International Track 2: Beyond MDSAP and ISO 13485: The Impact of the New EU Regulations on Audits

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The EU MDR Triangle

Clinical

Benefit-Risk-Analysis

§7 Claims

MedDev 2.7.1 Rev 4

R&D

Intended Purpose
[Intended Use] §2 (12)

Risk-Management

Usability

IEC 62366-1

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The EU MDR Triangle

Clinical

R & D

Intended Purpose [Intended Use] §2 (12)

§7 Claims

Risk-Management

Usability

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- Clinical
- Risk Management
- Usability

Labeling

- R&D
- Intended Purpose (Extended Use) (EU/CE)
- SF Claims

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- **Labeling**
  - (60+ requirements)
  - MDR+IVDR require consistency & validity of all labeling information to include websites

- Summary of Safety & Clinical Performance
- IFU
- User Training
- Labels [on packaging, marking on device]
- Information for Safety [warnings]
The EU MDR Triangle Pyramid
The EU MDR Triangle Pyramid
The EU MDR Triangle Pyramid

Post Market Surveillance

Clinical

Risk Management

Labeling

P & D

Intended Purpose (intended use)

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Post Market Surveillance System
Chapter VII § 83 - § 100

Clinical Evaluation Report

Incidents

Redesign

User Error

Off-Label Use

Literature Reviews

Labeling

Clinical

Risk-Management

Unability

Intended Purpose: Extended Use (EU)

R&D
4.1.1 The organization shall document a quality management system and maintain its effectiveness in accordance with the requirements of this International Standard and applicable regulatory requirements.

The organization shall document the role(s) undertaken by the organization under the applicable regulatory requirements.

NOTE: Roles undertaken by the organization can include manufacturer, authorized representative, importer or distributor.
Updating Your Quality Management System (QMS)

Must consider:

- New roles and responsibilities for Authorized Representative, Importers, Distributors etc.; and any needed supplier (internal or external) agreements
- New requirements for Person Responsible for Regulatory Compliance
Careful Attention to QMS Integration with Annex Requirements

- ANNEX I GENERAL SAFETY AND PERFORMANCE REQUIREMENTS (GSPRs)

- ANNEX II TECHNICAL DOCUMENTATION

**NOTE:** Functions of RA and QA must be integrated and constantly communicating in order for the QMS to successfully comply with the EU Regulations
Overview of GSPRs

Chapter I
General requirements

1. Achieve intended performance

2-6. Risk Management requirements

7. Transport & storage

8. Risks acceptable when weighed against the benefits


Chapter II
Requirements regarding design and manufacture

10.1 – 10.6. Chemical, physical and biological properties

11.1 – 11.8. Infection and microbial contamination

12.1 – 12.2. Medicinal substances, substances absorbed or locally dispersed

13.1 – 13.3. Devices incorporating materials of biological origin

14.1-14.7. Construction of device & interaction with environment

15.1 – 15.2. Devices with a diagnostic or measuring function

16.1 – 16.4. Ionising radiation

17.1 – 17.4. Electronic programmable systems (Software)

18.1 – 18.8. Active devices and devices connected to them

19.1 – 19.4. Particular requirements for active implantable devices

Chapter II
Requirements regarding design and manufacture

20.1 – 20.6. Protection against mechanical and thermal risks

21.1 – 21.3. Devices for supplying energy or substances to the patient

22.1 – 22.3. Devices intended by the manufacturer for use by lay persons

Chapter III
Requirements regarding the information supplied with the device

23.1 a-h. General info regarding information supplied by the manufacturer

23.2 a-s. Information on the label

23.3 a-j. Information on the packaging for (sterile packaging)

23.4 a-ab. Information in the instructions for use
Article 10.1
Design & Manufacture to (EU) 2017/745

Article 10.2
System for risk management

Article 10.3
Clinical evaluation & PMCF

Article 10.4
Establish & Maintain technical documentation

Article 10.5
Declaration of conformity

Article 10.6
System for Unique Device Identification

Article 10.7
Document & Record retention obligations

Article 10.8
Maintaining conformity to (EU) 2017/745 relating to changes

Article 10.9
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14
Article 10(9) Components
Basic Quality Management
System Requirements

Article 10.9 a
Strategy for regulatory compliance

Article 10.9 b
Identification of GSPR’s & options to address them

Article 10.9 c
Responsibility of management

Article 10.9 d
Resource mgt, including supplier control

Article 10.9 e
Risk management

Article 10.9 f
Clinical evaluation & PMCF

Article 10.9 g
Product realization

Article 10.9 h
UDI

Article 10.9 i
Post-market surveillance system

Article 10.9 j
Comms with CA / NB / Economic operators / Customers

Article 10.9 k
(Vigilance) Reporting serious incidents and FSCA’s

Article 10.9 l
Management of corrective and preventive actions.
Questions?

