European Medical Device Regulations

Preparing for the Storm

Moderator:

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Ibim Tariah, Technical Director, BSI Americas Inc.
MEDICAL DEVICE REGULATION

KARL VAHEY
VP QA CARDINAL HEALTH
What is the EU MDR about?

- A new regulation in Europe for medical devices and in vitro diagnostic products with many changes compared to the current directives.
- Consolidated trilogue text of EU MDR and EU IVDR were issued in June 2016 and was published in the Official Journal of the European Union in May 2017.

Why is EU MDR important?

- After a three-year transition period, all products must be CE certified to EU MDR requirements.
- There will be impacts across all Businesses and many functions for the commercialized product portfolio and products in development.
- There will also be impacts to other geographies as products and labelling are updated.

What will success look like?

- Recertification of products within the established timelines.
- Strategic investment opportunity assessment and execution.
- Partnering with Competent Authorities and Notified Bodies to align on a practical compliance strategy.
MORE ROBUST TEXT UNDER STRONGER POLITICAL PRESSURE

A FEW FACTS...

<table>
<thead>
<tr>
<th>MDD</th>
<th>MDR</th>
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</thead>
<tbody>
<tr>
<td>23 articles</td>
<td>97 articles</td>
</tr>
<tr>
<td>60 pages</td>
<td>355 pages</td>
</tr>
<tr>
<td>12 annexes</td>
<td>16 annexes</td>
</tr>
<tr>
<td>44 occurrences of &quot;clinical investigation&quot;</td>
<td>142 occurrences of &quot;clinical investigation&quot;</td>
</tr>
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MDR PROGRAM OVERVIEW

IMPACTS OF MDR

- The EU MDR release focuses on the overall product lifecycle from development through obsolescence.
- Requirements for CE marking have been enhanced in each stage of the lifecycle.

- More products require prior approval;
- Longer review timelines & increased costs;
- Enhanced clinical requirements;
- Scrutiny for new products.

- UDI reqs;;
- New QMS reqs;
- Quality agreements;
- Labeling reqs.

- Required PMS reporting;
- Required periodic safety update reports;
- Required CER updates;

- Continued scrutiny on State of Art reqs;
- More products requiring submissions;
- Introduction of new audits (MDSAP / Clinical).

NPD    Launch    Market    Cert Renewal
MDR PROGRAM OVERVIEW

IMPACTS OF MDR

- Below are examples of the specific requirements of MDR:

<table>
<thead>
<tr>
<th>Regulatory Files</th>
<th>Quality System</th>
<th>Haz Substance</th>
<th>Clinical Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Tech Files require updates;</td>
<td>SOP change to ref MDR</td>
<td>product codes require analysis for haz sub;</td>
<td>CER’s require review and if necessary updates;</td>
</tr>
<tr>
<td>All Declaration of Conformities require updates;</td>
<td>Post Market Surveillance reports for all tech files</td>
<td>Testing required for any product potentially having haz sub to quantify levels;</td>
<td>CER’s require updates annually;</td>
</tr>
<tr>
<td>More product families require submission to NB.</td>
<td>Periodic Safety Update Reports required;</td>
<td>Can lead to material changes or labeling reqs</td>
<td>Post Market Clinical Follow up required f</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SSCP require update &amp; annual submission.</td>
</tr>
</tbody>
</table>

RA, R&D, DQE, Medical Affairs, PMV

QA Man, Ops, DQE, Medical Affairs, RA, PMV

QA Man, RA, Ops, R&D, EHS

Medical Affairs, PMV, R&D, RA, Commercial

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## EU MDR CHANGES ARE EXTENSIVE

