PHARMA AERO
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MEDICAL DEVICES REGULATIONS PROJECT

Balancing Innovation and Regulations: from Care to Air

WHITE PAPER
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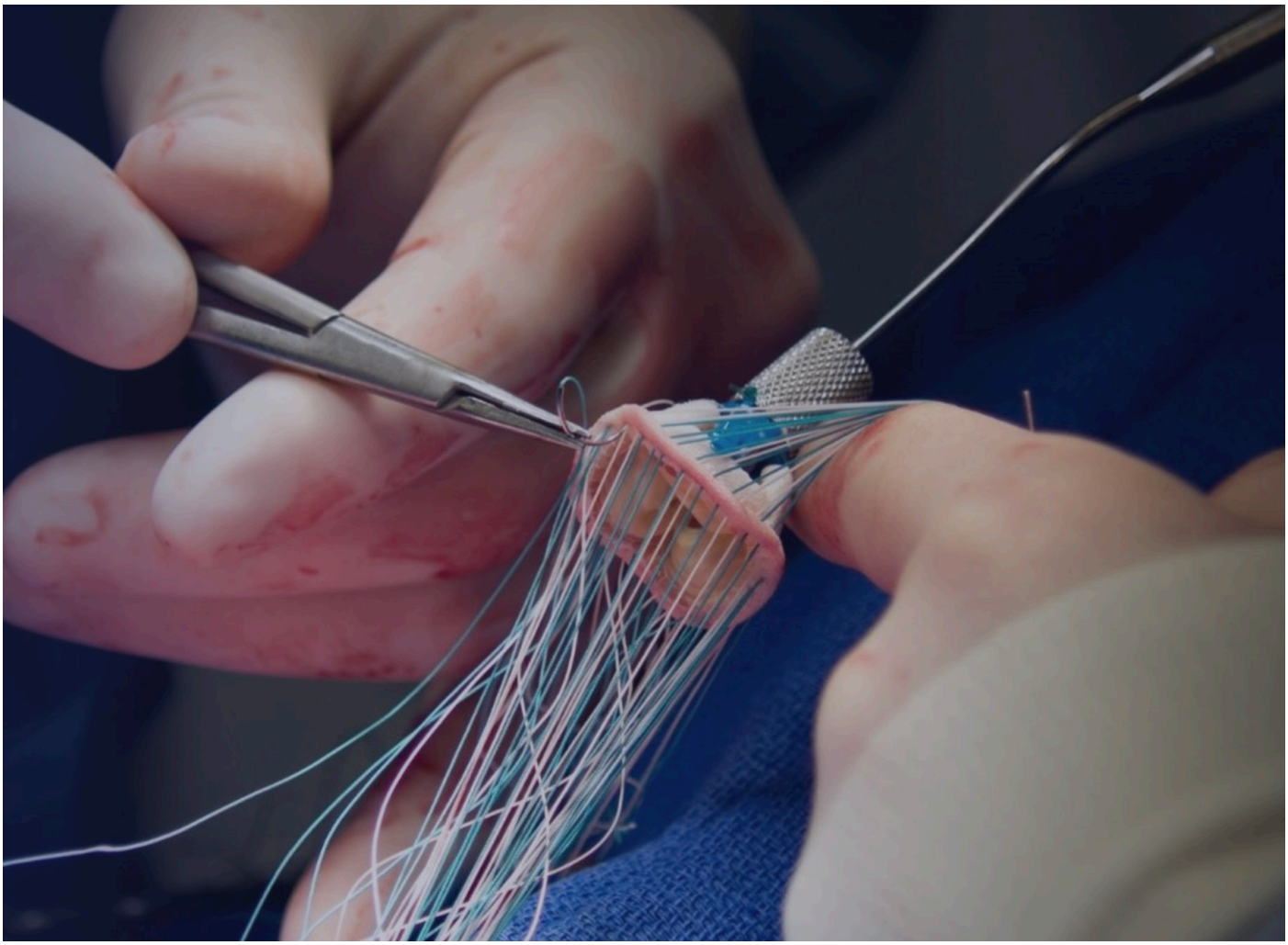
ABSTRACT

The effective management of logistics supply chain processes is pivotal for ensuring access to critical medical therapies, encompassing both pharmaceutical products and medical devices. Recent events, notably the Covid-19 pandemic, have highlighted the essential role of medical devices, such as masks, tests, ventilators, and oxygen supplies, in healthcare delivery.