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Beyond MDSAP and ISO 13485

Impact of the New EU Regulations on Audits

Rania Gerges
Consultant
Objectives

1. Learn MAIN changes between ISO 13485:2016 to MDR-QMS requirements

2. The Design and Development Process under the MDR

3. Readiness strategy for NB MDR-QMS audits
## From ISO 13485:2016 to the MDR

<table>
<thead>
<tr>
<th>ISO 13485</th>
<th>MDR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>4.2 Documentation requirements</strong></td>
<td>Technical Documentation – Annex II, III</td>
</tr>
<tr>
<td></td>
<td>Strategy for Regulatory Compliance – Article 10, Annex IX</td>
</tr>
<tr>
<td></td>
<td>Administrative Provisions – Annex IX</td>
</tr>
<tr>
<td><strong>5. Management responsibility</strong></td>
<td>Person Responsible for Regulatory Compliance – Article 15</td>
</tr>
<tr>
<td><strong>7.3 Design and development</strong></td>
<td>Strategy for Regulatory Compliance – Article 10, Annex IX</td>
</tr>
<tr>
<td></td>
<td>Use of Harmonised Standards – Article 8</td>
</tr>
<tr>
<td></td>
<td>Common Specifications – Article 9</td>
</tr>
<tr>
<td></td>
<td>General Safety and Performance Requirements (GSPR) – Annex I</td>
</tr>
<tr>
<td></td>
<td>o CMR and endocrine-disrupting substances – GSPR 10.4</td>
</tr>
<tr>
<td></td>
<td>o Labelling – Article 18, GSPR 23</td>
</tr>
<tr>
<td></td>
<td>Clinical Evaluation – Article 61, Annex XIV Part A</td>
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<td></td>
<td>Clinical Investigation – Article 62-82, Annex XV</td>
</tr>
<tr>
<td><strong>7.5.8 Identification</strong></td>
<td>Importers and Distributors Obligations – Article 13, 14</td>
</tr>
<tr>
<td><strong>7.5.9 Traceability</strong></td>
<td>Identification within the Supply Chain – Article 25</td>
</tr>
<tr>
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<td>UDI System – Article 27, ANNEX VI Part C</td>
</tr>
<tr>
<td></td>
<td>Registration of Devices and Economic Operators – ANNEX VI Part A</td>
</tr>
<tr>
<td><strong>8. Measurement, analysis and improvement</strong></td>
<td>Vigilance and Trend Reporting – Article 87-89</td>
</tr>
<tr>
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<td>Post Market Surveillance – Article 83-86, Annex III</td>
</tr>
<tr>
<td></td>
<td>Post Market Clinical Follow-up – Annex XIV Part B</td>
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</tbody>
</table>
(Medical devices - Quality management systems - Requirements for regulatory purposes) and European Medical Devices Regulation and In Vitro Diagnostic Medical Devices Regulation
Design and Development

Planning

Inputs/Outputs

V&V

Transfer

Post Market

Control of Changes
Strategy for Regulatory Compliance

- Identification of relevant legal requirements,
- Qualification,
- Classification,
- **Handling of equivalence,**
- Choice of and compliance with conformity assessment procedures

Quality management system assessment - Annex IX(2.2c)
General Safety and Performance Requirements

Annex I Chapters

I. General (1-9)
II. Design and Manufacture (10-22)
III. Information Supplied with Device (23)
Expanded Scope & New/Revised Requirements

Distance Sales - Article 6

Annex XVI Devices

CMR, endocrine disrupting substances
GSPR 10.4

Cleaning/disinfection/ re-sterilization
GSPR 11.2

Safe disposal
GSPR 14.7

Devices w/substances absorbed or locally dispersed, non-viable biological substances
GSPR 12, 13.3

Electronic programmable systems – GSPR 17

Devices used by lay persons – GSPR 22

Labelling – GSPR 23
Common Specifications & Harmonized Standards

Common Specifications (CS): a set of technical and/or clinical requirements, other than a standard, that provides a means of complying with the legal obligations applicable to a device, process or system.