<table>
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<th>Key EU MDR Changes</th>
<th>Business Implications</th>
<th>Implicated</th>
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<td><strong>Hazardous Substances</strong></td>
<td>Revenue impact from loss in portfolio</td>
<td>R&amp;D Supply Chain</td>
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<tr>
<td>Increased Scope and Depth of Requirements</td>
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<tr>
<td><strong>Restricted Equivalence Claim (Class III and Implants)</strong></td>
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<tr>
<td><strong>“Scrutiny” – EU Panel Clinical Data Review</strong></td>
<td>Increased Time To Market</td>
<td>R&amp;D Regulatory Affairs, Medical Affairs, Quality</td>
</tr>
<tr>
<td><strong>Notified Body Design Review for Class IIb Implants</strong></td>
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<td><strong>New (Up-) Classification</strong></td>
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<td><strong>Technical Documentation, DoC</strong></td>
<td>Administrative Burden</td>
<td>R&amp;D Regulatory Affairs, Quality Tech. Communication, Production</td>
</tr>
<tr>
<td>New Format and Content</td>
<td></td>
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<tr>
<td><strong>Expanded Labelling Requirements (including Implant-Information)</strong></td>
<td>Increased Transparency and Documentation</td>
<td>Quality Medical Affairs, Regulatory Affairs</td>
</tr>
<tr>
<td><strong>QM-System</strong></td>
<td></td>
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<tr>
<td>PMS, Vigilance, PSURs, Trend Reports</td>
<td></td>
<td>Regulatory Affairs, Supply Chain</td>
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<tr>
<td><strong>Clinical Evaluation/Investigation</strong></td>
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<tr>
<td>Summary of Safety and Performance</td>
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<tr>
<td><strong>UDI and Economic Operators</strong></td>
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</tr>
</tbody>
</table>
MDR PROGRAM OVERVIEW

IMPACTS OF MDR TO INDUSTRY

Product Lines

Revenue

Product Codes

Files to Remediate (Risk, Design, Clinical)
Economic Operators

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Economic Operators
MDR Article 2
Economic Operators – Definitions

- **Manufacturer** means 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.

- **Authorized Representative** means 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.

- **Importer** means any natural or legal person established within the Union that places a device from a third country on the Union market.

- **Distributor** means 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.
MDR Art. 25

Identification Within The Supply Chain

• Economic operators shall be able to identify the following to the competent authority, for 10 years in general and 15 years for implantable devices:
  
  (a) any economic operator to whom they have directly supplied a device;

  (b) any economic operator who has directly supplied them with a device;

  (c) any health institution or healthcare professional to which they have directly supplied a device.
MDR Art. 31 – Registration

• Before placing a device on the market any manufacturer, authorized representative, and importer must register in the European Databank

• The Competent Authority obtains a single registration number (SRN) and provides it to the manufacturer, authorized representative, or importer

• The manufacturer uses the single registration number when applying to a Notified Body for conformity assessment
Manufacturer

• The manufacturer has obligations under the regulations including:
  – Setting up a quality management system, QMS
  – Registering in EudaMed with a Single Registration Number, SRN
  – Creating the Technical Document in Annex II and Annex III
  – Drawing up a Declaration of Conformity
  – Ensure financial coverage for product liability
  – Establish relationships (contracts, etc.) with other economic operators (authorized representative, importers, and distributors)
Providing a Service

• The manufacturer implements EN ISO 13485:2016 as modulated by CEN/TR 17223:2018 (Planned date of availability is March 21, 2018)

• The manufacturer receives a service from the other economic operators, so they are subject to ISO 13485:2016, 7.4

• The manufacturer must evaluate, select, and re-evaluate the other economic operators under 7.4.1 Purchasing Process
  – Since the manufacturer is outsourcing a process, then control of the economic operators includes a written quality agreement under 4.1.5

• The manufacturer provides the information under 7.4.2 Purchasing Information to the other economic operators
Authorized Representative

• Where the manufacturer of a device is not established in a Member State, the device may only be placed on the Union market if the manufacturer designates a sole authorized representative.

