EU MDR & EU IVDR

THE PATH TO COMPLIANCE

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CONTENTS

The Medical Devices Regulation (2017/745/EU) (MDR) and the In Vitro Diagnostic Medical Devices Regulation (2017/746/EU) (IVDR) introduce new requirements and added responsibilities for manufacturers in order to place their devices on the EU market. These regulations mandate expanded regulatory oversight, increase requirements for clinical evidence, quality management systems, and other documentation, create new methods of device identification throughout the product lifecycle, and institute more direct supervision of notified bodies.

These regulations establish an expectation that all documentation will be seamlessly connected, easily traceable, translated into every member state language where the supplier's products are sold, and registered in the new EUDAMED database as well as on the company's website.

The MDR came into effect on May 26, 2021, following a postponement due to the COVID-19 pandemic. The IVDR was subsequently implemented on May 26, 2022, after thorough deliberations.

While it can feel overwhelming to know how to get started with MDR and IVDR, these nine high-level steps can help you get on the right path to complying with these regulations.

STEP 1: DETERMINE THAT YOU ARE MANUFACTURING A MEDICAL DEVICE AS DEFINED UNDER MDR OR IVDR

MDR Article 2

(1) 'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- Diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease
- Diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability
- Investigation, replacement or modification of the anatomy or of a physiological or pathological process or state
- Providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations

and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.

The following products shall also be deemed to be medical devices:

- devices for the control or support of conception;
- products specifically intended for the cleaning, disinfection or sterilization of devices as referred to in Article 1(4) and of those referred to in the first paragraph of this point.

IVDR Article 2

(2) 'in vitro diagnostic medical device' means any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, software or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on one or more of the following:

- (a) concerning a physiological or pathological process or state;
- (b) concerning congenital physical or mental impairments;
- (c) concerning the predisposition to a medical condition or a disease;
- (d) to determine the safety and compatibility with potential recipients;
- (e) to predict treatment response or reactions;
- (f) to define or monitoring therapeutic measures.

Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices.

If you find that you are unable to confidently make this determination, please skip directly to Step 2.

STEP 2: ENGAGE THE SERVICES OF A REGULATORY COMPLIANCE SPECIALIST

The complexity of these regulations is such that an expert should not only prove to be useful, they are also now required specifically by Article 15 of both regulations. Differences are highlighted in **bold**:

MDR Article 15	IVDR Article 15
Person responsible for regulatory compliance: Manufacturers shall have available within their organization at least one person responsible for regulatory compliance who possesses the requisite expertise in the field of **medical devices**. The requisite expertise shall be demonstrated by either of the following qualifications: • a diploma, certificate or other evidence of formal qualification, awarded on completion of a university degree or of a course of study recognized as equivalent by the Member State concerned, in law, medicine, pharmacy, engineering or another relevant scientific discipline, and at least one year of professional experience in regulatory affairs or in quality management systems relating to **medical devices**; • four years of professional experience in regulatory affairs or in quality management systems relating to **medical devices**.	Person responsible for regulatory compliance: Manufacturers shall have available within their organization at least one person responsible for regulatory compliance who possesses the requisite expertise in the field of **in vitro diagnostic medical devices**. The requisite expertise shall be demonstrated by either of the following qualifications: • a diploma, certificate or other evidence of formal qualification, awarded on completion of a university degree or of a course of study recognized as equivalent by the Member State concerned, in law, medicine, pharmacy, engineering or another relevant scientific discipline, and at least one year of professional experience in regulatory affairs or in quality management systems relating to **in vitro medical devices**; • four years of professional experience in regulatory affairs or in quality management systems relating to **in vitro medical devices**.

The Person Responsible for Regulatory Compliance (PRRC) is considered a new and separate role from your EU Authorized Representative (EC Rep), who must also have a PRRC in place. In fact, the EU Medical Device Coordination Group (MDCG) guidance referenced below states that it cannot be the same individual.

The PRRC essential functions will be to:

- Check that your devices conform with your Quality Management System (QMS) procedures prior to being released on the market
- Ensure that your Technical Documentation for the device as well any Declarations of Conformity are complete and up to date
- Monitor all Post-Market Surveillance (PMS) activities for your devices and ensure that all reporting obligations from these activities are fulfilled

Micro and small enterprises as defined by Commission Recommendation 2003/361/ EC (generally employing fewer than 250 people and having annual revenue of less than €50 million) are exempt from having a PRRC on staff, but are required to have "permanently and continuously at their disposal" a person or organization that meets these qualifications and is based in the EU.

For more on this new role see:

- MDCG 2019-7 Guidance on Article 15 of the Medical Device Regulation (MDR) and in vitro Diagnostic Device Regulation (IVDR) regarding a "person responsible for regulatory compliance" (PRRC)
- For additional assistance navigating the overall complexities of the regulations, here is a link to the European Association of Authorised Representatives (EAAR)

STEP 3: REVIEW YOUR PRODUCT PORTFOLIO TO DETERMINE ANY CHANGES TO CLASSIFICATION

MDR

Using the definitions and rules detailed in Annex VIII, evaluate any changes to classification and conformity assessment that may be required.

