Biomedical Alliance in Europe

October 2025

Towards an MDR and IVDR that provide high-quality care for patients while supporting safe and effective innovation

Biomed Alliance response to the Call for Evidence on Medical devices and in vitro diagnostics – targeted revision of EU rules

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Executive summary

The BioMed Alliance supports the objectives of the Medical Device Regulation (MDR) and In Vitro Diagnostic Regulation (IVDR) to safeguard patient safety and ensure innovation. However, implementation has revealed significant challenges that must be addressed to protect patients' access to safe, effective, and innovative technologies.

The most pressing need is **central coordination at EU level**. Unlike the pharmaceutical sector, the current EU system for medical devices lacks a robust, centralised scientific and clinical authority. Fragmented advice from national authorities and notified bodies creates inefficiency, unpredictability, and duplication, with negative consequences for both patient safety and innovation.

The **EMA is best placed** to assume this role. It already manages the Expert Panels and has a proven track record in regulatory science. Expanding EMA's remit to establish a **medical devices division** would provide the expertise, structure, and oversight which is urgently needed. This division should:

- Offer early EU-level scientific and clinical **advice to developers**.
- Coordinate and strengthen the work of **Expert Panels**.
- Coordinate involvement by clinical assessors from notified bodies and National Competent Authorities, together with Expert Panels to provide advice and develop **guidance**.
- Lead the development of **common specifications** and **methodological frameworks** for clinical evidence.
- Oversee **special regulatory pathways** for breakthrough, orphan, and paediatric devices.
- Provide a **single point of contact** for healthcare professionals and patients to report shortages, safety concerns, or device discontinuations.

Beyond central coordination, the revision of MDR and IVDR should focus on:

- **Transparency of evidence:** Full publication of clinical studies and clinical evaluation reports is essential to support evidence-based practice.
- **Proportionate requirements:** A methodological framework and common specifications are needed for medical devices; for IVDs, utilisation of laboratory quality data for post-market surveillance, and a patient-focus for in-house IVDs is needed.
- **Support for new technologies in special circumstances:** Specific pathways and requirements must be provided in legislation for breakthrough, orphan, and paediatric medical devices, and for niche IVDs.
- **System sustainability:** A harmonised EU approach is required for issues such as the safe reprocessing of single-use devices, reducing waste and unnecessary costs.

Europe's patients and healthcare systems need a regulatory framework that is predictable, science-based, and sustainable. Establishing central coordination at EMA is the single most important step to achieve this. Without it, fragmentation will continue to hinder access to safe and innovative medical technologies.

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Introduction

The BioMed Alliance published an analysis and recommendation document in March 2025 ‘: "Review of the EU medical device regulations – Analysis and recommendations from the Biomedical Alliance in Europe",[1] and an open letter with other stakeholders in September 2025. [2] We believe the conclusions and recommendations of these documents remain valid, and we call on the Commission to consider them as they prepare their proposal for the revision of the regulations.

We have reviewed the European Commission’s proposed aims for the revision as described in the document accompanying the call for evidence. We support the intention to improve the availability of devices and streamline procedures, however we reiterate that the goal of robust standards for safety and clinical evidence must be preserved.

The recommendations presented in this document have been based upon the aims of the European Commission for the revision of the legislation, which are as follows:

- reduce the administrative burden including reporting obligations;
- enhance the predictability and cost-efficiency of the certification processes of notified bodies;
- make the conformity assessment requirements more proportionate, especially for low- and medium- risk devices and those that cater to special patient needs;
- enable further digitalisation;
- streamline procedures including those on governance;
- enable the EU medical device sector to benefit from international cooperation including reliance, where appropriate;
- better align the regulatory framework with other relevant legislation.

Our key recommendations are summarised below as follows:

- Recommendations for the MDR.
- Recommendations for the IVDR.
- Recommendations for the regulatory system.