The "MDR Project", initiated by Pharma.Aero, is a collaborative effort of industry stakeholders aiming to offer a better understanding of the evolving regulations and their impact on supply chain operations. Key findings reveal the dynamic landscape of the medical device industry within the EU, its classification system based on risk, and the roles of various economic operators.

The project also identifies business opportunities for logistics service providers and support them in enhancing their value proposition within the medical device supply chain.



INTRODUCTION

Traditionally, medical devices have received less regulatory attention compared to pharmaceuticals. However, recent events, such as the Covid-19 pandemic, have underscored the critical importance of medical devices in healthcare delivery. The sudden surge in demand for items like masks, tests, and protective equipment highlighted the essential role of medical devices, including life-saving equipment like mechanical ventilators and oxygen supplies, in managing public health crises and saving lives.

This heightened awareness has prompted regulatory bodies, such as those in the European Union, to introduce the Medical Device Regulation (MDR), addressing various aspects of medical device oversight and introducing new stakeholders into the supply chain.

METHODOLOGY

Recognizing the pivotal role of logistics in ensuring timely access to both pharmaceuticals and medical devices, Pharma.Aero initiated the Medical Device Regulations project with the following objectives:

- Provide a comprehensive understanding of the regulatory landscape to offer clear insights into the implications on logistics supply chain operations of Medical Devices.
- Determine if specific certifications from the logistics supply chain partners and manufacturers are required.
- Identify variations (if any) from the current EU GDP regulations and their impact on the existing framework.

Project Structure and Methodology

Work Package 1: Engaging the stakeholders

The relevant stakeholders such as project leads and team members were identified and engaged on the project's objectives and expectations. The kick-off session was aimed to align on the timeline, deliverables, roles and responsibilities, project scope and communication channels. This stage is crucial for a successful project launch and a collaborative environment among stakeholders.

Work Package 2: Desk research and assessment

In this stage of the project, thorough desk research was conducted to gather relevant information on the current landscape of the medical device industry and the Medical Device Regulation. Additionally, the research focused on trends in the logistics environment in both the medicinal product and medical device industry to map out differences and create a gap analysis between the Medical Device Regulation and the current guidelines on Good Distribution Practices.

Work Package 3: Interviewing logistic stakeholders to understand the impact of MDR on their activities

Relevant logistic stakeholders were interviewed to gain insights into how the Medical Device Regulation affects their operations, processes, and overall business strategies. The set of questions was designed to focus on perspectives, challenges, and needs related to compliance with MDR requirements.

Work Package 4: Publications

The project's findings were presented in a detailed, comprehensive Technical Report accessible to Pharma.Aero members and partners only. This White Paper is made available for the broader industry community.

PROJECT TEAM

Project team composition

NAME	ORGANISATION	PROJECT ROLE
Andy Faes	Expeditors	Project Lead
Rashmi Karnad	Qatar Airways	Project Manager
Morgane Franck	PwC	Project Manager
Arno Parisis		Project Support
Sara Van Lerberghe	Pharma.Aero	Project Coordinator
Frank Van Gelder		Secretary General
Hugo Repolho	Guarulhos Airport	Board Liaison
Gergely Szorcsik	Zoetis	Board Liaison

RESULTS

1. The Medical Device sector

Within the EU, the medical device sector is dynamic and competitive, characterized by active participation from small and medium-sized enterprises. The EU market boasts over 500,000 types of Medical Devices (MDs) and In Vitro Diagnostic Medical Devices (IVDs), encompassing a wide range of products:

- Personal protective equipment (PPE) materials such as shoe covers and masks
- Implantable devices such as pacemakers and stents
- Diagnostic imaging technologies like X-ray and MRI machines
- Devices for supporting organ physiology such as external heart pumps

Software apps and breast implants are also categorised as medical devices.

