The European Medical Devices Regulation 2017/745
The European IVD Regulation 2017/746

Training May 2021

Bringing Ingenuity to Life
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Agenda

1. General Introduction
2. Economic Operators
3. Classification and conformity assessment changes
4. Clinical evaluation and post market surveillance
5. Labelling
6. Q&A
01
General Introduction
EU MDR and IVDR are the most significant regulatory changes in Europe impacting MedTech, IVD and pharma industry

Medical devices regulations bring a culture change to devices and pharma companies
• Software apps (SaMD) are regulated more stringently than in the US, some may require clinical data
• More than 80% of the in vitro diagnostic devices (IVDs) need approval from the Notified Body compared to less than 20% previously
• ~30% of IVD companies have not begun the compliance project with due date looming in one year, another 20% are in gap assessment phase
• Importers and distributors must perform verifications, and in some cases need a quality management system (QMS).
• Companies will spend 7% to 13% of EU sales on compliance expenses (source: MedTech Europe)
Why the new legislation?

- **One regulation applicable throughout Europe.** The old directives needed to be adopted into local law to become effective. Countries tended to bring in small changes/own interpretation when transposing into national law.
- **Increased focus on clinical data** because of problems with (implantable) devices that were marketed without any clinical evaluation.
- **Proactive Post Market Surveillance** with a feedback loop into the device design and risk management intends to support early detection and remediation of product failures.
- **Increased requirements for Notified Bodies** must ensure equal competencies and standards applied and as such a more level playing field for manufacturers.
- **Introduction of an implant card** creates transparency for patients on which devices they have been implanted with.

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**EU MDR transition period**


**Grace Period**

**IVDR Transition Period**

**Grace Period**
MDR/IVDR highlights

Scope expansion
‘cosmetic’ devices
Supply chain

Notified Bodies
Significantly increased requirements
Cumbersome re-designation procedure
leading to a shortage of NBs

New/updated classification rules
Up-classification of software, surgical meshes,…
New class lr
Class llb implantable devices treated as class lll

Economic Operators
Bringing in compliance requirements
for the supply chain
Person Responsible for Regulatory Compliance

EU medical devices database
EUDAMED
Implementation delayed until 2022
Device registration including UDI
clinical, labeling and safety data

Better traceability of medical
devices using UDI,
Verifications throughout the supply chain
UDI on the label, implant card and patient leaflet

Stricter requirements for clinical
evidence and safety
Throughout the lifecycle of the device
Post market clinical follow up
Pro-active post market surveillance
There are less Notified Bodies available due to the more stringent requirements

*Haemonetics uses TÜV SÜD (MDR and IVDR), MDC (IVDR), BSI (MDR)*

<table>
<thead>
<tr>
<th>Type of Devices</th>
<th>Active Notified Bodies</th>
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<tbody>
<tr>
<td>MDD</td>
<td>52</td>
</tr>
<tr>
<td>IVDD</td>
<td>18</td>
</tr>
<tr>
<td>MDR</td>
<td>20</td>
</tr>
<tr>
<td>IVDR</td>
<td>4</td>
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*Notified Bodies are designated under MDR/IVDR for specific types of devices*, only BSI and TÜV SÜD have applied for the full scope.
The path to CE marking has become a bit more cumbersome…
EU MDR affects all areas of the business

- **R&D, Clinical & Medical Safety**
  - Clinical evaluation strategy & post-market surveillance plans
  - *CEP, PMCF, PMSP(R), PSUR, SSCP
  - Usability/human factors, DHF creation

- **Quality Assurance**
  - *PRRC strategy
  - QMS ISO13485:2016 assessment and remediation strategy
  - Document management strategy

- **PMO**
  - Organization readiness assessment
  - Project governance
  - Communications, Training
  - Cost controlling

- **Master Data/change controls**
  - EUDAMED master data identification and risk assessment
  - Data governance & change management
  - Basic UDI-DI strategy

- **Regulatory Affairs**
  - Technical Files
  - Labeling strategy & coordination
  - Regulatory submission management
  - Notified Body strategy
  - Intelligent documentation management system