[1] See: https://www.biomedeurope.org/news/press-release-biomed-alliance-calls-for-the-establishment-of-a-new-coordinating-mechanism-within-the-european-medicines-agency-to-tackle-deficiencies-at-the-heart-of-mdr-and-ivdr/

[2] See: https://www.biomedeurope.org/news/users-of-medical-devices-call-for-urgent-reform-to-eu-medical-devices-regulation-mdr/

Recommendations for Medical Devices

1. Clinical and scientific co-ordination and advice on an EU basis are essential for a proportionate and predictable regulatory system

For developers planning a clinical investigation, advice from National Competent Authorities is fragmented and typically procedural. This is in marked contrast with international regulatory systems such as the US FDA, who can advise on acceptable clinical study design. This allows developers to proceed with greater confidence and clarity, unlocking funding and supporting translational development.

For market entry, 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 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 to the totality of clinical evidence presented in the Clinical Evaluation Report rather than the 'Clinical Evaluation Assessment Report' that they are currently permitted to see under MDR.

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. Concerningly, there have been cases in which a negative opinion was issued with respect to the sufficiency of clinical data, where the device appears to have been CE-marked.

Evidence

The current Team-NB Code of conduct (2024) clarifies that a notified body cannot discuss with a manufacturer its clinical development strategy for a new device.[3] 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, rationales and justifications on an average of 2-3 occasions. That significantly prolongs the duration of the review and increases its inefficiency; it should be avoidable.

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.

[3] 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

Recommendations

- It should be possible to obtain specific advice on an EU-basis from a central body that utilises notified body, National Competent Authority and Expert Panel expertise. This must be available, before submitting an application for a clinical investigation and before submitting a dossier for conformity assessment. This can be supported by specialist expertise from European clinical associations.
- 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.
- 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 to all devices and made permanent, so that they can support more manufacturers in the early stages of their route to conformity assessment.
- Expert Panels provide independent opinions on whether devices should be designated as an orphan device; this should also be used for the designation as a breakthrough device – thereby acting as unbiased gatekeepers for access to special regulatory pathways.

2. Transparency of clinical evidence is vital to the regulatory system

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 and 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.[4] These reviews demonstrated limited clinical evidence available in published literature.

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.

Recommendations

- The Clinical Evaluation Report should be publicly available. This will allow clinicians to see the evidence base for approval of medical devices, and it will allow developers to understand the clinical evidence that has been accepted by notified bodies for market access. This could take the place of the SSCP, which is poorly available in practice and hence reduce administrative burden. This would also empower health-technology assessment bodies to have a more complete understanding of the evidence base used to support market-entry.
- Notified bodies should be given authority to require manufacturers to 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 supporting market access 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.[5]
- 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

[4] For further information, see: https://www.biomedeurope.org/news/press-release-biomed-alliance-calls-for-the-establishment-of-a-new-coordinating-mechanism-within-the-european-medicines-agency-to-tackle-deficiencies-at-the-heart-of-mdr-and-ivdr/

[5] See, for example Siontis 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

recalls from the websites of EU and non-EU regulators.[6,7] Sustainable funding should be found for the maintenance of this useful resource.

3. Clarify clinical evidence requirements by preparing common specifications

Common specifications have not been developed for general medical devices. Common specifications have been prepared for IVDs and for 'Annex XVI' devices which do not have a medical purpose.

The lack of common specifications appears to be due to the lack of scientific and medical workforce and regulatory capacity to coordinate their preparation, whether in the unit in the European Commission and/or offered from the EU national regulatory agencies. Providing clinical evidence requirements *a priori* would ensure minimal safety standards for medical devices, clarify the development strategy for developers, and reduce the administration and cost of notified body assessments.

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.

Recommendation

- An EU-level central body must be utilised to identify the guidance and common specifications that are needed, and then to ensure that it is prepared with scientific experts, according to an efficient timetable.

