APACMed
The voice of MedTech

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

December 2020

Table of Contents

Executive Summary

The European Medical Device Regulation (MDR) ((EU) 2017/745) and *In Vitro* Device Regulation (IVDR) ((EU) 2017/746) will apply from 26 May 2021 and 26 May 2022, respectively. The MDR replaces the Medical Devices Directive (MDD) (93/42/EEC) and Active Implantable Medical Devices Directive (AIMDD) (90/385/EEC). The new Regulations create a robust, transparent, and sustainable regulatory framework, recognized internationally, which further improves clinical safety and creates fair market access for manufacturers. In contrast to the Directives, Regulations are directly applicable and do not need to be transposed into national law. The EU MDR and the EU IVDR will therefore reduce the risks of discrepancies in interpretation across the EU market. The EU MDR and the EU IVDR will govern how manufacturers of medical devices produce and distribute products in the EU as per new regulations and has implications for non-EU countries that distribute CE Mark products. The focus of this position paper is on the EU MDR as there will be a separate position paper that will be published for the EU IVDR.

While MedTech companies in most countries in APAC are not directly impacted by the new EU regulations, they will be indirectly impacted by the changes made to the global products imported into these countries. To avoid market disruption and allow a smooth transition from the Directives to the Regulations, several transitional provisions have been put in place by the European Union. Some devices with certificates issued under the Directives (AIMDD/MDD) may continue to be placed on the market until 26 May 2024 and made available until 26 May 2025. Considering the transition phases, changes in documentation triggered by the EU MDR are being gradually implemented and will continue until 26 May 2024. These changes may vary from product to product and not all changes will apply to all devices.

The regulatory frameworks in most countries in APAC are based on a risk-based approach and low-risk changes or administrative changes to the products are either exempted from a change notification or require very minimal documentary submission for a change notification. These include labelling changes such as the addition and removal of certain statements, symbols, and markings (e.g. Unique Device Identification (UDI)).

For countries with established regulatory frameworks to manage such changes being implemented as a result of the EU MDR, the regulatory burden may not be an immediate concern but for the rest, the regulatory burden can be very real if 'simplified' change management regulatory frameworks are not addressed. In addition, managing the sheer volume of labelling changes due to the EU MDR can be a challenge not only to the regulators but also to the industry. Even if the changes do not require an in-depth review, the preparation work for submission and correspondence alone can be overwhelming.

Therefore, to expedite and ensure continuum of patient access to existing CE-marked products, changing the current regulatory paradigm for changes due to the EU MDR is required. The following sections of this paper will present the categories of MDR-triggered changes as well as our recommendations to the Regulators based on some current best practices in the region as well as globally.

Background & Overview

What is EU Medical Device Regulation?

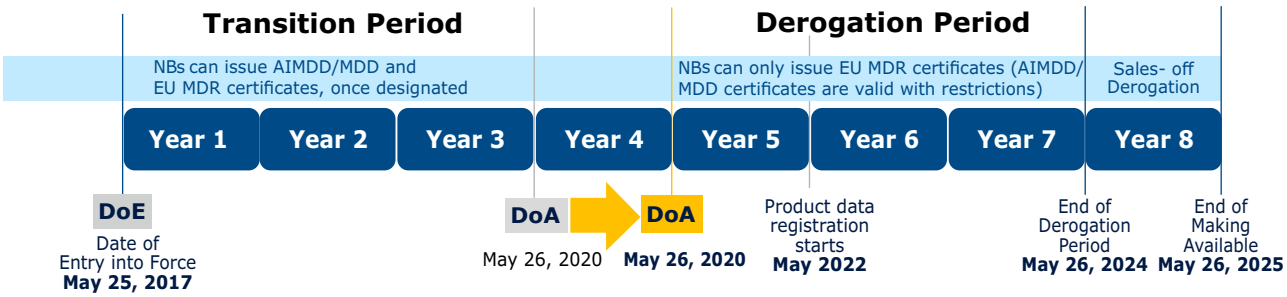
The new European Medical Device Regulation (EU MDR) was published in the Official Journal of the European Union on 05 May 2017. The Regulations entered into force on 25 May 2017, marking the start of the 4-year transition from Medical Devices Directive and Active Implantable Medical Devices Directive for manufacturers distributing medical devices into the European Union.

What has changed from the existing Directives?

The EU MDR replaces the Medical Devices Directive (93/42/EEC) and Active Implantable Medical Devices Directive (90/385/EEC). Compared to the current Directives, the EU MDR places more emphasis on a life-cycle approach to safety, backed up by clinical data. The EU MDR will govern how manufacturers of medical devices produce and distribute products in the EU. As mentioned earlier, there are also implications for non-EU countries that distribute CE Mark products. The EU-MDR is far reaching, strengthens the current system for "CE marking" of medical devices, and will impact the entire product lifecycle from R&D to post-customer, with major impact on the entire medical device industry, introducing new and substantial requirements, with no provision for grandfathering the products already on the market.