There is a notable impact on Class I devices under the MDR. Specifically, while reusable surgical instruments remain in Class I, they now necessitate Notified Body oversight for the validation of cleaning, repackaging, and reprocessing procedures. Any devices transitioning to Class IIa, IIb, or Class III will also require the involvement of a notified body. Additionally, a clinical evaluation consultation procedure for some Class IIb devices and for implantable Class III devices is introduced under Article 54, requiring an independent expert panel's assessment.

IVDR

Using the classification rules detailed in Annex VIII, evaluate any changes to classification and subsequent conformity assessment that may be required. The classification of IVDs has changed to a rule-based approach with four risk categories, from lowest risk, Class A, to highest risk, Class D. Instead of naming specific devices, risk classification is determined by the device intended use and analytes being measured. If more than one rule applies, the rule resulting in highest classification should be followed.

Under the IVDD, approximately 20% of IVD devices required a conformity assessment by a Notified Body, with the balance of devices being self-certified. However, recent updates from the European Commission suggest that under the IVDR, over 80% of previously self-certified IVDD devices now need Notified Body assessment to demonstrate conformity, contrasting sharply with ProClinical Life Sciences' initial estimate of 10-15%. Only unsterilized Class A devices will remain eligible for self-certification. Additionally, MDR and IVDR have escalated certain types of software, such as those assisting in drug dosage determinations or the interpretation of immunoassay analysis results, to higher risk classifications. Some could even be identified as Medical Device Software (MDSW), necessitating further documentation and conformity assessment.

The MDCG has again supplied useful guidance to assist in this determination.

STEP 4: NOTIFIED BODY IDENTIFICATION

As specified in Chapter IV of both MDR and IVDR, notified bodies must be designated and are required to meet more stringent criteria (especially regarding clinical competence) to perform conformity assessment. Your obligation as a manufacturer is to find an appropriate, designated notified body or verify that your current notified body has obtained designation, and that the designation will cover the requirements for assessing all your products.

You should begin working with your notified body immediately to schedule product certifications based on their availability and to uncover and perform any additional data gathering, performance studies, or documentation updates that may be required.

More information can be found in the database of EU Notified Bodies (NANDO).

STEP 5: UPDATE YOUR QUALITY MANAGEMENT SYSTEM (QMS)

Both regulations place an increased emphasis on risk and safety, with a heightened focus on device lifecycle management, including ongoing verification of compliance, post-market surveillance, and vigilance reporting. MDR and IVDR manufacturers will need a procedure for implementing and maintaining unique device identification (UDI) as part of their QMS. This includes the process for importing UDI information into EUDAMED and keeping a current list of all UDIs in service as part of their technical file.

Additionally, MDR and IVDR manufacturers need procedures outlining their planned use and uploading of information to EUDAMED, ensuring their information remains current and accurate.

Here is a master link page with EUDAMED and UDI information.

MDR

In accordance with Article 10(9) of the MDR, all manufacturers, including those in Class I, must establish a formal Quality Management System (QMS). Article 10 provides detailed guidelines for the necessary components of the QMS. While certification to EN ISO 13485:2016 is a significant step toward meeting this requirement, additional considerations may apply. Manufacturers are now required to comply with all post-market provisions of the MDR, including post-market clinical follow-up (PMCF), periodic safety update reports (PSUR), and vigilance reporting.

For Class I manufacturers, there is a notable change: certain devices that were previously exempt are now considered "in scope." Consequently, self-declaration is no longer permissible for these devices, necessitating modifications to the QMS and additional conformity assessments by a notified body. Notable examples include medical purpose devices and active implantable medical devices (AIMD), which fall under the MDR's scope. Additionally, the MDR introduces a new 15-day reporting deadline for serious incidents and requires vigilance reporting if there is any significant increase in the severity or frequency of such incidents.

IVDR

As with MDR, certification to EN ISO 13485:2016 is crucial for satisfying core QMS requirements for IVDR, including these key requirements:

- Establish a post-market surveillance (PMS) system and plan, as well as a post-market surveillance report (PMSR) with any corrective actions
- Prepare a periodic safety update report (PSUR) with additional risk analysis, sales volumes, user population characteristics, and use frequency
- Report serious incidents and field safety corrective actions (FSCA)

Annex III details the need for a "proactive and systematic process" of collecting information and mandates the preparation of a post-market performance follow-up plan (PMPF) or proof of exemption. These PMS processes will be subject to periodic audit by your notified body.

STEP 6: PERFORM A GAP ANALYSIS TO DETERMINE IF ADDITIONAL CLINICAL EVIDENCE IS REQUIRED

In many cases, the new regulations may increase the requirements for clinical evidence for both MDR and IVDR devices, which may add significantly to the cost of placing products on the EU market.

Compliance with current directives in terms of clinical evaluation and investigation is not guaranteed to ensure compliance with MDR and IVDR. Manufacturers may need to revise their overall clinical strategy or create one where none has been required before. Internal procedures for clinical investigation should be aligned with the new requirements and any gaps in clinical evidence remedied for both new and existing devices.

