Regulatory Affairs

"New IVD European Regulation: main changes for In-Vitro Diagnostic Medical Devices and new obligations for the economic operators."

Werfen

Introduction

Regulatory Affairs in the Medical Devices and In-Vitro Diagnostic Medical Devices market is vital in making safe and effective medical devices available worldwide.

Regulatory Affairs is intended in particular to ensure that companies comply with all of the regulations and laws pertaining to Medical Devices and In-Vitro Diagnostic Medical Devices and to work with federal, state and local regulatory agencies to enter (and remain) into each market.
The scope of Regulatory Requirements is to ensure quality of products and safety to patients, users, and any other stakeholders.

These guidelines provide a general overview on the main changes and requirements related to the new IVD European Regulation (IVDR), that is applicable in **every EU Country** and that will involve many stakeholders: Manufacturers, Distributors and Importers, National Authorities, Notified Bodies, Customers.

Contents

IVDR: Definitions

IVDR
The IVDR is the new In-Vitro Diagnostic Medical Devices Regulation that will be applicable in every EU Countries (2017/746/EU).

IVDR Publication Date: May 2017
The date in which the Regulation was published by the EU Comission. After the publication, a 5 years transition period started.

IVDR Application Date: 26 May 2022
This is the date of the effective entry into force of the new Regulation, at the end of the transition period.

IVDD
The current In-Vitro Diagnostic Medical Devices Directive (98/79/CE) that remains applicable in every EU country until the IVDR Application Date (22 May 2022).

Legal Manufacturer
A natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under its name or trade mark.

European Authorized Representative
Any natural or legal person established within the Union who has received and accepted a written mandate from a manufacturer, located outside the Union, to act on the manufacturer's behalf in relation to specified tasks with regard to the latter's obligations under the European Regulation.

Distributor
Any natural or legal person in the supply chain, other than the manufacturer or the importer, that makes a device available on the market, until the point of putting into service.

European Importer
Any natural or legal person established within the Union that places a device from a third country on the Union market. Werfen distribution center, located in Roncello, is included in this definition.

Notified Body
A conformity assessment body designated by the European Competent Authorities in accordance with the IVDR.

UDI (Unique Device Identifier)
A series of numeric or alphanumeric characters created through international indentification and coding standards, that allows unambiguous identification of a specific device on the market and includes the following information: device model, lagal manufacturer, lot/serial number, manufacturing date, expiration date.

CE Declaration of Conformity
Declaration signed by the Manufacturer to demonstrate the compliance of the In-Vitro Diagnostic Medical Devices with the IVDR essential requirements.

CE Certificate
Certificate issued by a Notified Body to demonstrate the compliance of the In-Vitro Diagnostic Medical Devices with the IVDR essential requirements.

IVDR: Transitional provisions

The new In-Vitro Diagnostic Medical Devices Regulation (2017/746/EU), also named as “IVDR”, was published by the EU Commisison in May 2017, marking the start of a 5 years transition period from the current IVDD.

During this transition, the IVDR will come into force gradually, so that the effective application date is May 26, 2022. During this transition, the current IVDD will continue to remain applicable in every European Country and for all In-Vitro Diagnostic Medical Devices, until May 26, 2022.

Table: Legal Manufacturers and Authorized Representatives in Werfen

Werfen Products Line	Werfen Legal Manufacturers	EU Authorized Representatives
Hemostasis	IL Co (US)	IL SpA (Italy)
	Accriva (US)	MDSS (Germany)
Acute Care	IL Co (US)	IL SpA (Italy)
	Accriva (US)	MDSS (Germany)
	TEM (Germany)	Not applicable (Manufaturer in EU)
Clinical Chemistry	IL SpA (Italy)	Not applicable (Manufaturers in EU)
	Biokit (Spain)	
Autoimmunity	Inova (US)	Promedt (Germany)
Serology	Biokit (Spain)	Not applicable (Manufaturer in EU)

IVDR: Requirements of the Manufacturers and main changes for In-Vitro Diagnostic Medical Devices (IVDs)

IVDs Classification

IVDs shall be classified by the Manufacturer into 4 different classes: **Class A, Class B, Class C, Class D.**
The classification will take into account the intended purpose of every device and its related risks.
An official guidelines on the IVDs Classification will be released by the EU Commission; an updated Regulatory Guidelines on IVDR will follow to include the classification for Werfen products.

Conformity Assessment

Prior to placing a device on the market, the Manufacturer shall undertake an assessment of the conformity of that device, based on the IVD classification.