Harmonized Standard: a European standard as defined in point (1)(c) of Article 2 of Regulation (EU) No 1025/2012.

QMS assessment - Annex IX(2.2c)
6.2. When is clinical evaluation undertaken and why is it important?
6.2.1. Clinical evaluation undertaken for the development of a medical device
6.2.2. Clinical evaluation for initial CE-marking
6.2.3. Updating the clinical evaluation
### Clinical Evaluation – Part of Technical Documentation

#### Clinical Evaluation – Article 61 & Annex XIV Part A

1. Clinical Development Plan (CDP)
2. Clinical Evaluation Plan (CEP)
4. Summary of Safety and Clinical Performance (SSCP) *(Class III, Implantable Only)* – Article 32

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![Diagram](https://via.placeholder.com/150)

**Planning** → **Inputs/Outputs** → **V&V** → **Post Market**

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“All activities carried out by manufacturers in cooperation with other economic operators to institute and keep up to date a systematic procedure to **proactively collect and review experience gained from devices they place on the market**, make available on the market or put into service for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions.”

The concept is not new
Design and Development – Under the MDR

Planning
- Strategy for Regulatory Compliance
- Clinical Development Plan (CDP)
- Clinical Evaluation Plan (CEP)

Inputs/Outputs
- Applicable GSPRs
- Applicable Common Specifications & Harmonized Standards

V&V
- Methods to conform to GSPRs
- Clinical Evaluation Report (CER)
- Clinical Investigations
- SSCP (Class III and Implantable)

Post Market
- PMS Plan
- PMS Report/PSUR
- PMCF Plan
- PMCF Evaluation Report
Readiness strategy for NB MDR-QMS Audits

1. What the NB Quality management system audits will be like – Annex VII (4.5.2)

2. Timelines & Transitional Provisions – Article 120

3. Compliance Roadmap – 10 steps
NB QMS Auditing – Annex VII (4.5.2)

1. audit the manufacturer’s QMS, ……..devices at every stage, from design through final quality control to ongoing surveillance……..

2. based on relevant technical documentation ...review and audit the manufacturer's processes and subsystems, in particular for:
   - CAPAs, including for post-market surveillance, and
   - PMCF,

3. and review and audit requirements and provisions adopted by the manufacturer, including those in relation to fulfilling the GSPR

4. conduct assessments of the technical documentation based on its sampling plan......
However, the requirements of this Regulation relating to
- post-market surveillance,
- market surveillance,
- vigilance,
- registration of economic operators and of devices
shall apply in place of the corresponding requirements in those Directives.

SOONER
than
26 May 2020
Compliance Roadmap

1. Set due dates and identify process owners.
2. Contact your NB to schedule Annex IX/X/XI for QMS assessment.
4. Perform gap Assessments (sampling).
   QMS & Technical Documentation & CERs
5. Perform Portfolio Rationalization.
6. Update and/or create of new procedures and records – and assess impact on other supporting procedures and records (Job descriptions, ASL, Definition lists, Quality Manual structure, etc.).
7. Remediate Technical Documentation and CERs.
9. Update internal audit program and perform 1 cycle.
10. Assess performance in the next Management Review meeting.
Thank you for your attention
EU MDR

Cross Functional Implementation

Laila Gurney
Sr. Executive & Head of Global Regulatory Affairs
GE Healthcare
EU MDR

Why did it happen?
Trigger → PIP breast implant scandal 2010... industrial grade silicon for breast implants → explants / adverse reactions

What is it?
Regulation overhaul... across the product lifecycle.... premarket, design, clinical, MFG, distribution, service, postmarket

Who impacted?
Cross functions (Engineering, Manufacturing, Supply Chain, Service, Quality, Regulatory)... led by Quality & Regulatory

When is it effective?
May 26, 2020... Compliance needed to ship products to Europe past May 26, 2020 (some requirements only apply to NPIs)

STAY ON MDD for forward production with valid certificate with no significant design change

MDR... NPI + MDD with significant design change

May 2020  May 2024  May 2025

• Audited to MDR & MDD
• NPI + significant design change to current products
• Postmarket Requirements
• Process & IT changes
• Economic Operators (Importer, Distributor, MFG, Authorized Representative)
• “PRRC”
• UDI registration to EUDAMED

Last date for devices to be certified to MDD
Last date for MDD inventory in the EU to be shipped to customers
### KEY Changes

