lengthy procedures, excessive costs, and comparability of reviews. It would now be extremely difficult and expensive to remodel the system completely since the NBs already employ 2,881 staff in 44 NBs to perform conformity assessments.<sup>74</sup>

Many of the recommendations in this document would be unnecessary if an adequate support structure for the MDR and IVDR had been created. There are too few expert staff in the unit in DG SANTE, and insufficient contributions from national regulatory experts.

**The option that is preferred, and recommended by the BioMed Alliance is to:**

- **Establish a medical devices division of EMA.**

The EMA is already managing the Expert Panels, so it is well placed to assume a broader management role to coordinate the regulatory system for medical devices. There would be considerable overlap with existing programmes within the EMA, for ‘regulatory science’ initiatives. This option would also be the least disruptive.

The EMA was known first as EMEA; now it could become “EMDA”  
(for the **European Medicines and Medical Devices Agency**) ..

Other options that have been considered but which are *not recommended* include:

- An expanded unit within the European Commission [but no precedent of a similar model, too few personnel, and budgetary constraints].
- A medical device agency (as a completely new EU agency) [which would be expensive, duplicative, and need a lengthy process to establish].
- Delegation to a national regulatory authority, with assigned responsibilities for the whole system [no better than a new agency].
- Development of a new structure managed collectively by the notified bodies [but NBs compete, and this reform would not guarantee transparency and predictability].
- A unit within the EU Joint Research Centre [would also be de novo, hence no benefit].

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<sup>74</sup> <https://www.team-nb.org/team-nb-2024-in-a-few-facts-and-figures/>



### **The functions of an enhanced, new European regulatory secretariat could include:**

- Provision of early dialogues (expanding the pilot initiatives led by the EMA).
- Management of scientific opinions from Expert Panels (already started by EMA).
- Development and coordination of specialist regulatory communities (with experts from notified bodies, medical associations and learned societies, doctors in regulatory agencies, and members of Expert Panels; “public-facing”).
- Oversight of specialist expertise within national regulatory agencies.
- Designation of lead agencies for specific (rare) device types.
- Designation of specialist responsibilities of individual notified bodies.
- Identification, supervision of preparation, and maintenance, of common technical specifications and other regulatory guidance on scientific methodologies.
- Coordination of joint approvals of clinical trials being conducted across the EU, and collaboration with Research Ethics Committees to develop combined procedures for ethical approval (through MedEthicsEU, which consists of member state representatives and whose remit covers both medicines and devices<sup>75</sup>).
- Coordination of the engagement of EU experts in the preparation of international standards (nominating members from academia and/or European specialist medical associations, and/or from regulatory agencies, and financially supporting their participation).
- Coordination of special clinical investigations and performance studies.
- Determination of eligibility for access to special regulatory pathways.
- Management of a special pathway for breakthrough or innovative devices.
- Designation and supervision of regulatory sandboxes.
- Management of a special pathway for orphan and paediatric devices.
- Maintenance of a register of approved European medical device registries.
- Maintenance of a register of not-for-profit European External Quality Assessment providers (for IVDs).
- Collection and analysis of real-world data on clinical outcomes related to devices.

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<sup>75</sup> [https://health.ec.europa.eu/medicinal-products/clinical-trials/medethicseu\\_en](https://health.ec.europa.eu/medicinal-products/clinical-trials/medethicseu_en)



## Biomedical Alliance in Europe

- Coordination of vigilance and market surveillance by EU regulatory agencies.
- Oversight of a mechanism to ensure that manufacturers meet any conditions that are placed on their certificates of conformity by notified bodies, or else the certificates are withdrawn and the device(s) taken off the market.
- Coordination with HTA agencies for joint reviews of clinical evidence.
- Coordination of EU participation in MDSAP, and other IMDRF projects.
- Leading the participation of EU medical device regulators in initiatives for global harmonisation of standards and approval processes for medical devices and *in vitro* diagnostic devices.
- Acting as a point of contact particularly for small and medium-sized enterprises and manufacturers of orphan devices and paediatric devices.



## 7. Conclusions

The first EU regulations for medical devices were developed during the late 1980s by a small team based in Directorate III of the European Commission. At that time, there was no medical expertise available within the Commission, so they arranged support from an *ad hoc* advisory committee. Together, these individuals were directed to develop proposals for a system that would apply the “New Approach” which had been adopted by the Council in 1985 as part of a drive to complete the internal market across the European Economic Community by 1992.<sup>76</sup> Medical devices were considered like any other manufacturing sector, and certification was delegated to notified bodies.

The regulatory framework for medical devices that exists now in the European Union is unlike that in any other major regulatory jurisdiction around the world, and it is very different from the system that is applied to evaluate new pharmaceutical products. From a clinical perspective such differences are illogical, as the need and methodologies required to establish that high-risk devices are safe and effective do not vary. The continuing challenges of implementing a regulatory system in Europe that is ‘fit for purpose’ can be traced back to the implications of the original decisions.

If a new system was being planned from first principles, it would probably not resemble the current structure – but a major upheaval would not be constructive. Instead, it is crucial that any further reforms of the EU regulations for medical devices and *in vitro* diagnostic medical devices should correct all the major deficiencies. If not revolution, then substantial evolution remains necessary.

The absolute priority – without which any other measures may fail – is to increase medical, scientific and managerial capacity significantly, preferably by establishing a dedicated division within the European Medicines Agency (which could become the “European Medicines and Medical Devices Agency”). Specialist regulators should have the capacity to engage with, and benefit from, much more clinical expertise. They should be qualified to prepare common specifications for specific types of devices, to advise developers, and to ensure that consistent standards are applied by notified bodies. Evidence-based regulation, as outlined in the recommendations that have been detailed in this report, should be proportionate to risk.

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<sup>76</sup> Fraser AG, Redberg RF, Melvin T. The origins of regulations for pharmaceutical products and medical devices – what can be learned for the governance of medical devices in Europe? *European Review* 2025 (in press).