Compliance & Risks

IVDR Compliance: What You Need To Know

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1. Introduction

The European Union's (EU) In Vitro Diagnostic Regulation 2017/746 (IVDR) became applicable on 26 May 2022 and thereby replaced the In Vitro Diagnostic Medical Devices Directive 98/79/EC (IVDD.)

The new IVD Regulations (IVDR) allow for a consistent regulatory approach across the EU, whilst maintaining high safety standards, and altogether has brought about important changes in the regulation of in vitro diagnostic medical devices (IVDs).

Firstly, the IVDR is now applied across the European Union, allowing for strict and uniform surveillance by regulatory bodies. Secondly, the IVDR introduced a new classification system for IVDs taking into account their risk, and placing them into one of four classes, from class A (low) to class D (high). With regards to the conformity assessment procedures, certain classifications of devices will now require certification by a notified body before being placed on the market.

Other significant changes include improved transparency, brought about by the EU database on medical devices (Eudamed) and a traceability system based on a unique device identifier (UDI). Traceability is of the utmost importance in the new IVD Regulations and the introduction of the Eudamed database has been instrumental in this change. Further changes also include the new requirement for a Summary of Safety and Performance (SSP) for class C and D devices.

As per Article 29 of the IVDR; “The summary of safety and performance shall be written in a way that is clear to the intended user and, if relevant, to the patient and shall be made available to the public via Eudamed.”[1] The SSP needs to be validated by a notified body and uploaded to Eudamed.

[1] 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

There are now more stringent rules on clinical evidence and post-market surveillance as well as clear obligations for economic operators with the new IVDR. The Periodic Safety Update Report (PSUR) is a new requirement for class C and D devices and needs to be submitted via Eudamed to the notified body.

As per Article 81 of IVDR, "Manufacturers of class C and class D devices shall prepare a periodic safety update report ('PSUR') for each device and where relevant for each category or group of devices summarising the results and conclusions of the analyses of the post-market surveillance data gathered as a result of the post-market surveillance plan referred to in Article 79 together with a rationale and description of any preventive and corrective actions taken."

In essence, the PSUR summarises actions and conclusions from post-market surveillance data and takes a lifecycle approach in that manufacturers are required to maintain and update it at least annually.

Within the IVDR, Post market performance follow-up (PMPF) is an important requirement, and involves continuously updating the performance evaluation. As per Annex XIII of the IVDR; "When conducting PMPF, the manufacturer shall proactively collect and evaluate performance and relevant scientific data from the use of a device which bears the CE marking and is placed on the market or put into service within its intended purpose as referred to in the relevant conformity assessment procedure, with the aim of confirming the safety, performance and scientific validity throughout the expected lifetime of the device, of ensuring the continued acceptability of the benefit-risk ratio and of detecting emerging risks on the basis of factual evidence."

Another important aspect of the IVDR, needed to ensure a high level of safety and performance, is compliance with the general safety and performance requirements set out in Annex I of the regulations.

As per the IVDR, general safety and performance requirements shall contain; “information for the demonstration of conformity with the general safety and performance requirements set out in Annex I that are applicable to the device taking into account its intended purpose, and shall include a justification, validation and verification of the solutions adopted to meet those requirements.”

Many challenges lie ahead for IVDR, in particular the shortage of notified bodies designated under Regulation (EU) 2017/746, which may make it difficult for conformity assessment procedures to be completed in time, however it is imperative for all involved, that a high level of safety and performance of devices is maintained, and that supply of essential devices is effectively sustained.

2. The IVDR Regulations

2.1 Regulation (EU) 2022/112- Transition periods

In January 2022, Regulation (EU) 2022/112[2] extended the transitional provisions of Regulation (EU) 2017/746 on in vitro diagnostic medical devices, in particular Article 110, in terms of scope and deadlines. The amendment extended the transitional provisions depending on the risk class of the device, with the date of application of the Regulation on in vitro diagnostic medical devices remaining the same.