- **Supply Chain**
  - Economic Operator mapping and remediation
  - Electronic labeling and implant card/Patient Leaflet delivery strategy
  - Labeling implementation/rollout
  - Inventory transition planning
  - OEM/PL strategy

- **Manufacturing**
  - UDI implementation
  - Label changes
  - In-line printing capabilities

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*CEP: Clinical Evaluation Plan
PMCF: Post Market Clinical Follow Up
PMSP: Post Market Surveillance Plan
PMIR: Post Market Surveillance Report
PSUR: Periodic Safety Update Report
SSCP: Summary of Safety and Clinical Performance
PRRC: Person Responsible for Regulatory Compliance
What are key challenges during implementation of the regulation

Quality Assurance
Companies have multiple quality management systems due to acquisitions, or try to combine a pharma QMS with a devices QMS resulting in gaps or too much bureaucracy
There is a lack of clarity on how to fit the Person Responsible for Regulatory Compliance into the organization

Regulatory Affairs
Outdated document management systems multiply the number of updates and risk of inconsistencies
Lack of transparency on global product registration status increases the cost of registrations and the risk of non-compliance
Lack of label standards/templates reduces efficiencies

Supply Chain
Lack of transparency in the supply chain challenges the identification and compliance of the economic operators
Change processes typically cannot manage the massive volume of labelling changes
Companies have to reconsider their approach to own branding products, as they need access to confidential product information

R&D, Clinical and Medical Safety
Companies struggle to collect clinical data for legacy products
Older products have outdated or missing design information which has to be created to ensure continued compliance
R&D, manufacturing, Clinical and Medical Safety have to work closely together to ensure the various regulatory reports are consistent and implement a robust lifecycle management system

Manufacturing
Long lead-times for labeling changes lead to non-compliance in the market and create a disconnect between manufacturing and the regulatory file
In-line printer capability/capacity may not be able to manage additional label content
Lack of space on labels can lead to packaging changes

Project management
Corporate risks losing oversight when the project management and responsibilities are delegated to the BUs
Implementation of MDR/IVDR is a large and complex project that affects all areas of the business and requires a strong PMO to maintain oversight and strong senior management support to move it forward
The Haemonetics MDR/IVDR team

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VP, Regulatory Affairs  

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Senior Manager, Global Regulatory Affa...  

Kerri DiPietro  
Vice President Global Quality Assurance
Economic Operators
Who are the Economic Operators

**MANUFACTURER**
- Only place compliant devices on the market
- Cooperate with Authorities
- Assign an AR where applicable
- Assign a PRRC
- Get liability insurance
- Has a QMS

**IMPORTER**
- Only place compliant devices on the market
- Register in EUDAMED
- Perform verifications
- Put name and address on label or accompanying documents
- Keep a copy of the DoC and certificate (where applicable)
- Keep a register and inform complaints

**DISTRIBUTOR**
- Only place compliant devices on the market
- Register in national database
- Perform verifications (languages)
- Keep a register and inform complaints

**AUTHORIZED REPRESENTATIVE**
- A mandate in writing from the manufacturer
- Liability insurance
- A PRRC permanently and continuously at their disposal
- Additional verifications of technical documentation before products are placed on the market
Who are the Economic Operators for Haemonetics

- **Manufacturer**
  - Haemonetics Corp
  - Haemonetics SA

- **Importer**
  - Depends on the product flow – the legal entity that has ownership of the product when it enters the European Union

- **Distributor**
  - Haemonetics owned distributors
  - Third party distributors

- **Authorized Representative**
  - Haemonetics Italy
A new role: the Person Responsible for Regulatory Compliance (PRRC)

PRRC at the Manufacturer
The PRRC is responsible for:
- Devices batch release
- Development and maintenance of the Technical Documentation and the Declaration of Conformity
- Post market surveillance
- Vigilance reporting
- Annex I compliance of devices used in clinical trials

The PRRC has to be part of the manufacturer’s organization
The PRRC has to be qualified (university degree or experience)
The PRRC function is protected
A manufacturer can have more than one PRRC

