Navigating the Transition: From IVDD to IVDR Compliance

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Abstract. The transition from the In Vitro Diagnostic Directive (IVDD) to the In Vitro Diagnostic Regulation (IVDR) represents a pivotal regulatory advancement in the EU for in vitro diagnostic (IVD) devices. Effective from 2022, the IVDR (2017/746) addresses the IVDD's limitations by introducing stringent requirements to enhance device traceability, performance evaluation, and risk-based classification. IVDs are categorized into Classes A to D, with Class D representing the highest risk, requiring conformity assessments by notified bodies. The regulation mandates comprehensive performance evaluation, post-market surveillance, risk management, and transparency through detailed labelling and usage instructions. Manufacturers must provide performance evaluation data and collaborate with notified bodies to achieve CE marking for legal distribution. By aligning with global standards, the IVDR enhances patient safety, product quality, and regulatory consistency. This framework ensures a higher level of protection for patients, healthcare providers, and the general public, reflecting the evolving landscape of diagnostic technologies.

Keywords: Invitro Diagnostics,Invitro Medical devices, IVDD, IVDR, Transition from IVDD to IVDR

1 Introduction

Invitro Diagnostics are defined as a medical device type typically used to examine human fluids such as skin, blood or urine in a test tube. This may include reagents, equipment and receptacles with specimens. Examples of invitro medical devices include HIV test, coagulation test system, urine test strips, pregnancy test.

Accessories for IVD are evaluated as separate IVD medical devices which include products that are not medical devices for in vitro diagnostic, but are designed for use with those devices. Accessories include tool for self-testing, tool for performance assessment.

Invitro diagnostic directive 98/79/EEC was known from 1998 and compliance were made compulsory from December 7, 2003. The IVDD exactly focuses on safety, quality, and performance of Invitro Diagnostics Medical Device.

The main desire of the directive is to assure that IVD’s does not compromises on health and the safety of the patients but later on European regulators has recognized the weakness of existing European Invitro Diagnostic Directives in protecting people and so they have spent

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years in creating an expanded sets of regulation which is said as Invitro Diagnostic Regulations.
Invitro diagnostics regulations are a crucial and most crowing to the global health care system as they add importance to patients, medical experts and the sector and improve the well-being of the general population.
The IVDR came into force in 2022. CE Marking certificates issued before the final implementation of the IVDR remained valid for a maximum of two years following the final implementation of the new regulations.
If your IVD is self-certified under the IVDD, and Class A sterile, B, C or D according to the IVDR, you must possess a Notified body issued CE marking certificate on 26 May 2022 in order to continue market the IVD in the EU
Key elements of the existing regulatory approach, such as the supervision of notified bodies, risk classification, conformity assessment procedures, performance evaluation and performance studies, vigilance and market surveillance should be significantly reinforced, whilst provisions ensuring transparency and traceability regarding in vitro diagnostic medical devices should be introduced, to improve health and safety.[1]

1.1 Classification

The IVD Medical Devices Directive (98/79 / EC) defines particular types of devices for the purpose of deciding the effective route of compliance evaluation. There is no explicit example of a risk hierarchy, although it is suggested by the criteria of the compliance evaluation to which each of those groups is subject. This implicit hierarchy of risk is as follows, starting with the highest category of risk and finishing with the lowest.[2]

- **Annex II List A** Determination of blood groups and the recognition of markers for blood types different blood-borne pathogens like HIV, HTLV, Vcjd
- **Annex II List B** Connected to the diagnosis of particular diseases
- Device for self-testing
- All other IVD device

Under the latest legislation (IVDR 2017/746) the entire classification scheme has been revised. A risk-assessment model that involves a new range of classification is now in place of the old framework. It was said that the scheme was based on the criteria of the Global Harmonization Task Force (GHTF), not unlike the existing Health Canada and TGA classification regulations. As follows, the classes introduced under IVDR 2017/746 are

- Class A - Low risk
- Class B - Low – Moderate risk
- Class C - Moderate risk
- Class D – High risk [3]

1.2 Requirements for compliance

- Many of the provisions of the Law apply irrespective of the danger class, such as:
- In the technical documents, the risk class and the rationale for the classification rules must exist.
- Enrolment with a description of the risk class at Eudamed.
- The risk classification of the devices concerned shall be identified by the certificates issued by the notified body.
- Specific specifications of Annex I for safety and performance
- On the declaration of conformity, the risk class must occur.
- Procedures for quality management systems must cover classification processes.

- The risk class of the device must be defined by different documentation relating to performance studies.