Specifically, as per Regulation (EU) 2022/112 of the European Parliament and of the council of 25 January 2022 amending Regulation (EU) 2017/746 as regards transitional provisions for certain in vitro diagnostic medical devices and the deferred application of conditions for in-house devices, Regulation (EU) 2017/746 Article 110 is amended by replacing paragraph 3 with the following; "the devices referred to in the second and third subparagraphs of this paragraph may be placed on the market or put into service until the dates set out in those subparagraphs, provided that, from the date of application of this Regulation, those devices continue to comply with Directive 98/79/EC, and provided that there are no significant changes in the design and intended purpose of those devices."

It is important to note that the transition periods will only be valid when there are no significant changes to the devices design and intended purpose.

[2] Regulation (EU) 2022/112 of the European Parliament and of the Council of 25 January 2022 amending Regulation (EU) 2017/746 as regards transitional provisions for certain in vitro diagnostic medical devices and the deferred application of conditions for in-house devices

As per Regulation (EU) 2022/112; "Devices with a certificate that was issued in accordance with Directive 98/79/EC and which is valid by virtue of paragraph 2 of this Article may be placed on the market or put into service until 26 May 2025". Furthermore, Regulation (EU) 2022/112 states; "Devices for which the conformity assessment procedure pursuant to Directive 98/79/EC did not require the involvement of a notified body, for which a declaration of conformity was drawn up prior to 26 May 2022 in accordance with that Directive, and for which the conformity assessment procedure pursuant to this Regulation requires the involvement of a notified body, may be placed on the market or put into service until the following dates:

A. 26 May 2025, for class D devices;
B. 26 May 2026, for class C devices;
C. 26 May 2027, for class B devices;
D. 26 May 2027, for class A devices placed on the market in sterile condition."

In relation to Article 110, paragraph 4 of Regulation (EU) 2017/746, Regulation (EU) 2022/112 further states that devices which were placed on the market in compliance with Directive 98/79/EC before 26 May 2022 may continue to be made available on the market or put into service until 26 May 2025.

As per Regulation (EU) 2022/112, paragraph 4 of Regulation (EU) 2017/746 states that devices placed on the market from 26 May 2022 under Article 110(3) "may continue to be made available on the market or put into service" until the following revised dates:

A. 26 May 2026, for devices with a certificate that was issued in accordance with Directive 98/79/EC valid per Article 110(2) IVDR, and class D devices referred to in Article 110(3);
B. 26 May 2027, for class C devices referred to in Article 110(3),
C. 26 May 2028, for class B devices, and class A devices placed on the market in sterile condition referred to in Article 110(3)

It must be noted that not all devices have benefited from an extension, with new IVDs, those that incorporated a significant change in design or intended purpose, and those that do not require notified body certification under the IVDR gaining no additional time.
IVDR was applied in full, from 26 May 2022 for such devices.

Furthermore, post-market surveillance, market surveillance, vigilance and registration requirements were still required for full compliance by all devices by May 2022.

Overall, these transition periods are important in ensuring there is no disruption in the supply of IVDs to the market for both health institutions and for the public.

2.2 Implementation of IVDR in Ireland

In Ireland, the In Vitro Diagnostic Regulations 2022 (S.I. 256 of 2022)[3], and the European Union (National Research Ethics Committees for Performance Studies of In Vitro Diagnostic Medical Devices) Regulations 2022 (S.I. 257 of 2022)[4] came into force on 26 May 2022 to further implement the IVDR.
Specifically, the In Vitro Diagnostic Regulations 2022 (S.I. 256 of 2022) confer functions on the Health Products Regulatory Authority (HPRA) in relation to enforcement of IVDR, in that the HPRA has been given powers of enforcement.

The regulation also describes a range of offences for breaches of the requirements of IVDR, including those committed by economic operators, notified bodies and sponsors. Moreover, part 3 of the regulations define the rules around the conduct of performance studies.

The European Union (National Research Ethics Committees for Performance Studies of In Vitro Diagnostic Medical Devices) Regulations 2022 (S.I. 257 of 2022) provide for the establishment of a national body responsible for ethical standards in the management of performance studies required under the IVDR, and for a National Office to administratively support the work of those committees.
This regulation also describes various offences relating to performance studies.