In order to gather, interpret, and communicate the evidence successfully to competent authorities and notified bodies, manufacturers may consider engaging the services of experts experienced with good clinical practice (GCP). GCP is an international quality standard that provides a framework to ensure the safety of human subjects and the integrity and validity of clinical data.

MDR

To demonstrate the conformity of an MDR device, manufacturers must provide evidence supporting an acceptable benefit-to-risk ratio based on clinical evaluation. The clinical data should include relevant clinical information regarding the safety and performance of the device as well as its clinical benefits for patients when used as intended by the manufacturer. The clinical data should generally include clinical investigations, clinical literature for the device or similar devices that has been peer reviewed, and any data from ongoing post-market surveillance activities.

IVDR

The IVDR introduces a risk-based classification system. Consequently, all IVD devices ranked above the low-risk Class A will typically require testing. This shift implies that over 80% of IVD devices might necessitate clinical performance evaluations, a stark increase from the earlier 20% mandate.

According to the regulation, the clinical evidence from these studies should focus on the accuracy of patient information obtained and the clinical benefits of the device as they are assessed against other diagnostic options and technology. The performance studies must demonstrate scientific validity in addition to analytical and clinical performance data that support the intended use of the device.

As with the MDR requirements, manufacturers must implement a post-market surveillance system and processes to update this data throughout the lifecycle of the device.

STEP 7: ASSESS THE COMPLETENESS AND ACCURACY OF TECHNICAL DOCUMENTATION

Both the MDR and IVDR's Annex II and Annex III detail a comprehensive list of information to be included in the device technical documentation. Manufacturers should review the technical file for each device to be sure it includes complete, accurate, and current information.

STEP 8: IDENTIFY AND REVIEW AFFECTED LABELING FOR UPDATES AND GAPS IN TRANSLATION

The definition of "labeling" has been expanded under MDR and IVDR. It now includes all the information provided concerning the device, whether to patient, user or third party, including promotional material, with an emphasis on clarity and accuracy. Article 7 of both MDR and IVDR references not only instructions for use (IFU) and the affixed product label, but also the information supplied when the device is put into service and any advertising to prevent distribution of information that "may mislead the user or the patient with regard to the device's intended purpose, safety and performance."

Manufacturers of MDR and IVDR devices, having taken the prior steps, should now be able to identify the labeling for each impacted device and assess the required changes to claims, warnings, and other information needing update. It is important to note that translation is not optional for most device information and may include software when it provides "instructions for use".

Article 10 of IVDR mandates manufacturers ensure devices are accompanied by the information outlined in Section 20 of Annex I, presented in an official Union language(s) determined by the Member State in which the device is made available to the user or patient. The particulars on the label shall be "indelible, easily legible and clearly comprehensible to the intended user or patient."

Article 10 of MDR makes the same statement, referencing Section 23 of Annex 1. Both regulation sections refer to labels and instructions for use. MDR and IVDR further state that, regarding conformity assessment procedures, "The Member State in which the notified body is established may require that all or certain documents, including the technical documentation, audit, assessment and inspection reports, relating to the procedures referred to in paragraphs 1 to 7 and 9 to 11 be made available in an official Union language(s) determined by that Member State. In the absence of such requirement, those documents shall be available in any official Union language acceptable to the notified body."

Other labeling requirements are detailed in the regulations:

- **Information Placement:** Ensure device and manufacturer identification, along with all relevant safety and performance information, are present on the packaging, in the instructions for use, and on the manufacturer's website.
- **UDI Display:** Labels must display the device's UDI code and clearly indicate its classification as a medical or an in vitro diagnostic medical device.
- **Infrastructure Details:** IFUs must contain any specific infrastructures required for the device's operation.
- **Reuse Guidelines:** Clear instructions must be provided detailing when the device should no longer be reused.
- **Disposal Instructions:** IFUs must give comprehensive guidelines for the safe disposal of the device, including any accessories and consumables.
- **Incident Reporting:** IFUs must contain a warning regarding the user and/or patient need to report any serious incident linked to the device to both the manufacturer and the relevant authority in the Member State where the user and/or patient resides.

STEP 9: REVIEW THE ADEQUACY OF LIABILITY COVERAGE

In light of classification and other changes arising from MDR or IVDR, manufacturers should assess whether current liability coverage is sufficient under the new regulations for any re-classified or newly classified devices in higher risk categories.

MDR

"In view of the fact that natural or legal persons can claim compensation for damage caused by a defective device in accordance with applicable Union and national law, it is appropriate to require manufacturers to have measures in place to provide sufficient financial coverage in respect of their potential liability under Council Directive 85/374/ EEC (1). Such measures should be proportionate to the risk class, type of device and the size of the enterprise. In this context, it is also appropriate to lay down rules concerning the facilitation, by a competent authority, of the provision of information to persons who may have been injured by a defective device."

IVDR

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SUMMARY

Many helpful EU MDCG templates and guidance documents regarding notified bodies, UDI, EUDAMED, clinical evaluation, and other topics can be found on this site from the European Commission.

Compliance remains essential to placing your products on the EU market. Have you ensured that adjustments based on these regulations are included in your release plans and factored into your budget?

ABOUT ARGOS

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