The IVDR 2017/746

In Vitro Diagnostic Regulation (IVDR) is the European Union (EU) law (IVDR 2017/746) that regulates the approval processes for the manufacturers to obtain CE marking for their *in vitro* diagnostics medical devices (IVDs) so that their devices can be marketed in the EU. The IVDR will replace the existing *in vitro* diagnostic medical devices Directive (98/79/EC) (IVDD). The IVDR was published in May 2017, marking the start of a five-year period of transition from the IVDD. Thereafter, on the 26th of May 2022, the enforcement of the IVDR came into effect.

The new medical devices Regulation (2017/745/ EU) (MDR) and the *in vitro* diagnostic medical devices Regulation (2017/746/EU) (IVDR) bring EU legislation in line with technical advances, changes in medical science, and progress in law making.

The new Regulations create a robust, transparent, and sustainable regulatory framework, recognized internationally, that improves clinical safety and creates fair market access for manufacturers.

In contrast to Directives, Regulations do not need to be transposed into national law. The MDR and the IVDR will therefore reduce the risks of discrepancies in interpretation across the EU market.

What is our role as Requalite in the process?

As an independent medical device Regulatory and Quality Consulting company, we consult manufacturers of IVDs on the planning, preparation, execution, and reporting of performance evaluations for existing as well as novel IVDs to ensure compliance with IVDR. Requalite prides itself with providing the very best services for planning, writing, and documentation of evaluations and reports provisioned in IVDR. We also provide resources for the manufacturers to help them navigate the system, keep current with the changes in the regulation, and train their personnel responsible for regulatory compliance.

Key dates for IVDD-IVDR transition:

26 May 2017: IVDR published and subsequently entered into force which began a 5 year transitional period from IVDD to IVDR

From 26 May 2022: IVDR enforcement begins and comes into effect with no new IVDD certificates being issued.

27 May 2024: Existing IVDD certificates expire

27 May 2025: All devices placed on the market must be in conformity with the IVDR

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What are the key changes from IVDD to IVDR?

In terms of their impact on manufacturers and products, the IVDD and the IVDR largely share the same basic regulatory process. No existing requirements have been removed, but the IVDR adds new requirements. The IVDR brings more stringent requirements for the designation of Notified Bodies, with increased control and monitoring by the national competent authorities and the Commission.

The biggest change concerns the risk classification of *in vitro* diagnostic (IVD) devices and the role of Notified Bodies (NBs). The IVDR also clarifies the obligations of economic operators (manufacturers, authorized representatives, importers and distributors).

The IVDD took a list-based approach to assigning risk classes, which in turn determined the process for assessing conformity and the level of supervision required from NBs. The IVDR instead uses rules recognized at international level to assign each device to one of the four risk categories, ranging from class A (lowest risk) to class D (highest risk). As a result, around 85% of all IVDs will need NBs oversight.

The IVDR also brings tightened requirements for clinical evidence and conformity assessment. For companion diagnostics, the NBs shall consult the competent authorities for medicinal products.

The conformity assessment of class D devices will require the involvement of an EU Reference Laboratory (if designated for that type of device) to verify the performance claimed by the manufacturer and compliance with the applicable Common Specifications. In addition, for innovative class D devices where no Common Specifications currently exist, an independent expert panel must provide its views on the performance evaluation report of the manufacturer.

The IVDR calls for increased transparency, with information on IVD devices and 'higher risk' performance studies being made public. The new European Database for Medical Devices (EUDAMED) will play a central role in providing more complete, accurate and accessible data.

The introduction of a unique device identifier (UDI) for every IVD device will significantly enhance traceability and support post-market safety activities.

A great reset is provisioned with the transition from IVDD to IVDR, where all currently approved IVDs (under IVDD) must be recertified for the new requirements (under IVDR) during the transition period.
Product coverage is expanded in IVDR to include all services that claim to determine a patient's disease state, predisposition and susceptibility to a disease, or potential benefit from a medical treatment (i.e., genetic, biochemical, physical, or online tests). Also reflected in the diagnostic arm, IVDs now include all services that claim to determine a patient's disease state, predisposition and susceptibility to a disease, or potential benefit from a medical treatment (i.e., genetic, biochemical, physical, or online tests).
Device classification is based on risk classes ranging from Class A (low risk IVDs) to Class D (high risk IVDs). Classification of an IVD is subject to approval by the Notified Body (NB).
Clinical evidence provided by the manufacturers is required to rigorously demonstrate clinical performance and safety of the IVD. Level of evidence is based the IVD's assigned risk class.

Premarket approval is required for IVDs intended for self-testing or near-patient testing.
Post-market surveillance is to be conducted by the manufacturer in order to assess and report safety risks periodically.
Technical documentation filed by the manufacturers is subject to more stringent requirements.
Traceability of any instrument is a requirement (through a unique device identification - UDI) for better traceability, assessment, and recall of flawed instruments.
Oversight is more rigorous, including the oversight by the NBs to reduce risks from unsafe devices (i.e., unannounced audits, product checks and testing, annual safety reporting) and greater scrutiny and reduced number of the NBs (currently, five NBs assigned for IVDs).
A qualified person responsible for regulatory compliance of the IVD is to be assigned by the manufacturer. This Regulation should include requirements regarding the design and manufacture of devices emitting ionizing
radiation without affecting the application of Council Directive 2013/59/Euratom (2) which pursues other objectives.