IVDs, on the other hand, are primarily used for conducting tests on samples, encompassing a range of products such as HIV blood tests, pregnancy tests, and blood sugar monitoring systems for individuals with diabetes.

Regulatory background

The first set of regulations regarding the medical devices at EU level came in 1990, in the form of the Active Implantable Medical Devices Directive (AIMDD) 90/385/EEC. Three years later, in 1993, the Medical Device Directive (MDD) came into force, aiming to harmonise the laws relating to medical devices within the European Union.

Prior to the implementation of the Medical Device Directives (MDD), the marketing of medical devices across European Member States necessitated compliance with individual national standards in each jurisdiction. Consequently, manufacturers encountered a disparate array of testing criteria, resulting in a complex trade environment within the EU. The Active Implantable Medical Devices Directive (AIMDD) and the Medical Devices Directive (MDD) introduced pivotal provisions and established standardized norms to ensure uniformity across Europe, facilitating the unhindered movement of goods.

While instrumental in fostering a unified market for medical devices in Europe since their inception, these directives exhibited certain shortcomings. As a result, the Medical Device Regulation (MDR) was published in the Official Journal of the European Union (OJEU) in May 2017.

Classification of Medical Devices

The marketing and sale of medical devices within the European Economic Area (EEA) are subject to stringent regulations by the European Union. Compliance with the Medical Device Regulation (MDR) or the In Vitro Diagnostic Medical Device Regulation (IVDR) is imperative for obtaining or retaining a CE marking (Conformité Européenne, or European Conformity).

MDR Article 51 categorises devices based on their intended purpose and inherent risks. Duration of use and invasiveness are also factors influencing the classification.

Transient duration devices
Used continuously for less than one hour
Short-term duration devices
Used continuously between one hour & 30 days
Long-term duration devices
Used continuously for more than 30 days

Invasive devices
Enter the body through an opening or surface
Non-invasive devices
Do not enter the body

Active devices
Require a source of energy for operation
Non-active devices
Do not require a source of energy for operation

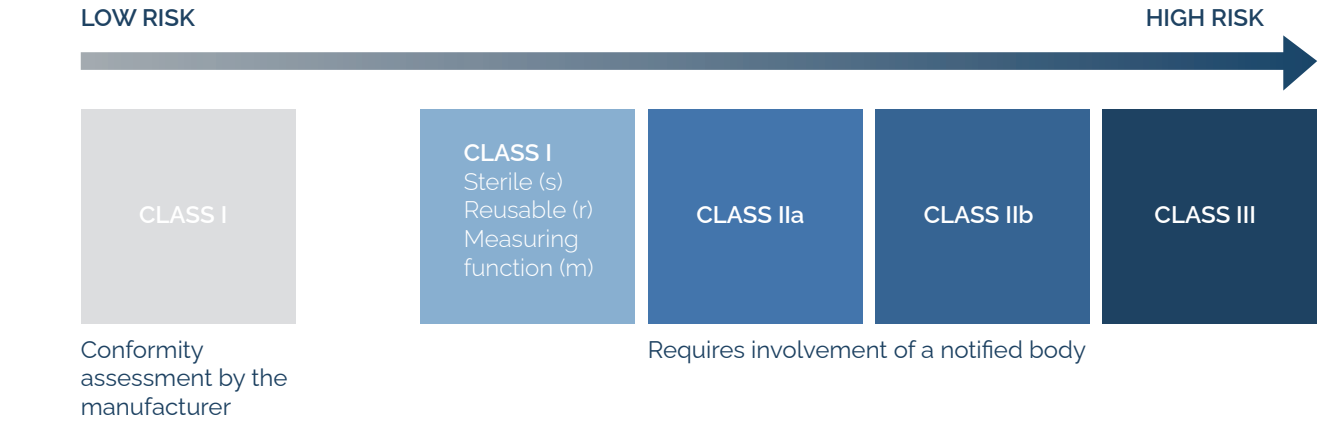
Class I devices are predominantly non-invasive and present a low risk to patients. This class is subdivided as follows:

- **Class I:** Devices that are non-sterile or lack a measuring function (e.g., wheelchairs, hospital beds)
- **Class Is:** Devices delivered sterile, requiring transportation in sterile conditions or sterilisation upon receipt (e.g., sterile gauze, personal protection kits)
- **Class Im:** Devices with a measuring function (e.g., stethoscopes, thermometers)
- **Class Ir:** Devices that are reprocessed or reused (e.g., surgical instruments, endoscopes)

Class IIa devices present a moderate risk to patients, typically being invasive and remaining in the body for less than 30 days. Approximately 20% of medical devices in the EU market belong to this category, including hearing aids, and ultrasonic diagnostic equipment.

Class IIb devices pose a medium to high risk to patients, primarily invasive and usually remaining in the body for over 30 days. Around 8% of medical devices fall under this category, such as infusion pumps, ventilators, and dialysis machines.

Class III devices present a high risk to patients, being invasive and designed to support human life or prevent the impairment of human health. Only 2% of medical devices fall into this category, including pacemakers and prosthetic heart valves.



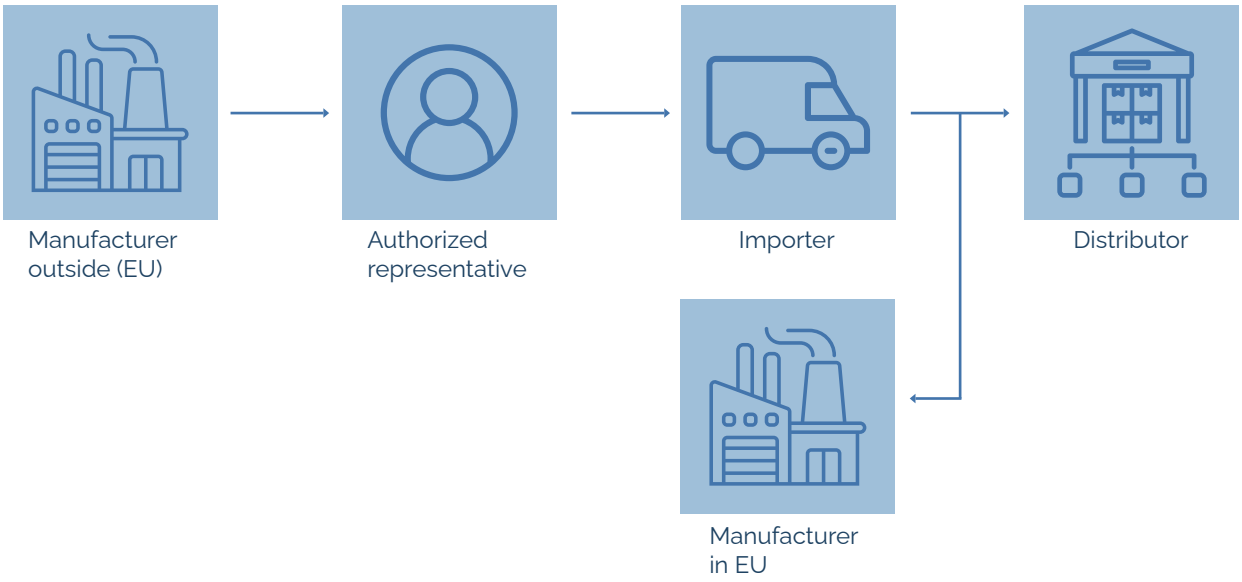
Main stakeholders

a. Economic operators

Under the European Union Medical Device Regulation, there are various stakeholders that need to collaborate. Having a clear understanding of the different roles is crucial to ensure compliance. The MDR focuses on four designated legal entities (economic operators):

- Manufacturers
- Importers
- Distributors
- Authorised representatives

Each of these entities bears distinct responsibilities (art. 10, 11, 13, 14 MDR), including record-keeping, reporting, and product handling. Collaborating with partners who fully adhere to these regulations is paramount, as it guarantees the safe and effective delivery of medical devices to the EU market.



