Establishing Regulatory Agility to manage changes due to

EU MDR in Asia Pacific

An Asia Pacific Medical Technology Association (APACMed) position paper on EU MDR

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Outline

- EU MDR overview
- APAC regulators best practices
- APACMed recommendations
- Learnings from EU MDR journey

EU MDR Overview

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Major changes MDD Vs EU MDR

1. EU MDR replaces the Medical Devices Directive (93/42/EEC) and Active Implantable Medical Devices Directive (90/385/EEC)
2. Greater emphasis on a life-cycle approach to safety
3. Govern production and distribution of products in the EU
4. Implications for non-EU countries distributing CE Mark products
5. Strengthened current system for "CE marking" of medical devices
6. Impact on the entire product lifecycle from R&D to post-customer, with major impact on the entire medical device industry, introducing new and substantial requirements

Overview of Eudamed Modules

EC EUROPA LINK

Eudamed Functional Specifications (draft)

EUDAMED

Economic Operators Registration (ACTORS)	UDI / Device Registration (UDID)	Clinical Investigations & Performance Studies (CIPS)	Vigilance & Post-Market Surveillance (VGL)
Activities: • Economic Operator registration functional ownership and maintenance process • Manufacturer (Alcon) registration activities	***Activities:*** • PIM Enhancements • Technical file UDI groupings • UDID attribute collection and PPLM process	***Activities:*** • Clinical investigation registration and record maintenance • Procedure and business process MDR compliance	***Activities:*** • IT application enhancements to enable Eudamed reporting requirement compliance • Business rules, process, and procedure updates to comply with reporting requirements
Scope • Registration of Economic Operators (i.e. manufacturers, importers, and distributors) by electronic submission to Eudamed	***Scope*** • Device registration, including UDI and UDI grouping data, by electronic submission to Eudamed	***Scope*** • Registration of clinical investigations conducted in EU member states • Abbreviated registration of clinical investigations conducted outside the EU to support commercialization of CE-marked product	***Scope*** • Electronic submission requirements for four (4) Vigilance reports: MIR (15 day reporting), FSCA / FSN, PSUR, and Trend Reporting
Module Leads • Carla Amstein / Paul Swift (registration of Actors)	***Module Leads*** • Trey Davis • Jennifer Ashlin	***Module Leads*** • Bertrand Paquette • Laura Wade	***Module Leads*** • Marcia Orozco • Hector Gutierrez