4. A standard methodological framework is needed for clinical evaluation

An extensive review by CORE–MD demonstrated that regulatory guidance documents almost always recommend only general principles.[8] The final recommendations from the CORE-MD project have been published, describing methodologies for clinical investigations of high-risk medical devices in a phased approach (See Figure), with specific recommendations for

[6] 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

[7] 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

[8] 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

breakthrough and orphan devices.[9]

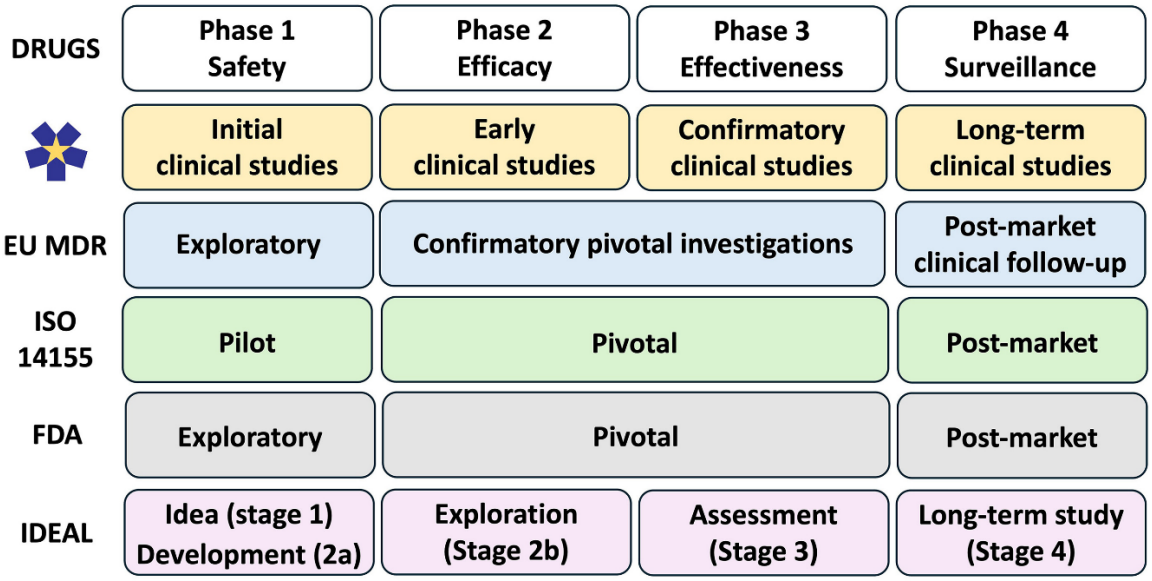

Figure 1. Comparison of terminologies for stages of clinical evaluation of new drugs and medical devices.

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 a subjective determination) and typically using observational study designs that are incapable of allowing valid claims of efficacy, effectiveness or clinical performance. In order to simplify the regulatory system, make clinical developments clearer, and hence reduce costs, the following are needed:

Recommendations

- Identify which types of medical devices require clinical trials designed to demonstrate clinical safety *and* efficacy (or effectiveness). This will streamline requirements with the HTA Regulation.
- 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.
- Identify the types of lower-risk medical devices which do not need pre-market clinical

[9] Recommended methodologies for clinical investigations of high-risk medical devices—Conclusions from the European Union CORE–MD Project. Fraser AG, et al. The Lancet Regional Health Europe, 2025. doi: 10.1016/j.lanepe.2025.101460 https://www.thelancet.com/journals/LANEPE/article/PIIS2666-7762(25)00252-2/fulltext

investigations.

- Utilise the CORE-MD approach for high-risk devices, and develop, publish and implement a scientific methodological framework for the clinical evaluation of lower-risk medical devices. This should place greater reliance on observational studies and post-market monitoring for surveillance of safety and clinical outcomes.
- Apply this methodological framework to specific technology domains, to understand differences between current and expected evidence, and determine when common specifications or guidance are needed. An example produced at the request of EU regulators was a report on coronary stents.[10]
- 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.