PRRC for the Authorized Representative
There are no specific responsibilities defined
The PRRC does not have to be part of the AR’s organization, but has to be based in the EU and be ‘continuously’ available
Classification & Conformity Assessment
Device classification is based on risk

MDR and IVDR Annex VIII

The intended use determines the risk classification

The three main criteria for risk classification in MDR:

• Duration of contact with the human body
• Degree of invasiveness
• Amount of interaction with the body

The two main criteria for risk classification in IVDR:

• Level of personal risk
• Level of public health risk

EU MDR Risk Classes

Class I, low risk:
Devices do not enter or interact with the body

Class IIA and IIB, medium risk:
Devices are invasive, implantable or interact with the body

Class III, high risk:
Devices are in contact with vital organs, the central nervous system, the central circulatory system or are absorbed

IVDR Risk Classes

Class A, low risk:
Low personal risk, low public health risk

Class B, medium low risk:
Moderate to low personal risk, low public health risk

Class C, medium high risk:
High personal risk, moderate to low public health risk

Class D, high risk:
High public health risk, high personal risk
## Haemonetics products and their classification

### Blood Bags and Blood filtration systems
- **Dry sets**: Class Ila and Ilib
- **Sets with a anti coagulant**: up classified to class III

### Automated Cell collection products
- NexSys PCS instruments and 24 associated disposables: mostly class Ilib
- MCS+ 9000 instrument and 34 associated disposables: mostly class Ilib

### Blood Management Products
- Cell Saver Elite/+ equipment and 17 disposables: Class Ila and Ilib
- ACP215 equipment and 4 associated disposables: Class Ila and Ilib

### Standalone Blood Management Software Products
- **SafeTrace Tx**: up classified from Class I to Class Ilib
- **BloodTrack**: up classified from class Ila to Ilib
- **eLynx** and **TEG Manager** are no longer considered medical device software
- **TEG 6S analyzer and 8 associated disposables**: 6 up classified from self-declared to Class C
- **TEG 5000 disposables**: 7 up classified from self-declared to Class C

### In Vitro Diagnostics:
Conformity assessment route for Haemonetics devices

Haemonetics has full quality assurance QMS certification (MDR Annex IX)

**Haemonetics**
- Establishes the QMS
- Draws up the Technical Documentation
- Lodges application

**Notified Body**
- Performs an audit of the QMS
- Checks a sample of the technical files per device category (class IIa) or per generic device group (class IIb)

**Applies the CE mark, issues the DoC**

**Issues the Annex IX certificate**

**Haemonetics**
- Informs the Notified Body of any plan for substantial changes to the QMS
- Keeps the technical documentation continuously up to date

**Notified Body**
- Performs annual surveillance audits of the manufacturer, suppliers and subcontractors
- Reviews the technical files on a sampling basis
- Performs unannounced inspections
Conformity assessment route for Haemonetics IVDs

Haemonetics has full quality assurance QMS certification (IVDR Annex IX)

Haemonetics
- Establishes the QMS
- Draws up the Technical Documentation
- Lodges application

Notified Body
- Performs an audit of the QMS
- Checks a sample of the technical files per device category (class B) or per generic device group (class C)

Applies the CE mark, issues the DoC

Issues the Annex IX certificate

Haemonetics
- Informs the Notified Body of any plan for substantial changes to the QMS
- Keeps the technical documentation continuously up to date

Notified Body
- Performs annual surveillance audits of the manufacturer, suppliers, and subcontractors
- Reviews the technical files on a sampling basis
- Performs unannounced inspections

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Clinical Evaluation and Post Market Surveillance
Clinical Evaluation

• Clinical evaluation is required for all devices, regardless of classification
• Clinical evaluation is a continuous process that continues after the device is placed on the market
• All claims need to be substantiated by clinical data, this includes promotional claims