IT Leads: Nikki Lyons, Colleen Metz (QIS), Harrison Doan

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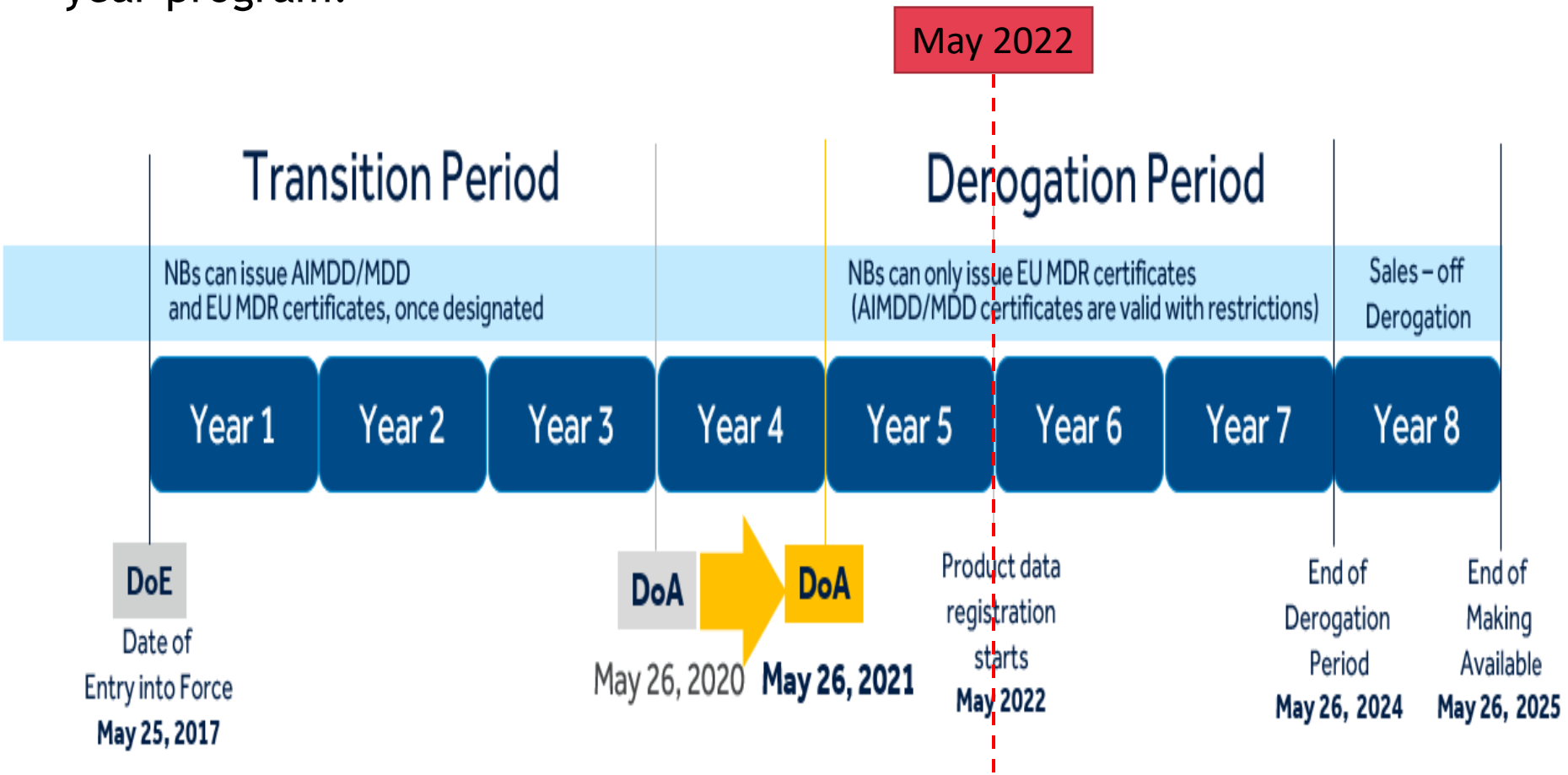
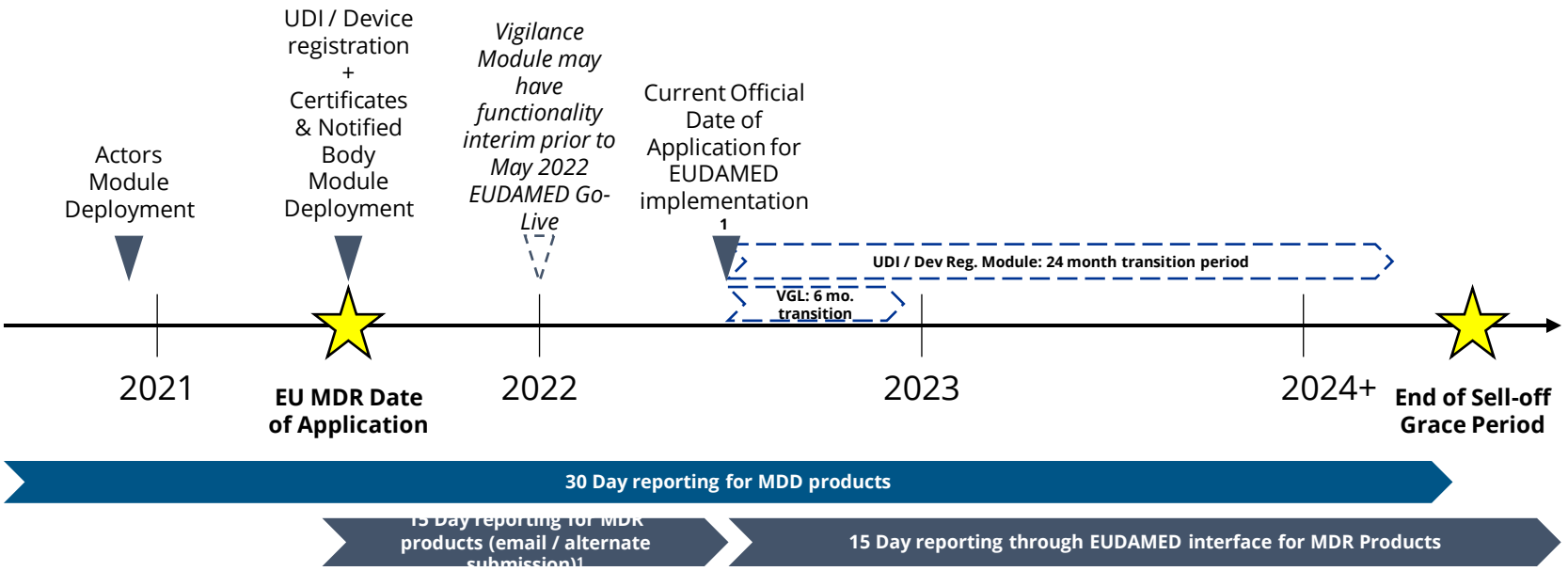
To avoid market disruption and allow a smooth transition from the Directives to the Regulations, the EU MDR implementation is a multi-year program:



Module Timelines



Notes:

1. EU Commission may publish notice prior to 21 MAY 2022 EUDAMED Go-Live date to denote delayed Eudamed full functionality.
2. Registration of Eudamed Actors will be required prior to registration of devices in the UDI/Device Registration Module
3. From November 2022, the device should be fully registered in Eudamed UDI/Device Registration Module, prior to filing the final report for any serious incidents / FSCAs in the Vigilance module (from post market and clinical investigations)
4. Assuming manufacturers receive additional 6 month transition period due to EUDAMED having **full functionality** by May 2022 EU MDR date of application

Changes and Additional Document/Regulatory Requirements for Compliance to the EU MDR

- Greater enforcement on advertising and labeling claims
- Prohibition of reprocessing of single use devices, unless allowed by specific national laws
- Substantially greater clinical evidence requirements
- Enhanced post-market surveillance
- Product-specific Notified Body assessment for all implants and reusable surgical instruments
- Up-classification of meshes and devices in contact with the spinal column
- Increased clinical data scrutiny procedures for certain innovative technologies
- Registration of the medical device, the Notified Body certification documents, and economic operators in the European Database (EUDAMED - European Databank on Medical Devices) to increase transparency
- The implementation of the Unique Device Identification (UDI) to ensure traceability and lifecycle requirements

Note: Most of the changes will result in additional information being added to the labels/IFU but not impact the safety, quality, and efficacy of the registered devices. Changes to the regulatory documentation do not imply changes to the products themselves.