• The manufacturer and the authorized representative agree, in writing, on a mandate that requires the authorized representative to:
  – Verify the declaration of conformity and technical documentation
  – Keep a copy of the technical documentation, the declaration of conformity, and a copy of the relevant certificates
  – Register and verify that the manufacturer has registered
  – Immediately inform the manufacturer about complaints and reports from healthcare professionals, patients, and users about suspected incidents related to the device

• The authorized representative is legally liable for defective devices on the same basis as, and jointly and severally with, the manufacturer.
Importer

• Importers shall place on the Union market only devices that are in conformity with the MDR
• The importer verifies:
  – The product has a CE Mark and a Declaration of Conformity
  – The manufacturer is identified and the authorized representative is identified
  – The device is labeled and has instructions for use
  – The manufacturer assigned a UDI
  – The device is registered in EudaMed – the importer adds information
• The importer adds information to the device: their name, registered trade name or registered trade mark, registered place of business, and the address at which they can be contacted
• Importers who receive complaints or reports from healthcare professionals, patients, or users immediately forward this information to the manufacturer and its authorized representative
Distributor

• The distributor verifies:
  – The product has a CE Mark and a Declaration of Conformity
  – The device is labeled and has instructions for use
  – The importer added the required information
  – The manufacturer assigned a UDI

• Distributors ensure that, while the device is under their responsibility, storage or transport conditions comply with the conditions set by the manufacturer

• Distributors who receive complaints or reports from healthcare professionals, patients, or users immediately forward this information to the manufacturer, the manufacturer's authorized representative, and the importer
Documentation Flow

Manufacturer

Authorized Representative

Verifies:
DoC
Tech. Doc.
Mfg. Reg

Keeps a Copy:
DoC
Tech. Doc.
Certificates

Importer

Verifies:
DoC
CE Mark
Mfg
Auth. Rep
Labeled
IFU
UDI
Device Reg.

Distributor

Verifies:
DoC
CE Mark
Labeled
IFU
UDI

Ombu Enterprises, LLC
Complaint Flow

Complaint

Healthcare Professional

Patient

User

Distributor

Importer

Authorized Representative

Manufacturer
Manufacturer’s QMS
Article 10 (9)

• A strategy for regulatory compliance
• Identification of applicable general safety and performance requirements
• Management responsibility
• Selection and control of suppliers and sub-contractors
• Risk management following Annex 1, Section 3
• Clinical evaluation and PMCF following Article 61 and Annex XIV
• Product realization, including planning, design, development, production, and service provision
Article 10 (9)

- UDI following Article 27(3) and Article 29
- Post-market surveillance system following Article 83
- Communication with competent authorities, notified bodies, other economic operators, customers, and other stakeholders
- Reporting serious incidents and field safety corrective actions
- Management of corrective and preventive actions
- Monitoring and measurement of output, data analysis, and product improvement
Person Responsible for Regularity Compliance
MDR Art. 15 – Qualification

- Manufacturers have at least person in the organization responsible from regulatory compliance
  - Micro and small enterprises only need a person permanently and continuously at their disposal

- 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 an equivalent course of study 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 \textit{in vitro} diagnostic medical devices
  - four years of professional experience in regulatory affairs or in quality management systems relating to medical devices.
SME Categories

SME
Small
Micro
Person Responsible

- Manufacturer
- Authorized Representative
- Importer
- Distributor

Person responsible in the organization
Person responsible available
SME Manufacturer
Person responsible available
Product Liability Insurance
Liability for Defective Products

• Natural or legal persons may claim compensation for damage caused by a defective device in accordance with applicable Union and national law.

• Manufacturers shall, in a manner that is proportionate to the risk class, type of device and the size of the enterprise, have measures in place to provide sufficient financial coverage in respect of their potential liability under Directive 85/374/EEC, without prejudice to more protective measures under national law.