[10] 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

Recommendations for IVDs

1. Established laboratory quality control procedures can simplify and streamline post-market surveillance for both CE-marked and in-house IVDs

European medical laboratories in various IVD disciplines are subject to stringent quality regulations. This includes internal and external quality assurance, with mandatory adherence in many countries, and compliance with EN ISO 15189, or national equivalents

In 2021, approximately 70% of academic hospital laboratories were in the process of ISO 15189 accreditation.[11] Utilising ISO 15189 accreditation to allow laboratories to comply with IVDR will simplify procedures, reduce bureaucracy, avoid confusion, and limit costs. Measures to harmonize EU application, in partnership with the European Accreditation Association,[12] will support the use of innovative diagnostics in clinical trials, thus attracting research and innovation to Europe. While accreditation is currently focussed on CE-marked IVDs, some Member States and centres also accredit their IH-IVDs. Dissemination of such practice will contribute to harmonized, reproducible and commutable confidence in IH-IVD results, and will support developers' readiness to work with European diagnostic laboratories, as empowered by initiatives such as the COMBINE program.

In addition to independent assessment of laboratory performance for obtaining accreditation, participation in External Quality Assurance (EQA) programs is usually required. For-profit and not-for-profit EQA providers operate across the EU and beyond, providing a multitude of quality assessment programs such as proficiency testing (PT) for analytical accuracy and precision.[13] As such, they are similar to CLIA evaluation in North America. Unfortunately, these quality management tools existing in the in-vitro diagnostic fields were not integrated into the IVDR regulatory framework.

For many IH-IVDs (including those based on modifications of CE-labelled tests), EQA subscriptions are available, allowing IH-IVDs to be integrated into established quality programs. In other cases, specialty EQA are available within the respective academic laboratory networks. By participating at regular intervals (6-weekly to annually, depending on the biomarker) in EQA rounds, longitudinal data accumulate in each laboratory. These data are currently used locally by laboratories but could be extended or adapted for the post-market surveillance of IVDs on a broader scale. This could provide a system allowing for:

- Improved and streamlined post-market IVD surveillance;
- Improved data curation and commutability initiatives between laboratories;

[11] Dombrink et al. Critical Implications of IVDR for Innovation in Diagnostics: Input From the BioMed Alliance Diagnostics Task Force. HemaSphere 6(6):p e724, June 2022. DOI: 10.1097/HS9.0000000000000724
[12] See https://european-accreditation.org/
[13] 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

- Significant savings for documentation since these data are currently generated independently for the medical laboratory and by each manufacturer for the individual IVD.

Evidence

According to IVDR Articles 5.5b and c, diagnostic laboratories are required to comply with the harmonized ISO standard EN ISO 15189 regarding analytical quality and competence in medical laboratories, or with applicable national conditions.

The European umbrella organization EQALM currently lists 49 full or associated member organisations providing EQA programs.[14] These are often associated with national scientific laboratory societies; for example, the German Reference Institute for Bioanalytics (RfB),[15] itself an EN ISO/IEC 17043 accredited conformity assessment body, currently offers 61 different EQA diagnostic programs,[16] and the COFRAC French equivalent recognizes 20 EQA providers.[17]

The importance of EQA and PT has been acknowledged by the WHO, the European Centre for Disease Prevention and Control (ECDC),[18] the European and the International Federation for Clinical Chemistry and Laboratory Medicine (EFLM and IFCC)[19] and many others. In 2023 the IFCC task force on Global Laboratory Quality (TF-GLQ) reported that:[20]

- 21 out of 26 European laboratory societies (EFLM members) who responded to a survey, run national EQA programs.
- 23 participate in nationally or internationally organized EQA programs covering 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 (EQA) structures already in place in Europe to support post-market surveillance of IVD devices.

➢ Aspects of EQA should be extended from evaluation of the laboratory users to surveillance of the IVDs products with regard to analytical precision and performance. Retrieval and harmonization of Europe-wide EQA data could be administrated through or with the support of networking organizations like EQALM. Since provisions made in ISO 15189

[14] See list of European organisations providing EQA at https://eqalm.org/eqalm/members
[15] More information available at www.rfb.bio
[16] See https://www.rfb.bio/pdf/2025/RfB-Programmheft-2025-en.pdf
[17] See https://tools.cofrac.fr/documentation/sh-inf-19
[18] See https://www.ecdc.europa.eu/sites/default/files/documents/EQA-strategy-2018.pdf
[19] See https://doi.org/10.1515/cclm-2023-0057
[20] See IFCC TF-GLQ: https://doi.org/10.1515/cclm-2023-0057

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.