Assessment of the changes due to transition to the EU MDR

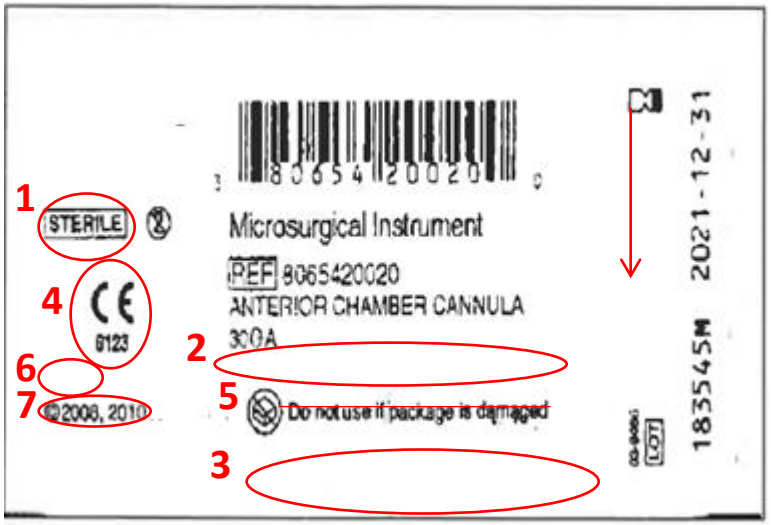
Type of information	Type of change	Change in risk/benefit profile of the device	Change in use of the device	Assessment of the impact of the change
Change to ingredients and manufacturing process	Amendment not permitted during EU MDR transition period	Not applicable	Not applicable	Not applicable
Labels	Additional information, including UDI, new symbols e.g. indication that a productis a medical device or that it contains CMR/ED substances,etc.	None	None	No impact on use or patient safety
IFU	Additional clarification or reduced claims (e.g. intendedusers, where applicable, information about CMR/ED substances, information to be supplied to the patient with an implanted device, explanation of new symbols that appear on the label), etc.	None	None	No impact on use or patient safety
Notified Body Certificates	Additional information e.g. UDI, registration number of the manufacturer (if already issued),etc. This certificate applies toEU member states only	None	None	No impact on use or patient safety

Note - Not all changes will apply to all medical devices. Changes to regulatory documentation because of the EU MDR are likely to vary from product to product.

Examples of Labeling Changes

- Alcon has combined safety information update, shelf life, storage temperature changes and multiple changes together.

EU MDR + JNJ Initiated Changes



Sleeve Label

1. Add method of sterilization
2. Add name and address of manufacturer
3. Add date manufactured YYYY-MM-DD
4. Confirm size of CE mark (min 5mm)
5. Remove “Do not use if package is damaged” → Symbol is sufficient
6. Add proposed MD symbol
7. Update copyright

Note: location and layout will be changed in artwork process

Type of information	Type of change	Change in risk/benefit profile of the device	Changein use of the device	Assessment of the impactof the change
Declaration of Conformity	Additional information, including UDI, registration number of manufacturer and of European authorized representative (if already issued), etc. APAC countries have their respective DoC formatting	None	None	No impact on use or patient safety
Classification	Changes to the classification rules in Annex VIII of the EUMDR may result in a higher risk class for some devices, leading to more stringent conformity assessment requirements. APAC countries have their respective classification ruleto comply to	None	None	No impact on use or patient safety
Certificate of Free Sale(CFS)	New data, including UDI and Notified Body certificate number. Possible new layout for the CFS as the EU MDR foresees the possibility to adopt a model format	None	None	No impact on use or patient safety

Current Best Practices from two Asia Pacific regulators

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Australia TGA

- The Australian medical device regulatory framework has been in place since 2002
- The regulations allow for various submission routes for approval onto the Australian Register Therapeutic Goods (ARTG), including conformity assessment through the Therapeutic Goods Administration or leveraging the approval of a comparable overseas regulator including EU notified bodies. (US, Health Canada, Japan, Singapore)
- Changes such as design, manufacturing, and labelling, or any other substantial changes should be reported to the NBs for assessment and not the TGA, as per the Australian regulations.
- Once the NBs have completed the assessment, the change is considered approved for implementation in Australia.
- Only if the change affects the information entered on the ARTG certificate such as changes to the intended purpose, functional description of the device or device variants is a change notification required to the TGA for assessment and approval.
- TGA does not review changes to products that have been included on the ARTG leveraging CE mark conformity assessment (or other comparable overseas regulator) which includes changes due to the EU MDR.
- For medical devices included on the ARTG via TGA Conformity Assessment certificate*, the manufacturer must notify the TGA of any plan for substantial changes prior to implementation of those changes