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 trademark"

The manufacturer stands at the centre of the medical device ecosystem, being responsible for creating, designing, and producing medical devices that meet strict regulatory requirements. This involves conducting risk assessments, clinical evaluations, and maintaining quality management systems to ensure compliance. Manufacturers also need to provide clear labelling and user instructions for their devices.

Importer

"Any natural or legal person established within the Union that places a device from a third country on the Union market"

Importers' responsibilities include ensuring manufacturers' compliance with regulatory standards, overseeing labelling and packaging, and collaborating with regulatory authorities on market surveillance efforts. Importers are essential for maintaining the safety and reliability of devices during the import process.

Authorised 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 this Regulation"

Non-EU manufacturers must appoint an Authorised Representative within the EU, serving as a connection between the manufacturer and EU regulatory bodies to ensure compliance with EU directives. The authorised representative must be located in the same member state as the authority. Its responsibilities include maintaining technical documentation, handling complaints, and working with authorities to ensure regulatory compliance.

In some cases, a company can serve as both the authorised representative and the importer for a medical device under the Medical Device Regulation. For instance, a multinational corporation that manufactures medical devices outside the European Union may choose to appoint one of its subsidiaries or a designated entity within the EU to act as both the authorised representative and importer. This approach allows for streamlined regulatory compliance and facilitates efficient communication between the manufacturer and EU regulatory authorities. It's crucial for the designated entity to understand and fulfil the distinct responsibilities associated with each role to ensure compliance with MDR requirements and uphold the safety and effectiveness of the medical devices being imported and marketed in the EU.

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, up until the point of putting into service"

Distributors serve as vital intermediaries linking manufacturers and end-users, facilitating the entry of medical devices into the EU market.
While sometimes mistaken for logistic operators, distributors may maintain European warehouses and oversee device delivery across Europe. However, they often enlist logistic service providers for wider distribution. Distributors also ensure adherence to labelling standards and promptly report incidents or compliance issues.

b. Other stakeholders

Besides economic operators, other stakeholders in the medical device value chain include Notified Bodies (NB) and Logistic Service Providers (LSP).
In the Medical Device Regulation, a Notified Body is an accredited independent organisation designated by an EU member state to verify if certain medical devices comply with regulatory standards. Notified Bodies are key in certifying devices by reviewing technical documents, conducting assessments, and issuing CE certificates, demonstrating compliance with MDR standards.

The relationship between Notified Bodies and economic operators (such as manufacturers, importers, distributors, and authorised representatives) revolves around collaboration. Economic operators depend on Notified Bodies to ensure their devices meet EU rules for market entry, relying on them for verification, certification, and guidance along the process. Conversely, Notified Bodies require accurate information from economic operators to perform their duties effectively. This highlights the importance of clear communication and teamwork in ensuring the safety and quality of medical devices.

Logistic Service Providers offer storage and/or transportation services, often subcontracted by pharmaceutical companies. In this setup, the LSP typically does not assume ownership of the devices and therefore is not classified as an economic operator (e.g. importer or distributor), under the MDR. The MDR compliance stays in the responsibility of the outsourcing company, holding ownership or possession rights over the devices. Therefore, clear agreements outlining each party's responsibilities are essential. Unlike regulations for medicinal products, LSPs are not required to hold specific authorisations to store or transport medical devices unless requested by the contracting medical device company.

This technical report aims to support logistic service providers in understanding the potential impact of the medical device regulation on their business and how they can add value to the medical device supply chain, as elaborated in chapter V of the report.

2. The impact of evolving medical device regulations on logistics service providers (LSP)

As part of Pharma.Aero's MDR project, the project team focused on assessing if and how the logistics providers were impacted by the transition from the Medical Device Directive (MDD) to the Medical Device Regulation (MDR) at EU level. For a correct assessment, a set of interviews were conducted with several logistic service providers and a gap analysis between MDR and Good Distribution Practices (GDP) was undertaken.

