Biomedical Alliance in Europe

BioMed Alliance position on the IVDR review

January 2025

Implementing regulatory science to protect Public Health

Introduction

Clinicians and healthcare professionals welcomed the general objectives of the In Vitro Diagnostic Medical Devices Regulation (IVDR), but they now highlight concerns and recommendations that need to be addressed urgently to ensure better availability of safe IVDs for patients in Europe. The review of the In Vitro Diagnostic Devices Regulation provides a chance to address pressing issues and prevent essential IVDs from diasppearing, while improving access to innovative devices and increasing investment in science, research and development within the European market.

About us

The Biomedical Alliance in Europe (BioMed Alliance) is a unique initiative of 35 leading European medical societies that together include hundreds of thousands of researchers and health professionals. It provides expert advice to policy makers and regulators on the implementation of the Medical Device Regulation and In Vitro Diagnostic Device Regulation, through the work of its dedicated Task Forces and its stakeholder membership of a number of working groups of the Medical Device Coordination Group.

Essential principles of a patient-centred regulatory system

Evidence based & transparent

Regulatory requirements for the safety, performance, and effectiveness of devices should be based on scientific principles, and their impact should be evaluated to determine if they are fit for purpose. All clinical evidence should be publicly shared and easily accessible.

Proportionate to risk & fair

High standards of safety and effectiveness are key, but the level of evaluation should be proportional to the potential risk for individual patients balanced by the potential clinical benefit while maintaining high standards of safety and effectiveness. Regulations should ensure that particular groups of patients are not disadvantaged, such as people with rare diseases, and children or adults requiring highly individualised treatment.

Consistent

There should be consistency between reviews of different diagnostic devices within the same type or used for the same clinical indication – so that similar clinical evidence is expected and similar criteria are applied, leading to predictable outcomes of conformity assessments performed by different notified bodies.

Flexible & interactive

Review and approval processes must be responsive to unmet needs, new technological developments, and changing healthcare needs. Procedures should be available to allow innovators, developers, manufacturers, and clinical trialists obtain advice on requirements for clinical studies, in face-to-face discussions with regulators / evaluators.

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”).

The In Vitro Diagnostic Regulation

The In Vitro Diagnostic Medical Devices Regulation (IVDR) that was adopted in 2017 was intended to revise the EU regulatory framework for In Vitro Diagnostics (IVDs) in order to enhance their safety. Nonetheless, the clinical community represented in the BioMed Alliance has in the past raised awareness of problems including delays in implementation, limited capacity of Notified Bodies, and the slow roll-out of EUDAMED. In addition, they focused on unintended consequences of the reform including high costs of certification, issues with the evaluation of rare/orphan IVDs, research and development leaving Europe, limited transparency and predictability, restrictive requirements for In-House IVDs. BioMed Alliance has presented its concerns at meetings of the Medical Device Coordination Group, in discussions with Commission officials and policy makers, at a STOA workshop of the European Parliament, and in statements.

Key issues

There is insufficient regulatory capacity to evaluate all in vitro devices and classifications.

The IVDR classifies in vitro diagnostic devices (IVDs) into four risk classes (A to D), with Class A posing the lowest and Class D the highest risk. The proportion of IVDs that require Notified Body approval has surged from 7% under the previous directives (IVDD) to 84% under IVDR[1] (all class B,

Recommendations:

- Differential management should be considered for class C and 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 and requirements for class B would allow concentration of resources for class C and D, with little or no significant risk to patients or society.
- Reducing the certification requirements of class C and D (which constitute 30% of approximately 40,000 tests[2]) would facilitate harmonisation and optimisation of management by the increasing number of notified bodies involved.

[1] van Drongelen A., de Bruijn A., Pennings J., van der Maaden T. RIVM Letter Report 2018-0082; 2018. The impact of the new European IVD classification rules on the notified body involvement. A study on the IVDs registered in the Netherlands.

[2] See MedTech Europe: https://www.medtecheurope.org/wp-content/uploads/2021/09/medtech-europe-survey-report-detailed-results.pdf

C & D IVDs). This increase presents challenges for notified bodies and manufacturers, especially SMEs, and may lead to delays in certifying Class D devices before the transition period ends.

Recommendations:

- Regulators should consider monitoring IVD performance through internal and external quality assessment (EQA) structures already in place in Europe to evaluate medical laboratories to support quality monitoring of IVD devices.
- Such expanded EQA use would allow post-market monitoring of the precision and performance of tests and devices, not just the users. Harmonising EQA data across Europe could be organised through networks such as the European Organisation for External Quality Assurance Providers in Laboratory Medicine (EQALM). Since ISO 15189:2022 already requires both internal and external quality assessments for accreditation, promoting ISO 15189 across the EU would support this effort.

There is insufficient recognition of established laboratory quality control procedures.

EU regulators have not sufficiently recognised existing laboratory quality management procedures, such as external quality assessment (EQA) and proficiency testing (PT), which have been in use for decades to monitor diagnostic performance. These well-established tools, developed by professional bodies, were not integrated into the IVDR framework.