Overall, the new Irish Regulations support the main features of the IVDR.

[3] S.I. No. 256/2022 - In Vitro Diagnostic Medical Devices Regulations 2022

[4] S.I. No. 257/2022 - European Union (National Research Ethics Committees for Performance Studies of In Vitro Diagnostic Medical Devices) Regulations 2022

2.3 Commission Implementing Regulation (EU) 2022/1107

The European Commission has adopted common specifications for some high-risk IVDs. Commission Implementing Regulation (EU) 2022/1107[5] of 4 July 2022 lays down common specifications for certain class D in vitro diagnostic medical devices in accordance with Regulation (EU) 2017/746 of the European Parliament and of the Council. Specifically, this regulation lays down common specifications for certain class D IVDs with regards to requirements regarding the performance characteristics set out in Annex I to Regulation (EU) 2017/746.

As per the transitional provisions of Commission Implementing Regulation (EU) 2022/1107, from 25 July 2022 until 25 July 2024, devices that are in conformity with the common technical specifications set out in Decision 2002/364/EC or devices that are in conformity with the common specifications set out in this Regulation (EU) 2022/1107, "shall be presumed to be in conformity with the requirements regarding the performance characteristics set out in Section 9.1, points (a) and (b), Section 9.3 and Section 9.4, point (a), of Annex I to Regulation (EU) 2017/746."

This regulation includes relevant definitions, transitional provisions and general common specifications and requirements applicable to particular devices for example, those devices intended for detection or quantification of Human immunodeficiency virus (HIV.)

This regulation entered into force on 25 July 2022 and will apply from 25 July 25 2024, with Article 3 on Transitional provisions applicable from 25 July 2022.

[5] Commission Implementing Regulation (EU) 2022/1107 of 4 July 2022 laying down common specifications for certain class D in vitro diagnostic medical devices in accordance with Regulation (EU) 2017/746 of the European Parliament and of the Council

2.4 Implementation and preparedness plan for Regulation (EU) 2017/746

An update to the Joint implementation and preparedness plan for Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR) was published by the EU Commission this year. It is a result of a review by the MDCG, with input from stakeholders and describes the implementation priorities for IVDR.

The actions and priorities set out in this document were established based on the objectives of "public health, patient safety and transparency."[6] As per the plan, "The priorities are split into two sets. Set A includes actions that are vital for devices to have access to the market (those related to a framework for contingency planning and availability of notified bodies). Set B includes legislation and guidance documents that, while not obligatory, would greatly facilitate the work of the actors as well as designation of EU reference laboratories for high-risk IVDs."

The Annex sets out a summary table of essential and high priority actions including actions surrounding the availability of notified bodies, adoption of implementing acts for common specifications, performance evaluation and expert panels and Eudamed.

[6] Joint implementation and preparedness plan for Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR) June 2022

2.5 Medical Device Coordination Group (MDCG) Guidance documents

The Medical Device Coordination Group (MDCG) was formed to assist in ensuring a harmonised implementation of both the MDR and the IVDR. Recently, the MDCG published several guidance documents to assist in applying Regulation (EU) 2017/746 (IVDR) to in vitro diagnostic medical devices.

MDCG 2022-8 on Regulation (EU) 2017/746 - application of IVDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2022 in accordance with Directive 98/79/EC[7], was published in May 2022 and provides information on the application of the IVDR requirements to both legacy devices and old devices and well as associated transition periods. Legacy devices are defined as "devices referred to in the 2nd or 3rd subparagraph of Article 110(3) IVDR, which are placed on the market or put into service after 26 May 2022 and until the end of the respective transition period set out in the 2nd or 3 rd subparagraph of Article 110(3), if the conditions laid down in the 1st subparagraph of Article 110(3)3 are fulfilled."

As per MDCG 2022-8, such legacy devices can be devices "covered by a valid EC certificate issued by a notified body in accordance with Directive 98/79/EC prior to 26 May 2022" or devices for which "a declaration of conformity was drawn up prior to 26 May 2022 in accordance with the IVDD and for which the conformity assessment procedure pursuant to the IVDR (contrary to the IVDD) requires the involvement of a notified body."