Chapter VI
Clinical Evaluation and Clinical Investigation

- Article 61 Clinical Evaluation
- Article 62 – 82, Clinical investigations

Annex XIV
Clinical Evaluation and Post-market Clinical Follow up

- Part A Clinical Evaluation
- Part B Post-market Clinical Follow up

Annex XV
Clinical Investigations
Clinical Evaluation

Literature
- Relevant scientific literature
- Focus on safety, performance, design characteristics and intended purpose
- Use of equivalency is significantly reduced

Meddev 2.7/1 rev 4 still applicable, with some additional requirements from MDR such as:
- Demonstration of clinical benefits
- Post-market surveillance and PMCF identified as a possible clinical data source

Clinical Investigations
Required for class III and IIb implantable devices expect if:
- Modification of an already existing design by the same manufacturer
- Demonstration of equivalency
- Clinical data of the reference device apply to the modified device

Elements of ISO 14155 have been incorporated in the legislation

Alternative treatments
The clinical evaluation has to include a comparison to alternative treatments

Clinical evaluation is required for all devices, regardless of classification!

This means that for every device you need a:
- Clinical Evaluation Plan
- Clinical Evaluation Report
- PMCF plan (or justification that PMCF is not required)
- PMCF report
Equivalent devices

In order to claim equivalence, a comparison of the new device to the predicate device must be completed for technical, clinical and biological aspects.

1. Similar design
2. Similar specifications
3. Similar conditions of use
4. Similar principles of operation and critical performance requirements

1. **Same** materials/substances in contact with same human tissues/body fluids
2. Similar kind and duration of contact
3. Similar release characteristics of substances

1. **Same** clinical condition or purpose
2. Similar severity or stage of disease
3. **Same** site in the body
4. Similar population
5. **Same** kind of user
Post Market Surveillance

• Post Market Surveillance is required for **all devices**, regardless of classification

• Post Market Surveillance is a **proactive process** that is **planned** before the device is placed on the market
Post Market Surveillance Plan

The Post Market Surveillance Plan is part of the Technical Documentation

Scope

- A PMS Plan must be developed for every device, regardless of classification

Minimal content of the PMS Plan

- Process to collect the information
- Methods for assessing the data
- Threshold values related to the Risk Assessment
- Methods and tools to investigate complaints and market feedback
- Methods and threshold values for trend reporting
- Methods to communicate with competent authorities
- Procedures for corrective actions
- PMCF plan or justification as to why PMCF is not applicable

Information Sources

- Serious incidents, FSCA
- Non-serious incidents, undesirable side-effects, PSUR
- Trend reporting
- Literature, databases, registries
- Feedback and complaints
- Relevant NCRs, CAPAs and Audits
- FMEAs
- Design changes
- User surveys / focus groups
- Publicly available information on similar devices

Refer to WI2478, Global Work Instruction - Post Market Surveillance Plan for details.
PSUR – Periodic Safety Update Report

Scope

PSUR summarizes the results and conclusions of the analyses of the post-market surveillance data gathered as a result of the post-market surveillance plan with a rationale and description of any preventative and corrective actions taken.

PMS collaborates with stakeholders identified per the PMS plan to determine any significant safety actions that have occurred worldwide during the PSUR reporting interval which may have had:

1. A significant influence on the benefit-risk determination of the authorized product and/or

2. An impact on the conduct of a specific clinical trial(s) or on the overall clinical development program

Examples of significant actions taken for safety reasons

Actions related to investigational uses:
- Refusal to authorize clinical trial for ethical or safety reasons;
- Partial or complete clinical trial suspension or early termination of an ongoing trial because of safety findings or lack of efficacy;
- Recall of investigational product or comparator;

Actions related to marketing experience:
- Failure to obtain or apply for a marketing authorization renewal;
- Withdrawal or suspension of a marketing authorization;
- Actions taken due to product defects and quality issues;
- Suspension of supply by the company;

Refer to WI2479, Global Work Instruction - Post Market Surveillance Output Reports for details.
Device lifecycle management framework

Actively seeking feedback to confirm the device risk/benefit conclusion

<table>
<thead>
<tr>
<th>Class</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>III, IIb</td>
<td>Annual</td>
</tr>
<tr>
<td>IIa</td>
<td>Bi-annual</td>
</tr>
<tr>
<td>I</td>
<td>5 Years</td>
</tr>
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</table>