**Regulatory Affairs, Quality, Engineering, Clinical, Product Management**

<table>
<thead>
<tr>
<th>TODAY</th>
<th>Changes TOMORROW</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Technical Documentation / File</strong></td>
<td><strong>23 requirements... NEW: requirements to document / justify</strong></td>
</tr>
<tr>
<td>• 13 Essential Principles</td>
<td>• NEW: Label, labeling change, chemical substances</td>
</tr>
<tr>
<td>• Review of Tech File in “next” audit (we do not have devices classified as Class III in the EU)</td>
<td>• NEW: Class I move to MDR</td>
</tr>
<tr>
<td></td>
<td>• NEW: Review / approval of 1st Tech File per class &amp; modality</td>
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<tr>
<td></td>
<td>• NEW: Significant Change Assessment for changes to MDD products.... Can move to MDR</td>
</tr>
<tr>
<td></td>
<td>• NEW: Tech File completion dates cannot move → impact: QMS audit / delay to market</td>
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<tr>
<td></td>
<td>• NOTE: Review classification and data requirements for portfolio</td>
</tr>
<tr>
<td><strong>Clinical Evaluation</strong></td>
<td><strong>1. NEW: Clinical Eval Plan; continue with report for CE mark... include support for claims / tied to risk</strong></td>
</tr>
<tr>
<td>• Report (CESR) prepared with NPI;</td>
<td><strong>2. UPDATE as before</strong></td>
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<tr>
<td>• Update required periodically (frequency depends on product, technology – see MEDDEV)</td>
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**UDI**

- NEW: Some unique requirements vs. US
KEY Changes

Regulatory Affairs, Complaint Handling Unit, Quality, ENG, Product MGMT, Supply Chain, Service, Economic Operators

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<thead>
<tr>
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<tr>
<td>Complaint Handling &amp; Incident</td>
<td>AER timeline: 30 days</td>
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<tr>
<td>Reporting</td>
<td>AER timeline: 15 days</td>
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<tr>
<td></td>
<td>New requirements on reporting events, trends, &amp; actions</td>
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<td>Economic operators – obligations expressly included in EU MDR</td>
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<tr>
<td>Postmarket Summary Report</td>
<td>N/A</td>
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<tr>
<td></td>
<td>NEW: Requires preparation and maintenance... postmarket trend</td>
</tr>
<tr>
<td></td>
<td>analysis, investigation, report</td>
</tr>
<tr>
<td>EUDAMED</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Registration of devices, UDI, postmarket (incidents, FSCA, PSUR),</td>
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<tr>
<td></td>
<td>clinical investigations, economic operators</td>
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A lot of procedures require updating
Almost every function has a role and has to do something new / differently
Cross functional planning required for product launch / timing
Planning required with Notified Bodies for audits
EU MDR Planning for Readiness

IMPACT:
- **RA / ENG**: Technical docs, labeling
- **RA / ENG**: Portfolio: MDD or MDR?
- **QA / RA / ENG**: MDD/MDR site certs
- **QA / All**: QMS/ Training
- **Supply Chain (Economic operators)**: Registration, Reporting
- **RA / ENG / Supply Chain / Modality / IT**: UDI, postmarket, EUDAMED

Our Plan:
- **8 task forces formed, led by RA & QA, with cross functional members**:
  - Premarket
  - Postmarket
  - UDI
  - Clinical Evaluation
  - Clinical Investigation
  - EUDAMED
  - Economic Operators
  - QMS
  - Task force leaders with detailed project plans – complete 2018
  - Develop & deploy EU MDR implementation playbook – complete 2018
  - Train / Execute / Implemente across sites - ongoing
  - Executive Sponsor reviews (weekly)
  - Cross task force reviews (monthly)
  - Review with Senior Leadership (monthly)

Cross Functional Engagement is Key to Ensure Timely Implementation
Challenges

- Eudamed Technical Specifications not available yet – delaying IT tool development for connection to Eudamed
- UDI using Italian CND nomenclature vs. GMDN (IMDRF)
- Several Implementing Acts are still being worked on...
- SW classification

Advice

- Determine “MDD” vs. “MDR” products and plan accordingly
- Develop written positions for significant change assessment, classification, unclear / non defined areas
- Escalate challenges / issues ... e.g. through COCIR, AdvaMed & other Trade Associations
- THIS IS AN “ALL HANDS ON DECK” activity.... It is cross functional and can only be effective if functions work together seamlessly & do their part / hand offs