• Directive 85/374/EEC
  – The producer is liable for damage caused by a product defect [Art. 1]
  – Damage includes death or personal injury [Art. 9]
  – A product is defective when it does not provide the safety which a person is entitled to expect [Art. 6]
MDR - Technical Documentation

Ibim Tariah
Technical Director, BSI Group America
April 4th 2018
CE Marking Process

1. **Is it a medical device?** (Articles 1 & 2)
2. **Determine device classification** (Annex VIII)
3. **Select conformity assessment route** (Article 52)
4. **Assemble technical documentation** (Annex II)
5. **Certificate and complete Declaration of Conformity** (Annex XII, IV)
6. **Affix CE mark** (Annex V)
7. **Notified Body conducts conformity assessment** (Annexes IX, X, XI)
8. **Post Market Surveillance (MDR Annex III)**

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*Image credits: BSI*
MDD – Technical Documentation Requirements

The technical documentation must allow assessment of the conformity of the product with the requirements of the Directive. It must include in particular:

— a general description of the product, including any variants planned and its intended use(s),
— design drawings, methods of manufacture envisaged and diagrams of components, sub-assemblies, circuits, etc.,
— the descriptions and explanations necessary to understand the abovementioned drawings and diagrams and the operations of the product,
— the results of the risk analysis and a list of the standards referred to in Article 5, applied in full or in part, and descriptions of the solutions adopted to meet the essential requirements of the Directive if the standards referred to in Article 5 have not been applied in full, in the case of products placed on the market in a sterile condition, description of the methods used and the validation report,
— the results of the design calculations and of the inspections carried out, etc.; if the device is to be connected to other device(s) in order to operate as intended, proof must be provided that it conforms to the essential requirements when connected to any such device(s) having the characteristics specified by the manufacturer,
— the solutions adopted as referred to in Annex I, Chapter I, Section 2,
— the pre-clinical evaluation,
— the clinical evaluation in accordance with Annex X,
— the label and instructions for use.
MDR - Technical Documentation Requirements

Annex II: Technical Documentation

1: Device description
2: Information to be supplied by the manufacturer
3: Design and manufacturing information
4: General safety and performance requirements
5: Benefit-risk analysis and risk management
6: Product verification and validation

Annex III: Technical Documentation on Post-Market Surveillance

“The technical documentation and, if applicable, the summary thereof to be drawn up by the manufacturer shall be presented in a clear, organised, readily searchable and unambiguous manner.....”

Key Change: The MDR is very prescriptive regarding the Technical Documentation content and formatting.
MDR Requirements for technical documentation

Annex II: Technical Documentation

1: Device description

- Product name, description, intended purpose
- Product identification including basic UDI-DI
- Principles of operation and mode of action
- Technical and material specification, description of key functional elements and any novel features
- Overview of previous generations of the device
- Overview of similar devices available in the EU or elsewhere
MDR Requirements for technical documentation

Annex II: Technical Documentation

1: Device description

2: Information to be supplied by the manufacturer

- Complete set of labels, inserts, brochures, operating manuals, instructions for use etc
MDR Requirements for technical documentation

Annex II: Technical Documentation

1: Device description
2: Information to be supplied by the manufacturer
3: Design and manufacturing information

- Information to allow key design stages to be understood
- Description of manufacturing processes
- Manufacturing validations, monitoring and final product testing
- Identification of all suppliers and subcontractors undertaking design or manufacturing processes for the manufacturer
MDR Requirements for technical documentation

Annex II: Technical Documentation

1: Device description
2: Information to be supplied by the manufacturer
3: Design and manufacturing information
4: General safety and performance requirements

Evidence of conformity with the General Safety and Performance Requirements set out in Annex I, including:

- Identification of applicable GSPRs
- Methods used to demonstrate conformity
- Applicable standards, Common Specifications or other requirements
- Links to specific documents demonstrating conformity with SPRs
MDR Requirements for technical documentation

Annex II: Technical Documentation

1: Device description
2: Information to be supplied by the manufacturer
3: Design and manufacturing information
4: General safety and performance requirements
5: Benefit-risk analysis and risk management

• Risk management documentation and risk-benefit analysis
MDR Requirements for technical documentation

Annex II: Technical Documentation

1: Device description
2: Information to be supplied by the manufacturer
3: Design and manufacturing information
4: General safety and performance requirements
5: Benefit-risk analysis and risk management
6: Product verification and validation