*Tech File and labeling updates depend on conclusions from CER & PSUR
### MDR Documents update Schedule

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class IIb implantable</th>
<th>Class III</th>
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</thead>
<tbody>
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</tbody>
</table>

- **CER** = Clinical Evaluation Report
- **PMCF** = Post Market Clinical Follow-up
- **SSCP** = Summary of Safety and Clinical Performance
- **PSUR** = Periodic Safety Update Report
- **PMS** = Post Market Surveillance Report
- **RMR** = Risk Management Report
Vigilance – Serious Incident Reporting

15-day Reporting Timeline for Initial Report

IMDRF Codes

Submission into EUDAMED in the Future

Refer to SOP04.06, Compliance Program for the Medical Device Directive Vigilance system.
Labelling
MDR/IVDR bring new symbols to be put on labels

Introduction of Unique Device Identifier (UDI)
There are several types of UDI

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic UDI-DI</td>
<td>The primary identifier of a device model, assigned at the level of the device unit of use.</td>
</tr>
<tr>
<td>UDI-DI</td>
<td>Unique (alpha)numeric code specific to a model of device.</td>
</tr>
<tr>
<td>UDI-PI</td>
<td>(alpha)numeric code identifying the unit of device production</td>
</tr>
<tr>
<td>Unit of Use DI</td>
<td>Allows association of a device with a patient in cases where the UDI is not available on the single device (e.g. multipacks)</td>
</tr>
</tbody>
</table>

Only UDI-DI and UDI-PI are printed on the label

Only the manufacturer can assign the UDI
How are the different UDIs related

Unit of Use DI 1

UDI-DI 1

UDI-PI 1

UDI-PI 2

UDI-PI 4

UDI-PI 5

UDI-PI ...

Basic UDI-DI

UDI-DI 2

UDI-PI 1

UDI-PI 2

UDI-PI 4

UDI-PI 5

UDI-PI ...

Unit of Use DI 3

UDI-DI 3

UDI-PI 1

UDI-PI 2

UDI-PI 4

UDI-PI 5

UDI-PI ...

UDI-DI ...

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UDI is the basis for devices registration in EUDAMED

### Basic UDI-DI
- Basic UDI-DI value
- Manufacturer SRN
- Name and address of manufacturer
- Name, address and SRN of AR
- Risk class
- Implantable, measuring function, reusable surgical instrument, active device, intended to administer/remove a medicinal substance
- Medical device nomenclature code
- Name or device model associated with the basic UDI-DI per the technical documentation, DoC, certificate

### UDI-DI
- UDI-DI value
- Reference, article or catalog number
- Direct marking
- Quantity of devices
- Type of UDI-PI
- Unit of use UDI-DI
- Clinical size
- Storage/handling conditions
- Name/trade name
- Additional trade names (including languages)
- Additional product description
- URL for additional information (label website)
- Labelled as single use, maximum number of reuses, labelled as sterile, need for sterilization before use, containing latex, CMR/Endocrine disruptor
- Critical warnings, contra-indications
- Medical device nomenclature code
- Status
- Reprocessed single use
- Annex XVI
- Name, address and contact detail of contract design/manufacturer

### UDI-DI (container package DI)
- UDI-DI value
- Quantity per package
- Status

Each UDI-DI inherits the attributes of its linked basic UDI-DI and devices DI
Questions?
About PA.

We believe in the power of ingenuity to build a positive human future in a technology-driven world. As strategies, technologies and innovation collide, we create opportunity from complexity. Our diverse teams of experts combine innovative thinking and breakthrough use of technologies to progress further, faster. Our clients adapt and transform, and together we achieve enduring results.

An innovation and transformation consultancy, we are over 3,200 specialists in consumer, defence and security, energy and utilities, financial services, government, health and life sciences, manufacturing, and transport. Our people are strategists, innovators, designers, consultants, digital experts, scientists, engineers and technologists. We operate globally from offices across the UK, US, Europe, and the Nordics.

PA. Bringing Ingenuity to Life.