2. There needs to be appropriate, harmonised and coordinated regulatory capacity and expertise to evaluate CE-marked IVD in a risk-proportionate fashion.

The IVDR classifies IVDs based on risk (class A-D), with 70% of tests in low-risk categories A or B. The massively increased workload required to certify well-established IVDs represents significantly increased bureaucracy and costs, and a risk that resources may not be prioritized for high-risk class C and D devices.

Recommendations

➢ Differential management should be considered for class C and class B IVDs, since only the former is of high individual risk to patients (and neither to public health), while the latter represent half of all IVDs. Reduction of regulatory complexity for class B would allow concentration of resources for the assessment of class C and D IVDs, with little or no significant risk to patients or society.

3. No special provisions have been made for orphan/niche IVD tests

The development of personalized medicine is leading to a constantly increasing need for more individualized diagnostic testing. By definition, the respective IVDs are so-called “rarely used”, “niche” or “low volume” tests (referring to them as orphan tests is misleading, as this designation does not fit the term “orphan” as used in the context of orphan diseases, orphan medical devices or orphan drugs). We will refer to these tests as “niche IVDs”, which include tests for a wide range of rare inherited genetic disorders but also individualized diagnostic biomarkers in common and rare cancers.

The costs of establishment, validation, certification or recertification of niche IVDs are challenging. Niche IVDs are produced for small numbers of patients, leaving manufacturers with insufficient or limited return on investment.

Without a special regulatory pathway, there is a risk that patients will lose access to essential specialty diagnostics that guide or even determine their treatment. The concept of ‘actionable’ is used here when referring to an IVD result that can directly determine individual patient management and trigger therapeutic action by the treating physician.

Evidence

Cancer patients increasingly need disease monitoring at timely intervals by actionable niche IVDs.[21] In some situations, the IVD may even be specific to an individual patient, and these tests are virtually always IH-IVD (see below). The most promising 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?
3) Can alternative druggable targets be identified that would allow adaptation of therapeutic regimens?

Without a special regulatory pathway for relatively low throughput, niche IVDs, there is a risk that patients will lose access to essential actionable diagnostic tests that guide/determine their individual treatment.

Most IVD devices for liquid profiling start as IH-IVD, particularly when considering individualized test-set ups, but many of those with sufficient frequency of uniform testing should be transferred to the manufacturing sector as CE-marked IVDs.

Recommendations

➢ A special regulatory pathway should be created to facilitate the conformity assessment of rare/niche IVDs by notified bodies and expert panels.

➢ Pre/early certification access models should be developed (equivalent to conditional approval), preferably in collaboration with appropriate diagnostic experts in expanded/adapted IVD Expert Panel(s) and EU Reference Laboratories.

➢ Validation should be focussed on the analytical methods underlying the IVD test, rather than its specific molecular targets. Otherwise, every single molecular deviation would need its own validation, which would be impossible.

4. Facilitate the use of in-house developed tests and related reporting

The IVDR limits clinically necessary in-house IVD (IH-IVD) testing. IH-IVDs allow the appropriate testing of diagnostic biomarkers when there are no suitable CE-marked IVDs to test a patient. An IH-IVD may correspond to a modified CE-certified test, an RUO (research use only) device validated for diagnostic use or an IVD device developed "from-scratch" to accommodate the needs of a smaller patient cohort. IH-IVD are developed and validated in specialty (often academic) laboratories based on their methodological excellence or long-standing research interest in a specific diagnostic field in diagnostics in the blood or specialty

[21] See European Parliament: https://www.europarl.europa.eu/topics/en/article/20200131STO71517/

biospecimens (e.g. cerebro-spinal fluids, CSF) or "minuscule specimen volumes" (e.g. in paediatrics).

While the IVDR exempts IH-IVDs from most requirements that apply to CE-marked devices, it defines specific provisions outlined under various subheading within Article 5.5.