No special provisions are in place to safeguard the continued availability of legacy IVD tests.

The EU system now requires procedures for the approval and certification of routine laboratory diagnostic tests (legacy IVD tests), that are unnecessary since the tests are standard and well-established. These stricter compliance

Recommendations:

- New and/or alternative regulatory pathways or provisions are needed for legacy devices without shortcomings or inadequacies. This could be assured, for example, by providing legacy devices with provisional certificates with conditions, and indicating so in the EUDAMED database ('grandfathering'). The IVD Expert Panel could provide advice on specific cases.

requirements for clinical evidence, performance evaluation, and post-market surveillance are unnecessary and could lead to the withdrawal of standard assays, potentially impacting clinical care and public health.

Recommendations:

- A special regulatory pathway should be created to facilitate the conformity assessment of rare/niche/orphan IVDs and reduce the costs for their certification, while also ensuring against inappropriate use of this pathway.
- 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), the European Commission, Competent Authorities and registered stakeholders in the Medical Devices Coordination Group (MDCG).
- Analytical validation should be focused on the generic methods underlying the IVD device, rather than the specific molecular targets measured. Otherwise, every single molecular deviation would need its own validation, which is impossible to achieve.

The cost and challenges of certifying rare/orphan IVDs threaten patient access to vital diagnostics.

The cost of recertification is particularly challenging for rare/orphan IVDs. They are produced for small numbers of patients, so manufacturers will have a limited return on investment.

The increase in personalised medicine has led to an increased need for rare/orphan IVDs. Due to the bureaucratic and economic burden of developing these IVDs, patients face a risk of losing access to essential diagnostics and care.

Procedures for removing outdated IVDs should be clarified & implemented

Recommendations

- Medical disciplines should be encouraged and supported to participate in the development of clinical guidelines to identify optimal indications for IVDs, including the removal of outdated tests from diagnostic pathways.
- There should be a framework developed between medical societies and regulators for removing obsolete IVD devices from the market, as a form of “diagnostic pruning”.

There is a large number of tests currently on the market that may not play an essential role in clinical practice because they are no longer necessary or because there are more effective alternatives. Standardised procedures for removal from the market of outdated tests are not clear.

- This would free diagnostic budgets for more appropriate tests, thus encouraging access to innovative tests.

Recommendations:

- Additional support and provisions are necessary to help laboratories comply with regulatory requirements when using In-house IVDs.
- Article 5-5 of the IVDR should be amended. Conditions (a) and (d) through (i) for in-house exemptions should be removed, while conditions (b) to (c) should be retained. Failure to do this will increase health care costs and jeopardise ability to design "personalised" laboratory tests (necessary for precision medicine) and to adapt to shifting test needs, as happened with the repurposing of instruments for Covid-19 testing.
- In-house IVD activity categories should be evaluated by the reviewers of ISO 15189 accreditation bodies and participation in appropriate External Quality Assessment (EQA) provided, in order to demonstrate delivery of reproducible results and facilitate clinical evaluation.
- The Medical Device Coordination Group (MDCG) should participate in evaluation and development of the ongoing ISO 5649 on in-house IVDs. Once finalised, this document will support regulatory surveillance of in-house IVD activity.

There is no support to ensure in-house tests can continue their vital role in the health system

In House Devices play a key role in the system, as they allow laboratories to develop customised tests to respond to specific patient needs, or to fill a gap where commercial tests are unavailable or inadequate.

The new IVDR introduces specific obligations for in-house IVDs under Article 5.5, which replaces most requirements for CE-marked devices but adds administrative burdens.

Article 5.5d mandates that health institutions must provide justification of In-house IVD use when an (apparently) equivalent CE-marked device is available or does not meet the needs of the target patient group. This may discourage academic laboratories from continuing to develop and implement new tests, if a manufacturer can take over sole production of a test, many of which were developed in an academic institution or hospital. The risk inherent to Article 5.5d is that of monopolies. A CE-marked IVD will discourage optimisation, competition and design of new standards.

Incentives are needed to encourage innovation in the diagnostic field

There is a risk that increased requirements and higher certification costs discourage entities from introducing new innovative IVDs on the EU market. Support and special pathways may enhance the access to breakthrough technologies for European patients.

Recommendations

- The European Commission and member states should increase financial support to encourage the academic sector to continuously maintain and optimise test portfolios for diagnostic patient care.
- Most jurisdictions have programmes for innovative, break-through devices, to facilitate their early certification. If a new IVD promises to satisfy an unmet need for a serious, life-threatening, or irreversibly debilitating condition, for which no similarly effective diagnostic exists, then it should be possible for that device to be approved with limited evidence but with conditions.