CLASS B, CLASS C, CLASS D devices:
The Conformity Assessment shall be performed through an external Notified Body.
The Notified Body will review and assess the quality system of the Manufacturer and the technical files of the products in order to demonstrate whether the requirements of the IVDR relating to the devices have been fulfilled. At the completion of the assessment, the Notified Body will release the CE Certificate for the involved device. The labeling and the CE Declaration of Conformity prepared by the Manufacturer will report the identification number of the Notified Body.

CLASS A devices:
The Conformity Assessment will be performed without an external Notified Body. At the completion of the assessment, the Manufacturer will issue and sign the CE Declaration of Conformity for the involved device. Anyway, the quality system of the Manufacturer shall comply with ISO 13485.

Notified Bodies

The IVDR requires Notified Bodies to be designated by the European Competent Authorities. Notified Bodies will be required to meet more stringent criteria, in particular in terms of scientific and technical evaluation competence. The process of designation may take 12 months or more, following the application by a Notified Body, and it will involve assessors from different European authorities.

Clinical Evidence

The clinical evidence for each device shall be based on scientific literature, analytical performance and clinical performance studies (where needed). The collection of the Clinical Evidence is intended to proof the clinical benefit of a device.
The level of Clinical Evidence needed to demonstrate the conformity of a device becomes progressively more stringent as the device risk class increases.

Eudamed

Eudamed is the European central database of medical devices and IVDs, that will be operative under the IVDR. The database will include the following data:

- UDI (unique device identification) assigned by the Manufacturer;
- CE Certificate issued by the Notified Body (for Class B, C, D);
- Legal Manufacturer, European Authorized Representative, Importer;
- Incidents and Field Safety Corrective Actions issued by the Manufacturer.

Most of the these information will be accessible to the public.
The levels of accessibility will be defined by the EU Commission; an updated Regulatory Guidelines on IVDR will follow to include more details on Eudamed structure and levels of accessibility.

IVDR: Main changes and requirements for the European Authorized Representative

Under the IVDR, the EU Authorized Representative shall be legally liable for defective devices on the same basis of the Manufacturer.

In addition, the EU Authorized Representative shall have the following obligations:

- Have a designation in a written mandate signed with the Manufacturer. This mandate shall remain available and at disposal of National Authorities.
- Verify that the CE Declarations of Conformity and Technical Files have been drawn up and the appropriate conformity assessment procedure has been completed.
- Keep available copy of Technical Files, CE Declarations of Conformity and CE Certificates (including updates and amendments);
- Comply with registration obligations in Eudamed database;
- Provide any information required by the National Authorities and cooperate with the National Authorities;
- Cooperate with the Manufacturer in Field Safety Corrective Actions and Incidents handling, in connections with the Importer and the Distributors;
- Forward to the Manufacturer any request recived from the National Authorities;
- Forward to the Manufacturer any complaint received from customers, users or patients.
- EU Representative shall have within its organization at least 1 person responsible for regulatory compliance.

The Legal Manufacturer cannot delegate to the EU Representative the following actions: design, risk management, performance evaluations, technical files, CE Declaration of Conformity and Conformity Assessment.

IVDR: Main changes and requirements for Distributors

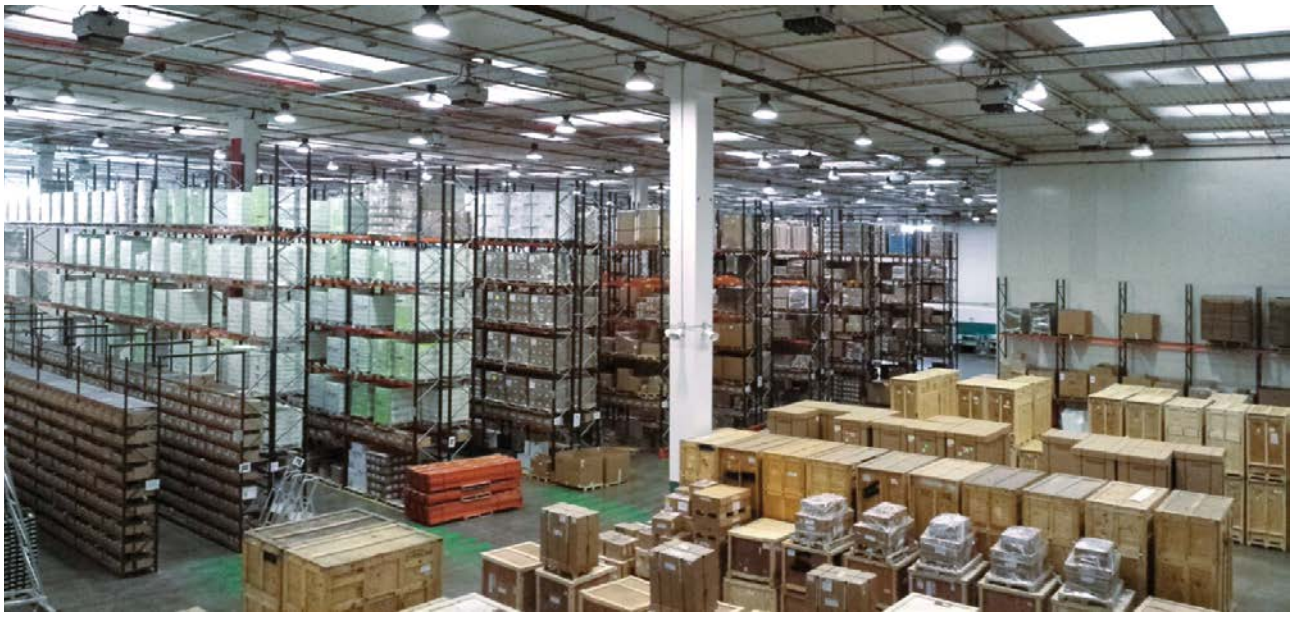
Every Distributor (Werfen Affiliates or third-party distributors) shall have the following obligations under the IVDR.