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-marked IVDs and IH-IVDs. Article 5.5d is a significant disincentive to establishing and validating innovative IH-IVDs because it is unclear how long this test can be used before a CE-marked IVD is placed on the market for the intended purpose, as development costs do not justify a short-term use.

Article 5.5.d presumes a gold standard to any CE-marked IVD, which brings about a significant paradigm shift that does not place the choice and use of the most effective and appropriate diagnostic test for the individual patient on the side of the physicians responsible and liable for the diagnostics, but ascribes it to industry, which naturally also pursues market interests. As a result, if there is a CE-marked IVD that only targets a specific population (eg. adults) and the health institution's target population also includes other patients (eg. paediatric) the health institution would have to conduct two tests: the CE-IVD for adults and the IH-IVD for children, which increases costs and documentation.

If there is a CE marked device for test A (e.g. an immunophenotypic panel for leukaemia characterisation) which is linked to a (often expensive) platform A, whereas another CE marked device for test B (e.g. an immunophenotypic panel for MRD diagnostics in leukaemia) which is linked to a distinct (equally expensive) platform B, the health institution has to buy and maintain both platforms, with smaller batch sizes, poorer experience per platform, non-commutability of data, need for parallel documentation, and maintenance and increased costs for the healthcare system and, ultimately, the patients.

Evidence

In a central laboratory of a large academic health care provider generating 11.5 million test results per year:[22]

- (58%) of the 922 tests within the laboratory´s portfolio were IH-IVDs (including methodologically complex flow cytometry, mass spectrometry, special chemistry and molecular diagnostics);
- 70% of the IH-IVDs had no commercial alternatives on the market;

[22] Vermeersch et al. 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

A survey of, predominantly academic, European laboratories published in 2022 by the Biomedical Alliance showed that:[11]

- the most frequently performed tests were CE-marked IVDs (50%);
- about 25% of tests were IH-IVD;
- 25% were modified CE-IVD/RUO;
- IH-IVD use was most frequent in genetics, therapeutic drug monitoring (TDM) and microbiology.

In the United States, LDT activity will be governed by the CLIA/CAP federal system, independently of the FDA, which has been permanently blocked in 2025 from regulating LDTs as marketed products, after an initial ruling in 2024 describing enforcement.[23] CLIA accreditation, while not identical, is similar to ISO 15189 accreditation in Europe.

The lack of flexibility in the EU is particularly challenging for companion diagnostics used in oncology. For example the novel medicine Elacestrant (Oserdu, Menarini), at the time of market approval, had no CE-marked companion diagnostic available, forcing medical laboratories to establish appropriate IH-IVDs. Similar examples exist for other cancer biomarkers, such as leukaemia and lymphoma, where not-for-profit European EQA providers encourage and evaluate optimised, standardised IH-IVD diagnostic practices.[24] Similar strategies to warrant analytical proficiency for IVDs should be supported within the EU regulatory framework.

Recommendations

➢ The responsibility for interpretation and execution of an IH-IVD test in a clinical setting 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).

➢ There should be a special pathway for approval of IH-IVDs outside of the IVDR (a European CLIA equivalent).

➢ Article 5.5 of the IVDR should be amended.

- Conditions (b) and (c) of Article 5.5 should be retained.
- Conditions (a) and (d) to (i) should be removed or significantly modified.

[23] See https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests

[24] Alary et al. Improvement of standardization of molecular analyses in hematology: The 10-year GBMHM French Experience. Hemasphere. 2021;5(12):e658. https://journals.lww.com/hemasphere/fulltext/2021/12000/improvement_of_standardization_of_molecular.6.aspx

➢ Article 5.5a may be modified using unambiguous terminology applied across all Member States, explicitly permitting the transfer of IH-IVDs between health institutions under strictly defined conditions. Such conditions must ensure that the safety and efficacy of the transferred device are fully maintained in the receiving health institution. The modified section could read: "*A health institution manufacturing an IH-IVD under Article 5(5) may transfer the device to another health institution´s diagnostic laboratory, provided that the receiving institution complies with Article 5(5)(b) and (c)*"

➢ Article 5.5d should be rephrased to encourage both the manufacturing and Health Institution sectors to prioritise optimal access to innovative diagnostics. We suggest (ESHG suggestion during the 2/10/25 IVD TF VC) "*Healthcare institutions are required to demonstrate that the in-house developed IVDs comply with the state-of-art as defined by professionals in the respective field*."