The definition of old devices are those that were "placed on the market or put into service before 26 May 2022 in accordance with the IVDD or the applicable national rules before the IVDD had become applicable and which are still on the market or in use after 26 May 2022."

[7] MDCG 2022-8: Regulation (EU) 2017/746 - application of IVDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2022 in accordance with Directive 98/79/EC

MDCG 2022-8 provides a summary on the transition periods for IVDs. Specifically, the transition period ends on 26 May 2025 for devices covered by a valid EC certificate per IVDD requirements prior to 26 May 2022, however the 'sell-off date' is 26 May 2026 as per 2nd subparagraph, point (a) of Article 110(4) IVDR). For devices with a declaration of conformity pre 26 May 2022 (per IVDD requirements) that now requires the involvement of a notified body (per IVDR requirements), transition periods end on different dates depending on the class of the device as defined in the IVDR.

For class D devices, the transition period ends on 26 May 2025, with a 'sell-off date' of 26 May 2026 as per 2nd subparagraph, point (a) of Article 110(4) IVDR). For class C devices, the transition period ends on 26 May 2026, with a 'sell-off date' of 26 May 2027 as per 2nd subparagraph, point (b) of Article 110(4) IVDR). The transition period ends on 26 May 2027 for class B devices or class A sterile devices with a sell-off date of 26 May 2028.

IVDR states that legacy devices must comply with the new requirements on post-market surveillance, market surveillance, vigilance, registration of economic operators and devices. Therefore, manufacturers must pay attention to Article 78 and 79 of the IVDR on Post-market surveillance system and Post-market surveillance plan. Article 82 on vigilance, article 83 on reporting and article 84 on serious incidents and field safety corrective actions, must also be adhered to.

Furthermore, as per MDCG 2022-8, "Article 80 IVDR (PMS report) should, as a minimum requirement, apply to all legacy devices, unless a manufacturer of 'legacy devices' that will fall under class C or D voluntarily prepares a PSUR pursuant to Article 81." Finally, the annex in MDCG 2022-8 provides a helpful table illustrating IVDR requirements applicable or not applicable to legacy devices.

MDCG 2022-6 on Guidance on significant changes regarding the transitional provision under Article 110(3) of the IVDR[8] was issued in May 2022 and clarifies the concept of 'significant changes in the design and intended purpose' under IVDR Article 110(3). Importantly, the transition periods for IVDs outlined in Article 110(3) IVDR, only apply when devices do not undergo any significant change in the design or intended purpose after 26 May 2022.
MDCG 2022-6 offers guidance for devices that were compliant under IVDD and that are placed on the market or put into service after 26 May 2022 during the applicable transition period.

Section 4 of this guidance document describes the assessment that needs to be made in order to establish if changes are significant with regards to the design or intended purpose, in accordance with IVDR Article 110(3). The Annex to the guidance displays useful flow charts on design changes and changes of the intended purpose which may be considered 'significant' when interpreting the first sentence of IVDR Art. 110(3).

In July 2022, MDCG published MDCG 2022-12, guidance on harmonised administrative practices and alternative technical solutions until Eudamed is fully functional (for Regulation (EU) 2017/746 on in vitro diagnostic medical devices).[9]

As per Article 30 of Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR), a European database on medical devices ('Eudamed') must be established. As per paragraph 2 of Article 30, Eudamed must be composed of six different modules which will function to collect and process information including that relating to registration, UDI and notified bodies and certificates under the IVDR.