However, those criteria common to all systems should be fulfilled in a manner proportionate to the risk category:

- QMS
- PMS
- Performance Evaluation

1.3 Timeline Transition from IVDD to IVDR[4,5,6]

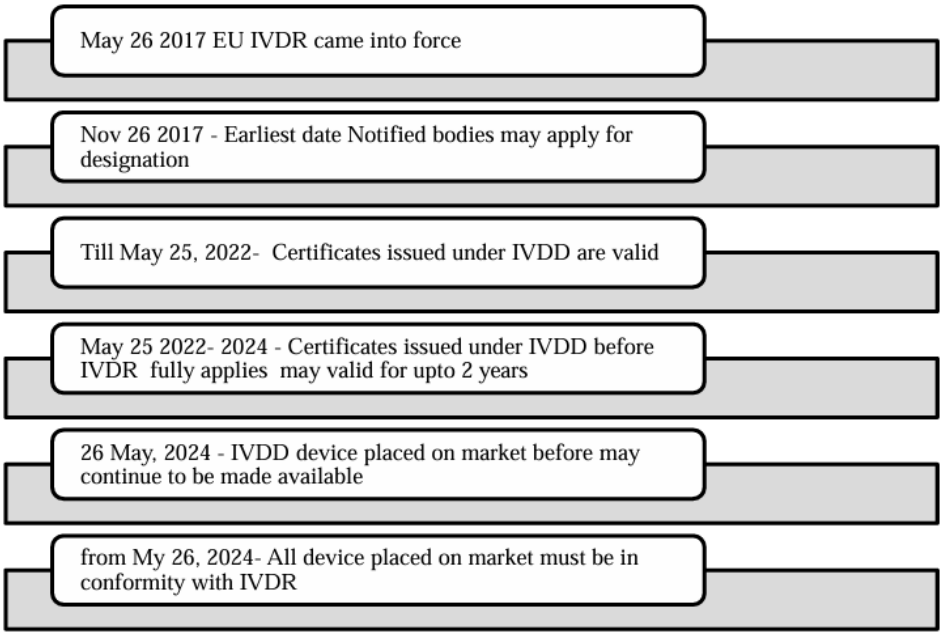

Fig. 1 Timeline

1.4 Principles on Labelling

The following rules to be followed by IVDR are:

The label must indicate that the IVD medical device is for in- vitro diagnostic use.

- Instruction for Use
- The guidelines for usage should include a statement of the theory of testing
- A summary and volume of the reagent, calibrators and controls and any limits on their use should be included in the guidelines for use.
- The guidelines for usage should list the criteria for the use included and omitted for sample selection, shipping, storing, and planning.
- A list of materials given and a list of any materials needed but not provided should be included in the guidelines for use.
- The assay process, including the measurement and analysis of the results, any additional software or reference database needed, should be specified in the instructions for use and, where appropriate, any confirmatory testing should be addressed.
- Where applicable, the reference intervals in regular and affected populations should be included in the guidelines for usage.

- Where appropriate, a bibliography or citations section should be included in the guidelines for usage.[7]

1.5 Structure of IVDR includes

Table 1. Structure of IVDR

Chapter - 10, Articles - 113, Annexes - 15	
Annex I	General safety and performance requirements
Annex II	Technical documentations
Annex III	Technical documentation on post market surveillance
Annex IV	EC declaration of conformity
Annex V	CE marking of conformity
Annex VI	Information's to be submitted upon the registration of devices and economic operators in accordance to articles 26(3) and 28, core data elements to be included in the UDI database together with UDI-DI in accordance with articles 25 and 26 of UDI
Annex VII	Requirements to be met by notified bodies
Annex VIII	Classification rules
Annex IX	Conformity assessment, based on a QMS and on assessment of technical documentation
Annex X	Conformity assessment based on type examination
Annex XI	Conformity assessment based on production quality assurance
Annex XII	Certificates issued by notified body
Annex XIII	Performance evaluation, performance studies and post market performance follow up
Annex XIV	Interventional clinical studies and certain other performance studies
Annex XV	Correlation table

1.6 Clinical Evaluation report

Information obtained from analytical performance studies or (valid) research literature on aspects of IVD clinical and analytical performance and, where appropriate.
Clinical performance studies are presented in a performance assessment study [8]. At least the following argument should be included in this report:

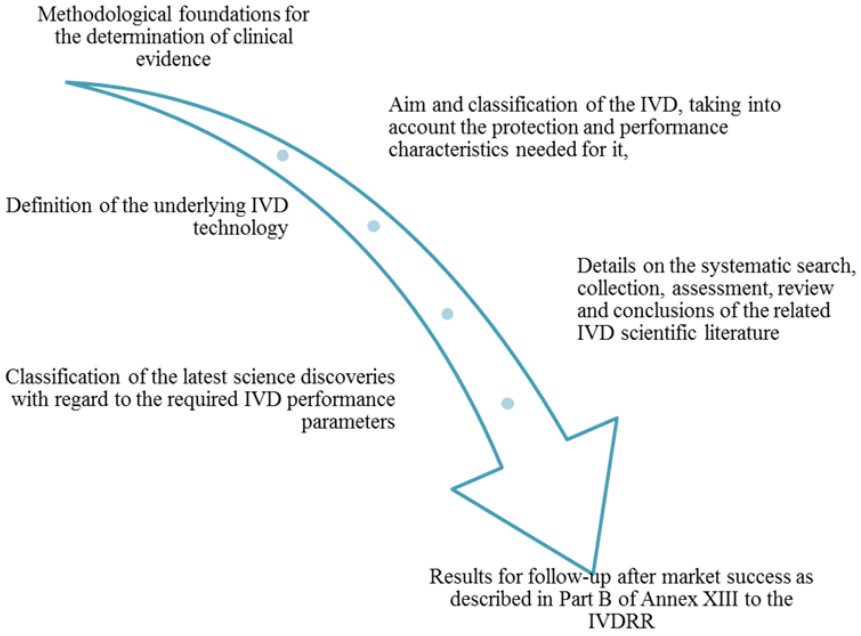

Fig. 2 Clinical Evaluation report

1.7 CE mark

For all IVD devices to be marketed in Europe, CE marking is required. The CE marking means that an IVD device is in compliance with the European Directive on In-Vitro Diagnostic Devices (98/79 / EC) and that it can be lawfully marketed in the EU.

1.7.1 Approval process of CE marking

- Determine your device's classification using IVD (98/79/EC)
- QMS is not generally required for general IVD
- Design a dossier for list A IVD's, which offers detailed information about your IVD
- Appoint an authorized representative who is qualified to handle the regulatory
- No notified body audit for general IVD. Self-certified device manufacturers must affix the CE marking to their units
- Prepare declaration of conformity for all the classes
- IVD shall be registered with the competent authority of the European Union where your approved representative is located
- For the general IVD, the Self-certified CE labelling certificate does not expire as long as you adhere to 98/79/EC
- On-going batch testing is conducted and the results are forwarded to NB[9]

Table 2.
Conformity appraisal techniques are related to the risk groups

Classes	**Conformity assessment**
Class A	Self certify
Class B	Requires QMS with their NB sampling atleast one technical file as per generic device group as part of onsite audits unless these device are self testing

Class C	Requires either full QMS combined with review of technical documentation of at least one device per generic device group
Class D	Same as class C plus batch verification and reference laboratory involvement

1.8Role of Authorized Representative

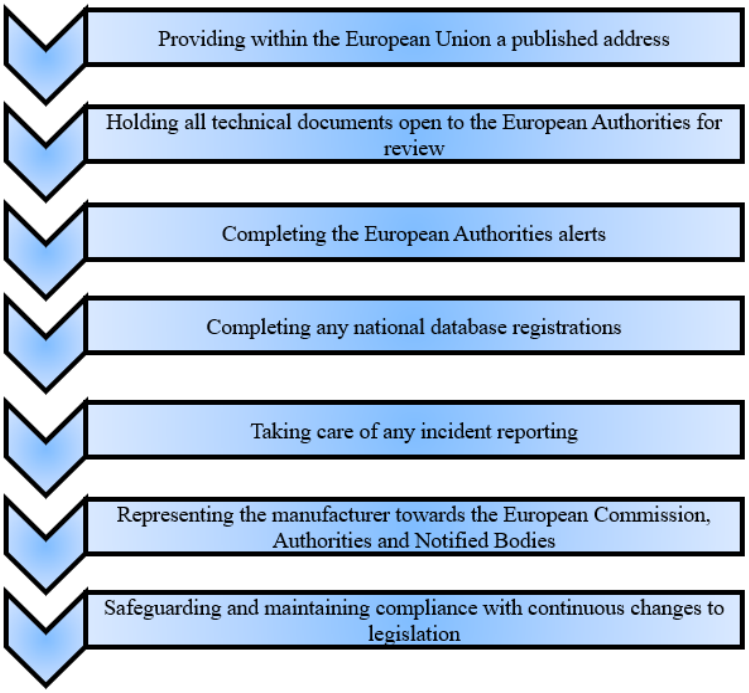

Fig.3 Role of Authorized Representative

1.9 Post market surveillance

New post-market surveillance (PMS) demands have raised interrogations among manufacturers of medical devices when IVD came into force on May 25, 2017. These new regulations afford what information's should be included and specifies that this PMS plan is component of the Technical Documentation Device.Throughout the life time the post marketing surveillance is much needed for each device to converge data on quality, safety and performance of the device. For class A and class B device, the manufacturers must provide post market surveillance report and in case of class C and class D devices the manufacturer has to provide the periodic safety update report at most once a year.

1.10 Difference between IVDD & IVDR

When comparing the In-Vitro Diagnostics Directive (IVDD) and the latest In-Vitro Diagnostics Regulation (IVDR), it is apparent that IVDR increases the consistency and protection of IVD instruments and enhances the transparency and traceability of details throughout the chain delivery process. In the IVDR, the IVDD also covers most of the specifications. The IVDR now takes a bit further and gives even more clarification on how these criteria can be fulfilled. This, together with the reality that the expanded meanings of the IVDR make it less vulnerable to interpretation, tends to provide a legislative structure that is straightforward and sustainable. With that in perspective, the IVDD and the IVDRR still have certain important variations.[10]

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