Logistics Service Providers' perspectives

1. None of the logistic operators could be classified as an economic operator according to the regulation. As mentioned above (Section III.4), the roles and responsibilities are related to entities/companies that would be in the ownership of the medical device.

2. The impact of the transition from MDD to MDR on the Quality Management System (QMS) is heavily linked to the companies' roles. While manufacturers and distributors had to rethink the processes and designate working groups to ensure full compliance, the logistics service providers were not directly impacted. Nevertheless, the logistics service providers detected new requirements from the contracting companies, indirectly leading to an update of the QMS.

3. The logistic service providers already serving the pharmaceutical / healthcare industry refer to the Good Distribution Practices as standard. Some interviewees also referred to the ISO9001 and ISO13485, indicating high level quality processes. While ISO13485 certification is not generally considered a decisive factor in the procurement process, it might influence the decision when two providers are in equivalent positions, in terms of quality system and compliance.

4. Interviewed LSPs did not notice any change across territories, as QMS is designed to cover procedures globally. Local requirements are embedded locally or in quality agreements between parties.

5. LSPs didn't face any additional challenge posed by the shift in the regulation framework. Medical devices are generally stored/transported in environments that have no temperature monitoring, although labelling indicates certain temperature ranges. In the MDR context, the temperature ranges should be taken into account or at least analysed from a risk-based approach.

To date, medical device companies didn't have additional or stricter requirements towards their service providers. However, it is important to note that authorities are not yet performing inspections on a regular basis for the medical device economic operators. Should verification intensify, it is expected that contracting companies will have inspections-related additional requirements.

Good Distribution Practice and Medical Devices

The Good Distribution Practice for medicinal products for human use is a widely known standard within healthcare logistics. It applies to pharmaceutical companies and logistics service providers, aiming to ensure a robust supply chain and avoid product falsification and loss of quality. The GDP is mandatory for transporting medicinal products. However, it is not applicable to medical devices. are not in scope and a logistic service provider has therefore less restrictions when performing activities with medical devices. But how does the new regulation for medical devices impact this?

A Gap Analysis was undertaken to compare the GDP principles and requirements with the MDR. The aim of the analysis was to determine whether a logistic service provider engaged in activities involving both medicinal products and medical devices can adhere to GDP standards, or if additional requirements should be considered for the devices.

As a general conclusion, if GDP is already integrated as a standard approach within the QMS of the logistic service provider, no changes are necessary, as GDP offers comprehensive and strict guidance on the handling of (medicinal) products. If GDP is not standard embedded in QMS, no immediate changes are required unless requested by the medical device company. In such cases, the company functioning as an economic operator holds the ultimate responsibility for ensuring all requirements (e.g. environmental monitoring) are met. Nevertheless, it is beneficial to ascertain whether any local requirements from the local health authority pertain to distribution activities concerning medical devices. For instance, the Belgian Federal Agency for Medicines and Health Products (FAMHP) has formulated guidelines on Good Distribution Practices for medical device distributors.

CONCLUSIONS

The medical device market is experiencing rapid growth and playing an increasingly significant role in the healthcare industry. In terms of logistics, the new regulations have had a greater impact on medical device manufacturers and entities within the EU that will take ownership of the device, rather than service providers that are working as a subcontractor for these entities with ownership of the product. Manufacturers have been compelled to ensure compliance with a myriad of requirements and enlist appropriate economic operators in their value chains, both in the EU and indirectly on a global scale. However, given that the medical device market is often overlooked, investing in understanding the regulations and requirements faced by medical device companies could unveil untapped opportunities to enhance the value chain. While conducting the comprehensive evaluation of the Medical Device Regulation, within the scope of the Pharma.Aero project, the MDR project team identified several opportunities for logistics service providers to offer additional services in support of various economic operators within the medical device sector. These opportunities encompass facilitating market entry, efficient returns management and new opportunities in the handling of special (hazardous) materials. They are elaborated in detail in the project's Technical Report, accessible exclusively to members of the Pharma Aero community.

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