- Before making a device available on the market, the Affiliate/Distributor shall verify that:
  - ✓ The device has the CE mark and the CE Declaration of Conformity (CE mark must be readable on label, packaging and instructions for use, along with the Notified Body code if applicable);
  - ✓ Manufacturer and EU Authorized Representative are identified;
  - ✓ The device is labelled in accordance with the IVDR requirements and is accompanied by the required instructions for use (instructions for use shall be provided in the language required by the EU countries where the device will be commercialized);
  - ✓ The Manufacturer assigned the UDI (Unique Device Identification code), that must be reported on labelling;
  - ✓ Importer's name/address is reported on device, packaging or other document provided along with the device (for example the invoice).
- Where the Distributor considers that a device is not in conformity with the requirements of the IVDR, they shall not make the device available in the market until it has been brought into conformity, inform the Manufacturer and EU Representative and cooperate with them to ensure that the necessary cor rective actions are taken.
- Distributor shall ensure that storage and transport conditions are met.
- Distributor who receives complaints from users and customers, shall immediately forward the information to Manufacturer and EU Authorized Representative.
- Distributor shall keep records of complaints, non-conforming devices and recalls, and cooperate with Manufacturer, EU Authorized Representative and National Authorities.
- Distributor can translate locally the information provided by the Manufacturer (example: instructions for use) in order to market the device in the relevant Member State. In this case the Distributor shall indicate on the device, on the packaging or in a document accompanying the device, the translation activity and the name/address of the Distributor itself. The Distributor shall have in place a quality system including a procedure on the translation process. 28 days prior to making the device available on the market, Distributor shall inform the Manufacturer and the National Authority of the relevant Member State and, upon request, provide a copy of the translated documents.