Recommendations

- The IVD Working Group of the Medical Device Coordination Group (MDCG) should produce guidance on the interface between regulatory market approval, including clinical utility, and Health Technology Assessment (HTA).
- The MDCG IVD Working Group should recommend identification of more specialised Expert Panels, rather than the single IVD panel. At a minimum, clinical chemistry, molecular genetics, infectious disease, and cell/tissue-based (including transfusion and tissue typing) specific panels should be identified, and their potential extended beyond observation and consultation.
- There is a need to identify appropriate HTA assessment of IVDs and to pay attention to coherence between IVDR and HTAR.
- 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.

Regulatory standards and guidance on demonstrating clinical relevance are needed

There is still uncertainty about how to demonstrate clinical relevance for many IVDs, beyond technical performance, although initiatives such as STARD exist. Gaps exist in EU guidance on post-market surveillance and quality assurance. Additionally, IVDs requires demonstration of clinical utility for Health Technology Assessment (HTA), but clarity on how to meet these requirements is lacking.

Need to strengthen stakeholder involvement

As recognised stakeholders to the Medical Device Coordination Group, the BioMed Alliance and other healthcare professional and patient organisations contribute to the MDR implementation.

Recommendations:

- Travel costs for clinicians, patients, and civil society representatives who attend the MDCG should be reimbursed by the European Commission.
- 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.
- Consultations and requests for input from stakeholders need to have sufficiently flexible deadlines, that take into account the busy schedules of clinicians, patients, and other volunteers.
- Draft guidance documents and consultations with stakeholders should be conducted in an open and transparent manner, similar to the EMA and US FDA approaches to guidance development.

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 and IVDs should be simple and clear, as proposed by the Coalition for Reducing Bureaucracy in Clinical Trials.

Increasing regulatory complexity

The European regulatory framework for health technologies is becoming increasingly complex. The In Vitro Diagnostics Regulation interlinks with several key new regulations including the Medical Devices Regulation, the European Health Data Space, the Regulation on Health Technology Assessment, and the Clinical Trials Regulation, among others. There is an important need for legal clarity on the overlap between these regulations.

Need to streamline governance

There is limited capacity within DG SANTE Unit D3 and a lack of a coordinated regulatory support system.

Recommendations

- There is a need to make the system more efficient, and different options should be considered, including an overview of the specialisations of each notified body, to match specialised expertise with the specific needs of manufacturers.
- There is a critical need for more regulatory staff and expertise within the European Commission's Directorate General for Health and Food Safety (DG SANTE) and particularly for staff with clinical expertise.
- Many of the persisting issues could be addressed if an adequate support structure for the MDR and IVDR is created.

Need for a new coordinating mechanism to address pressing issues in the system

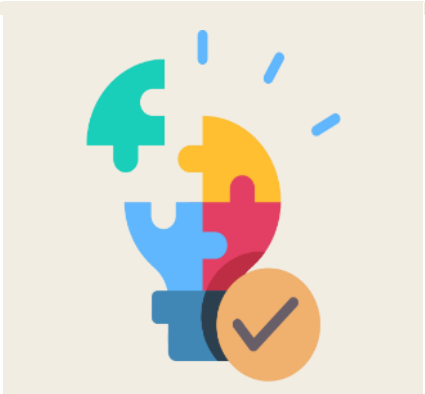
There is a clear need for a new body that can coordinate the EU regulatory system and serve as a point of contact particularly for small and medium-sized enterprises, health institutions and manufacturers of rare/orphan and/or legacy diagnostic devices. There are different options to create such a mechanism, and their disadvantages and benefits must be carefully evaluated to identify the most effective way forward.

Notified Bodies have gained responsibilities, functions and workload under the Medical Device Regulation and In Vitro Diagnostic Medical Device Regulation. While notified body capacity under the MDR has significantly expanded, there are still only 19 notified bodies designated under the IVDR. The optimal number of notified bodies for IVDR is unclear, given the highly diverse categories of tests, as is the ideal degree of specialisation or complementarity.

Notified bodies are private organisations that are designated by Competent Authorities, which are also in charge of overseeing their performance. Cooperation and coordination are foreseen through the Notified Body coordination group NB-MED, but this coordination does not go far enough to address excessive costs, lengthy procedures, issues in communication and heterogeneity of practice. BioMed Alliance believes that the role of the European Medicines Agency in the field of medical devices could be expanded, so it can take on a broader management role to coordinate the regulatory system for medical devices.

Functions of the new coordinating mechanism

- Enhance coordination in the system and ensure synergies and complementarities within and between the different actors, including notified bodies, manufacturers, the Commission, healthcare professionals, laboratory professionals and other jurisdictions at the global level.



- Early dialogue and advice, particularly for rare/orphan IVDs, breakthrough innovation and SMEs.
- Support for health institutions developing in-house devices.
- Designation of rare/orphan IVDs.
- Manage an affordable pathway to conformity assessment for rare/orphan IVDs, and breakthrough technologies.

- Maintenance of a register of disease-specific registries which allow clinical evaluation of IVD performance, as for example via ERNs or other reference networks.
- Coordination of market surveillance.
- Joint reviews with HTA, joint horizon scanning.
- EU participation in the IMDRFs international Medical Devices Single Auditing Programme (MDSAP).