[8] MDCG 2022-6: Guidance on significant changes regarding the transitional provision under Article 110(3) of the IVDR, May 2022

[9] MDCG 2022-12: Guidance on harmonised administrative practices and alternative technical solutions until Eudamed is fully functional (for Regulation (EU) 2017/746 on in vitro diagnostic medical devices), July 2022

As per Article 30, "Eudamed shall include the following electronic systems:

A. the electronic system for registration of devices referred to in Article 26;
B. the UDI database referred to in Article 25;
C. the electronic system on registration of economic operators referred to in Article 27;
D. the electronic system on notified bodies and on certificates referred to in Article 52;
E. the electronic system on performance studies referred to in Article 69,
F. the electronic system on vigilance and post-market surveillance referred to in Article 87;
G. the electronic system on market surveillance referred to in Article 95

MDCG 2022-12 offers guidance and solutions to consider during the absence of Eudamed and describes some "alternative technical solutions" for the exchange of information in the interim. The guidance displays the provisions related to the use of Eudamed, alternative solutions to submit and/or exchange information and the responsible actor(s), in a table for ease of access.

On 26 August 2022, MDCG 2022-14, Transition to the MDR and IVDR - Notified body capacity and availability of medical devices and IVDs10 was published. As per the guidance document, "The MDCG recognises that significant and urgent challenges remain in ensuring sufficient capacity of notified bodies and readiness of manufacturers in order to allow medical devices and in vitro diagnostic medical devices to be certified in accordance with the MDR and the IVDR within the transition periods provided for in the Regulations."[10]

As a result, this document details several actions in relation to notified bodies that may help avoid a shortage of medical devices. The document states that the MDCG will "implement and/or support" the execution of the actions listed.

[10] MDCG 2022-14: Transition to the MDR and IVDR - Notified body capacity and availability of medical devices and IVDs, August 2022

The document lists actions relating to enhanced notified body capacity, access to notified bodies as well as other actions which may help in avoiding a situation where there is a shortage of devices in the future.

3. Conclusion

The European Union's new In Vitro Diagnostic Medical Device Regulation 2017/746 (IVDR) is now in effect, and while its implementation is an important step in guaranteeing safe and effective IVDs, it has also highlighted certain challenges for all involved, including stakeholders, the European Commission and Member States. Concerns remain about notified body capacity and potential lack of availability of IVDs on the European market. The COVID-19 pandemic further compounded challenges felt by all.

Several significant changes were brought about by the new In Vitro Diagnostic Medical Device Regulation 2017/746 (IVDR) including greater involvement of notified bodies in conformity assessment and new regulatory structures such as the EU reference laboratories. Overall however, significant strides have been made in adapting the new regulatory framework for IVDs, including the development of the Eudamed database and the publication of many guidance documents to aid in its implementation.

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Prior to joining Compliance & Risks, Denise worked in the medical device industry for 13 years across a number of areas including regulatory affairs, post-market surveillance, customer complaints, quality, and technical support.

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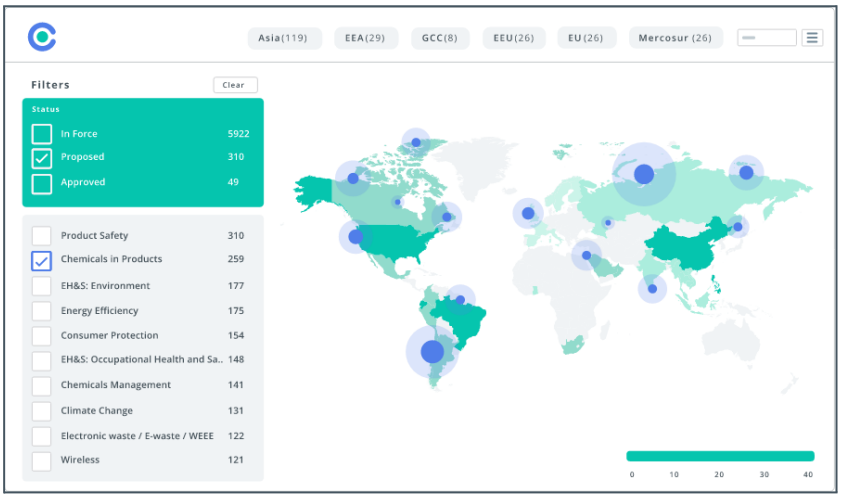

These changes, in general, mean that manufacturers of medical devices need to continuously monitor and assess regulatory requirements to ensure compliance.

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