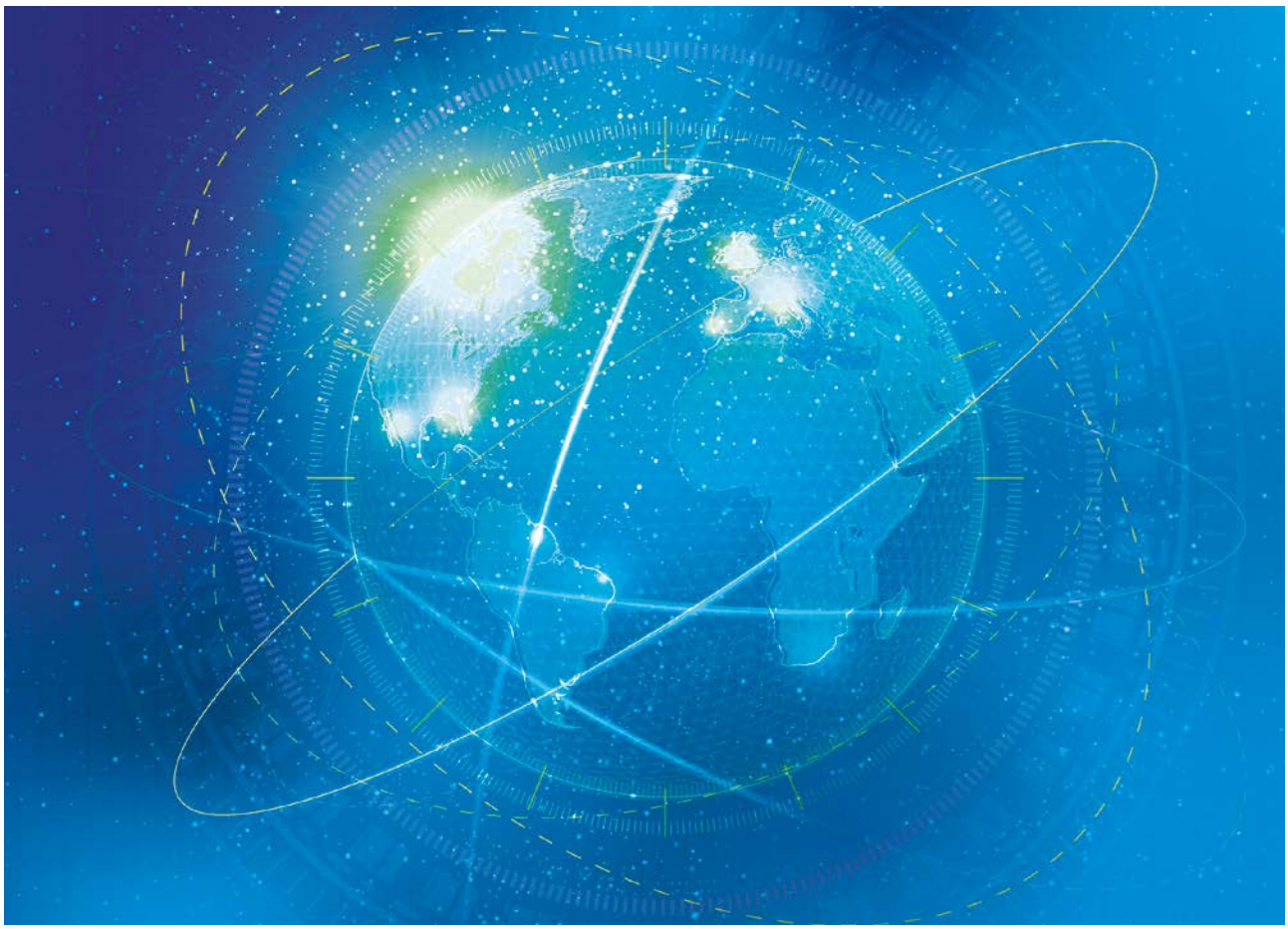
IVDR: Main changes and requirements for the European Importer (Werfen European Distribution Center)

Under the IVDR, the Werfen European Distribution Center (Roncello) will be the European Importer for all Werfen product lines.
The European Importer shall have the following obligations under the IVDR.

- Before making a device available on the market, the Importer shall verify that:
  - ✓ The device has the CE mark and the CE Declaration of Conformity (CE mark must be readable on label, packaging and instructions for use, along with the Notified Body code if applicable);
  - ✓ Manufacturer and EU Authorized Representative are identified;
  - ✓ The device is labelled in accordance with the Regulation and is accompanied by the required instructions for use (instructions for use shall be provided in the languages required by the EU countries where the device will be commercialized);
  - ✓ The Manufacturer assigned the UDI (Unique Device Identification code), that must be reported on labelling;
  - ✓ Importer's name/address is reported on device, packaging or other document provided along with the device (for example the invoice).
- Where Importer considers that a device is not in conformity with the requirements of the IVDR, they shall not make the device available in the market until it has been brought into conformity, inform the Manufacturer and EU Representative and cooperate with them to ensure that the necessary corrective actions are taken.
- Importer shall verify that the devices are registered in Eudamed, and shall be registered as well in Eudamed.



- Importer shall keep a copy of CE Declaration of Conformity and CE Certificate at least for 10 years after the last device is placed in the market.
- Importer shall ensure that storage and transport conditions specified by the Manufacturer are met.
- Importer who receives complaints from users and customers, shall immediately forward the information to Manufacturer and EU Authorized Representative.
- Importer shall records of complaints, non-conforming devices and recalls, and cooperate with Manufacturer, EU Authorized Representative and National Authorities.
- European Importer can translate locally the information provided by the Manufacturer (example: instructions for use) in order to market the device in the relevant Member State.
  In this case the Importer shall indicate on the device, on the packaging or in a document accompanying the device, the translation activity and the name/address of the Importer itself.
  The Importer shall have in place a quality system including a procedure on the translation process.
  28 days prior to making the device available on the market, Importer shall inform the Manufacturer and the National Authority of the relevant Member State and, upon request, provide a copy of the translated document.



Notes

Working *together*

To speed up **time to market**

To ***meet both*** regulatory requirements *and commercial goals*

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