The new regulation is far more comprehensive than IVDD and it will require an estimated 80-90% of IVDs on the EU market to undergo a conformity assessment by a Notified Body (NB).

One of the keys to understanding whether your in vitro diagnostic device requires review by an NB—and how that affects its path to market—is the IVDR classification system for devices. The new, risk-based system is governed by a set of rules that all IVD manufacturers will need to use to classify their devices.

What is the IVDR classification system?

Under the IVDR classification system, IVD devices are grouped by risk, similarly to how other medical devices are grouped under the EU Medical Device Regulation (EU MDR).

However, because in vitro devices are used with biological material that has been removed from the body, they may also pose a risk to public health due to transmissible agents within the biological material. As a result, IVDR classification also takes public health risk into account.

The IVDR establishes four risk classes based on both patient and public health risk:

- **Class A - Low patient and public health risk**
- **Class B - Moderate patient risk and/or low public health risk**
- **Class C - High patient risk and/or moderate public health risk**
- **Class D - High patient risk and high public health risk**

Examples of IVD devices that fall into each of these four risk classification types include:

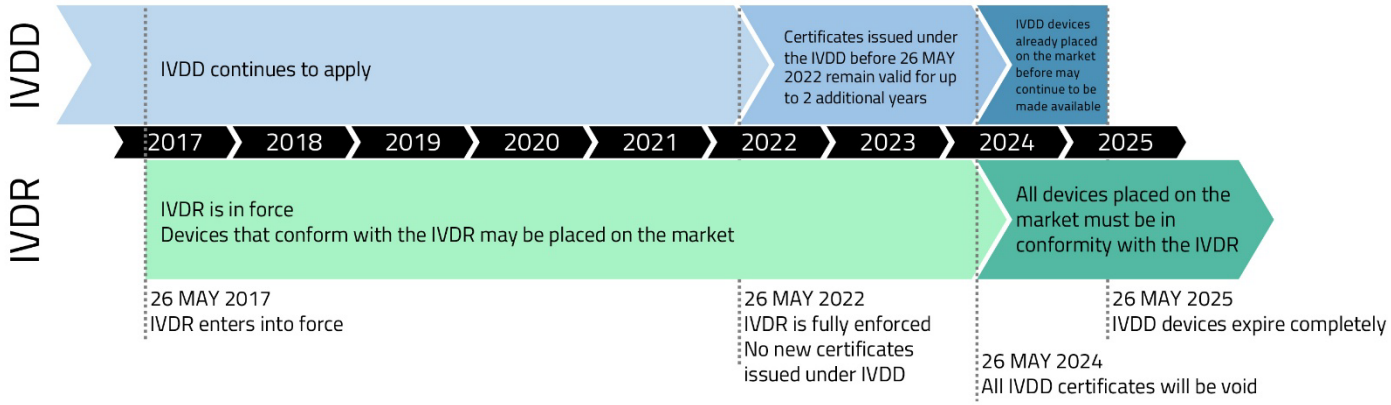
Class A: Examples of Class A IVDs include specimen receptacles, laboratory instruments, and buffer solutions.

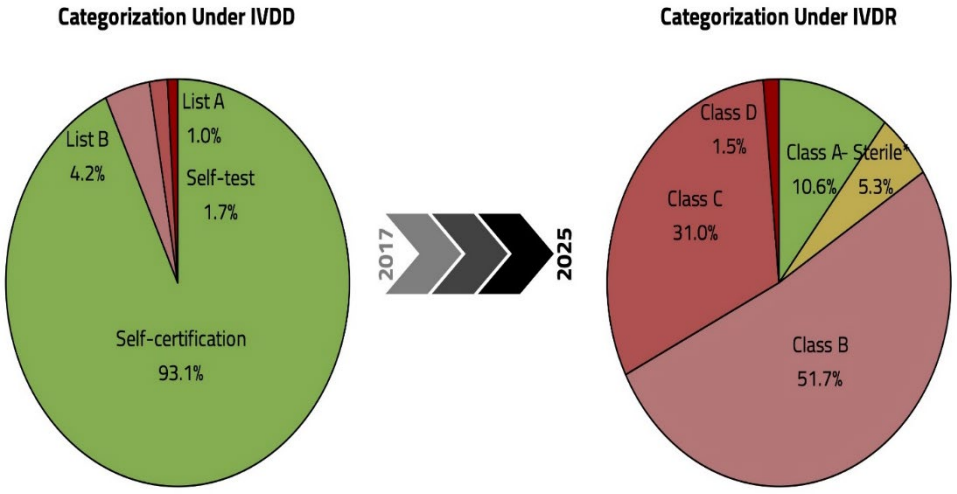
Class B: Class B devices include IVDs for self-testing with less risk to the patient than those in Class C. For example, Class B devices include pregnancy tests, fertility tests, and cholesterol tests. Class B is also the default classification for IVDs that are not covered by any other rules.

Class C: Class C devices include IVDs that are intended to be used for detecting an infectious agent *without* a high risk of propagation, or for detecting the presence of an infectious agent with the potential to cause death or severe disability in the case of an erroneous result.

Class D: This device class includes IVDs that detect or are exposed to life-threatening transmissible agents or transmissible agents and infectious diseases with a high risk of propagation.

Figure 1 showing IVDD to IVDR transition





Reference: van Drongelen A, *et al* . (2018) The impact of the new European IVD-classification rules on the notified body involvement; a study on the IVDs registered in the Netherlands.

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