➢ A policy that is equivalent to "enforcement discretion" could be applied for Health Institution laboratories that:

- have demonstrated a clear application of regulatory requirements;
- have sufficient annual activity to assure appropriate experience;
- participate satisfactorily in relevant EQA and surveillance of regional/national/European activity within their field of reference;
- are approved by their scientific societies and national competent authorites.

These criteria would allow Health Institution laboratories to act as 'reference laboratories' for niche tests, 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 for rare blood cell typing.

➢ Pre/early certification access models should be developed (equivalent to conditional approval), preferably in collaboration with academic diagnostic experts, the IVD Expert Panel, the European Rare Disease networks (ERN), and EU regulators.

Failure to modify Art. 5.5 will increase healthcare costs and jeopardize ability to design personalized laboratory tests (necessary for precision medicine) and to adapt to shifting test needs (as with the repurposing of instruments for Covid-19 testing). An appropriate Art 5.5 could provide the basis for a fit-for-purpose "European CLIA equivalent" which could contribute to the European Life Sciences Strategy and optimize access to innovative diagnostics in the precision medicine era.

Excessive bureaucratic regulatory control will discourage research and innovation, which provides a significant proportion of the innovative diagnostics which later become CE-marked IVDs. Maintenance of IH-IVD activity within an appropriately modified IVDR Art. 5.5 will accelerate optimization and harmonization of innovative diagnostics, and their integration in

clinical trials of personalized medicine.

System improvements

1. Regulatory reform will fail without scientific resources and coordination

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.

Many of the recommendations in this document would be unnecessary if an adequate support structure for the MDR and IVDR had been created.

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.[25]

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.[26]

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.

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

The EMA is already managing the Expert Panels, so it is well placed to assume a broader

[25] https://www.team-nb.org/team-nb-2024-in-a-few-facts-and-figures/

[26] 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

management role to coordinate scientific aspects of the regulatory system for medical devices. There would be considerable overlap with existing programs within the EMA, for 'regulatory science' initiatives. This option would also be the least disruptive.

Recommendations

- Additional expert staff must be appointed, and external recruitment for suitably qualified experts should be permitted. There should be a substantial expansion of staff.
- Establish a medical device division of EMA.

The functions of this division have been described in our previous recommendations.[1]

2. Specific pathways need to be introduced

Most jurisdictions have special programs to facilitate the early approval 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 clinical 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.[27,28]

Recommendation

- The EU should establish a special pathway that will enable orphan, paediatric and breakthrough technologies to undergo an accelerated conformity assessment; if a device is approved by such a route, there should be mandated post-market clinical follow-up.

[27] 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

[28] 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

- Market approval of medical devices with limited evidence, requires enhanced transparency of clinical evidence and the Clinical Evaluation Report being publicly available.
- 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 should be a task for Expert Panels.

3. A single reporting mechanism is needed for healthcare professionals in the EU

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".

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".[29] This provision is important and must not be diluted – particularly if a device that is going to be withdrawn is the 'last-in-class' for a clinical or diagnostic indication, meaning that no alternative will be available.

Manufacturers should tell their national regulator. It is unclear how "health institutions and healthcare professionals" across the EU will then 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".

Both incident and availability reporting would be managed more efficiently and effectively, if there was a single reporting point (or portal) for clinicians and patients in the EU.

Currently, healthcare practitioners learn that a device is no longer available, once it is too late for them to 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.

Evidence

[29] 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 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

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

- The targeted evaluation should include provision for critical medical devices, which are essential for the provision of healthcare, in a similar way to the Critical Medicines Act.
- 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 (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 incidents, shortages or non-availability of devices that are needed for patient care.

4. Reducing costs for the healthcare system

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.[30]

An institution or company that reprocesses a devices 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

[30] 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

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