- Pre-clinical – biological safety, sterilisation validations, packaging, shelf-life, software validations, usability etc
- Clinical evaluation report and associated documentation
- PMCF plan
- Specific validations for devices incorporating medicinal substances, animal or human tissues, CMR or endocrine-disrupting substances, absorbable devices, sterile devices, devices with measuring function, devices used in combination
MDR Requirements for technical documentation

Annex II: Technical Documentation

1: Device description
2: Information to be supplied by the manufacturer
3: Design and manufacturing information
4: General safety and performance requirements
5: Benefit-risk analysis and risk management
6: Product verification and validation

Annex III: Technical Documentation on Post-Market Surveillance

- Includes PMS Plan, PMS Report (Article 85), PSUR (Article 86) and PMCF plan or justification for no-PMCF
- Minimum requirements for PMS Plan sources of information
- Specific guidance on how to evaluate PMS data
- Requirement (via Article 83) to update clinical evaluation, SSCP, design and manufacturing information and information for use on the basis of PMS output
Post Market Surveillance:
all activities carried out by the manufacturer in cooperation with other economic operators to institute and keep up to date a systematic procedure to proactively collect and review experience gained from their devices placed on the market, made available on the market or put into service for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions;
EU MDR Article 10 Requirement Mapping
04 April 2018

Robert G. Ruff
Executive Director, Medical Device Certification and Training
This document is intended to facilitate an oral briefing. It is not intended for use as a stand-alone report.
EU MDR Article 10

Quality system correspondence table: EU MDR, EN ISO13485:2016 and MDSAP Audit Model

<table>
<thead>
<tr>
<th>Article 10 ref</th>
<th>Requirement</th>
<th>MDR Article / Annexes</th>
<th>Typical QMS Process / Procedure</th>
<th>EN ISO13485:2016 Clause(s)</th>
<th>MDSAP chapter and Task</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>When placing their devices on the market or putting them into service, manufacturers shall ensure that they have been designed and manufactured in accordance with the requirements of this Regulation.</td>
<td>-</td>
<td>Design control Product realisation</td>
<td>7.3 7.1, 7.5.1</td>
<td>Chapter 5 Chapter 6</td>
</tr>
<tr>
<td>2.</td>
<td>Manufacturers shall establish, document, implement and maintain a system for risk management as described in Section 3 of Annex I.</td>
<td>Annex I S3</td>
<td>Risk Management</td>
<td>7.1</td>
<td>Ch1, T7 Ch3, T3 - T7, T9, T12 Ch5, T8-T10, T12 – T13 Ch6, T10 – 11, T16, T21, T22, T28</td>
</tr>
<tr>
<td>3.</td>
<td>Manufacturers shall conduct a clinical evaluation in accordance with the requirements set out in Article 61 and Annex XIV, including a PMCF.</td>
<td>Article 61 Annex XIV</td>
<td>Clinical Evaluation</td>
<td>7.3.7</td>
<td>Ch5, T11</td>
</tr>
<tr>
<td>4.</td>
<td>Manufacturers of devices other than custom-made devices shall draw up and keep up to date technical documentation for those devices. The technical documentation shall be such as to allow the conformity of the device with the requirements of this Regulation to be assessed. The technical documentation shall include the elements set out in Annexes II and III.</td>
<td>Annex II Annex III</td>
<td>Technical documentation</td>
<td>4.2.3</td>
<td>Annex 1 (Audit of technical documentation)</td>
</tr>
</tbody>
</table>
3. Manufacturers shall establish, implement, document and maintain a risk management system. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall:

(a) establish and document a risk management plan for each device;
(b) identify and analyse the known and foreseeable hazards associated with each device;
(c) estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse;
(d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4;
(e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; and
(f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.
7.1 Planning of Product Realization

The organization shall document one or more processes for risk management in product realization. Records of risk management activities shall be maintained.
Process: Management

Task 7. **Verify that management has committed to and has responsibility for overall risk management planning, including ongoing review of the effectiveness of risk management activities ensuring that policies, procedures and practices are established and documented for analyzing, evaluating and controlling product risk throughout product realization.**