Australia TGA (cont)

- For medical devices included on the ARTG via TGA Conformity Assessment certificate*, the manufacturer must notify the TGA of any plan for substantial changes prior to implementation of those changes. Substantial changes include:
  - ❖ Changes to Quality Management system
  - ❖ Changes to product design
  - ❖ Changes that are likely to introduce new hazards
  - ❖ Changes to sterilization processes
  - ❖ Changes to product labelling, including intended use, warnings and precautions

Note: TGA conformity assessment is required for medical devices which contain a drug, material of animal origin, human blood or tissue or where a suitable comparable overseas regulator approval cannot be leveraged.

Singapore HSA

- The Health Sciences Authority Medical Device Regulatory Framework established since 2010 regulates all medical devices and IVDs supplied in Singapore based on a risk-based approach.
- Changes to medical devices and IVD products may require approval from HSA prior to implementation if they fall under a certain category. These changes are categorized based on the level of the risk.
- Low-risk labelling changes such as layout, color, font sizes, addition of languages, addition of UDI, and change in date format do not require submission of change notification.
- On 6 October 2020, HSA published Change Notification applications arising from the EU MDR/IVDR related changes to registered medical devices based on a proposal made by the Medical Technology Industry Group of Singapore Manufacturing Federation (SMF MTIG) to simplify the review and evaluation of changes due to the EU MDR.
- With EU's recent regulatory framework transition to MDR and IVDR, the related changes will impact existing registered medical devices, especially IFU and labels. Major categories of changes resulting from the transition to the EU MDR:
    - ❖ Changes to label and IFU with no new information related to safety and performance (GMD and IVD) => Change Notification is not required
    - ❖ Changes to label and IFU related to material “-Free” claims (GMD) => Change type 5E, Change Notification
    - ❖ Changes to IFU related to clarification of existing content and addition of safety information (GMD and IVD) => Change type 5E, Change Notification

Sharing from JNJ

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Lessons learned from EU MDR journey

- Rationalize if CE-mark is required
  - Ideal opportunity to rationalize product portfolio
- Confirm Notified Body is accredited
  - Check official list at https://ec.europa.eu/growth/tools-databases/nando/index.cfm?fuseaction=directive.notifiedbody&dir_id=34
- Define scope of remediation
  - # of technical files and product classifications
  - Gap assessments
- Meet with Notified Body to secure commitments and lead times
- Prioritize remediations based on MDD-cert expiry dates

Lessons learned from EU MDR journey (cont)

- Account for other country change registration lead time & transition plan
- Secure funding and allocate adequate resources
  - R&D, Quality, Supply Chain, Manufacturing in addition to RA
- Closely track MDR DoC dates
- Work closely with Notified Body

Conclusion

- The new EU MDR creates a robust, transparent, and sustainable regulatory framework, recognized internationally which further improves clinical safety and creates fair market access for manufacturers.
- New regulations to impact not only the manufacturers but also all the respective stakeholders including Regulators as well as importers
- Several transitional provisions are put in place to avoid market disruption and allow a smooth transition from the Directives to the Regulations.
- The aim in the non-European countries, where EU approved products are also supplied, is to also ensure that there is no market disruption and patients continue to receive high quality and safe products
- Local authorities in the countries to review and simplify their regulatory framework for changes due to the EU MDR.

Key stakeholders include (but are not limited to) national trade associations, chambers of commerce, manufacturers, health institutions, procurement bodies, customs officers and importers

Questions?

Please contact me alex.budiman@bd.com

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APACMed Recommendations

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Recommendations for Philippines FDA

- Work with industry bodies to provide clear regulatory guidance and timelines on changes as a result of the EU MDR to industry
- Allow bundling of similar changes of the same risk classification under one application
- Allow exemptions for low-risk and minor changes (e.g. administrative changes) to be implemented without submission
- Allow submission of changes by product families