Transition Period and Product Availability

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



26 May 2021: The COVID-19 pandemic severely disrupted the preparation for the entry into application of the EU MDR. As a consequence, the EU MDR was amended by Regulation EU 2020/561 and on 17 April 2020, the EU Parliament approved the postponement of the EU MDR Date of Application (DoA) by 1 year from 26 May 2020 to 26 May 2021.

May 2021 - May 2024 (Derogation Period): MDD certificates for medical devices will remain valid until their date of expiration or May 2024 at the latest. The derogation period will allow manufacturers and other economic operators to prepare for the implementation of the Regulations. This means that both MDD (under valid certificates) and MDR conforming devices can be placed on the market during the Derogation Period. Both will have equal status under the law, and no discrimination in public tenders may take place. Certificates delivered by Notified Bodies under the MDD will remain valid - substantial changes to design or intended purpose require MDR certification.

From **27 May 2024:** Only MDR compliant devices can be placed on the market and MDD devices already placed on the market may be made available until 26 May 2025 and used according to its label.

From **27 May 2025:** MDD products may no longer be made available. Devices that are in stock in health institutions can still be used after May 2025 until they reach their expiration dates or end of life since some devices such as instruments and capital equipment do not have expiration date.

With the transition timeline provided by the European Commission (EC) as previously shared, manufacturers have the duration of the transition period to update their technical documentation and processes to meet the new requirements. These new requirements will impact other key stakeholders like importers, distributors, Notified Bodies, the EC and National Health Authorities, as they span across the overall functioning of the system to ensure patient safety and to increase transparency and traceability.

There are various changes and additional document/regulatory requirements for compliance to the EU MDR, which include but are not limited to:

- 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

While changes in requirements/documentation triggered by the EU MDR are being gradually implemented and will continue until the derogation period completes, it is important to note that the design, performance and manufacture of the medical devices are not necessarily impacted by these changes. 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.

Types of Change

The key EU MDR changes influencing global registrations can be categorized in two major categories:

1. Labeling Changes

The requirements of the new regulation will trigger changes to the labels of medical devices. These changes will include

- **Presence of certain substances**

  Where applicable, indication of presence of certain substances that are carcinogenic, mutagenic or toxic to reproduction (CMR) of category 1A or 1B, and/or substances having endocrine-disrupting properties (ED) where there is scientific evidence of probable serious effects to human health. This information will be available for products that contain such substances in a concentration above 0.1% weight by weight. This labelling requirement does not mean that the device is unsafe. The fact that the device has been CE marked means that both the manufacturer and the Notified Body have established a positive benefit-risk ratio analysis, justifying the use of the substance in the device.

  The EU MDR lays down several new requirements asking various kinds of information to be indicated on the label of medical devices. To comply with these requirements, the information required to be supplied on the device's label may take the form of symbols.

- **Increased IFU content with no changes to product claims**

  The EU MDR identifies the information that needs to be included in the instructions for use (IFU) to inform the user of a device's intended purpose and proper use, as well as of any precautions. For devices CE-marked under the EU MDR, additional information will be provided in the IFU in comparison to devices that have been CE-marked under the MDD.

  Intended user: The IFU will include information regarding the device's intended purpose and the intended user.

  Reprocessing of single use devices: The EU MDR provides that the name and address of the manufacturer of the original single use device shall no longer appear on the label but shall

be mentioned in the IFU of the reprocessed device with other relevant information in accordance with the EU MDR.

Substances: Considering space limitation in case of labels of certain devices, the presence of substances that are CMR and ED substances is indicated on a label by the means of a symbol, further information about the substances can be found in the IFU.

Symbols: Explanation of the new symbols that appear on the label.

It's important to reiterate that none of these changes is considered to impact the functionality or risk profile of the medical device and simply serve to explicitly state additional information (if needed), allow for the traceability of the device (UDI) and reflect the new regulatory oversight (NB number).

2. Administrative document Updates

Design Examination Certificates, Declaration of Conformity's, EC Certificates, Certificate of Free Sale, technical files, and risk management documents will be re-issued/revised/updated as explained below:

- New Notified Body certificates will be issued under the EU MDR. These Notified Body certificates contain new information, such as the categorization for the devices which they cover.

- New declarations of conformity (DoC) will be issued under the EU MDR. These reflect not only the fact that conformity will be claimed to the Regulations but will also include additional information, such as UDI, or where applicable, references to any common specifications (CS).

- In general, the EU MDR has an extended scope in comparison to the scope of the MDD, which will result in CE marking of new products under the EU MDR. The scope of the EU MDR expands to products that were not subject to the requirements of the MDD. In addition, the classification of some medical devices may change under the EU MDR.

- New Certificates of Free Sale (CFS/FSC) will refer to the new Regulations. However, they will be covering essentially the same devices as before. The devices may be identified in a new way as UDI and even catalogue numbers may change for the medical devices under the new Regulations. The derogation period is also important to note when it comes to CFS. During the remaining validity of a NB certificate, a device can be covered by a certificate under both the current Directives and the new Regulations. CFS may therefore be issued with the corresponding certificates under both the MDD/AIMDD and the EU MDR and both types of CFS will be equally valid.

Impact Assessments

Assessment of the changes due to transition to the EU MDR

It is important to note that not all changes will apply to all medical devices. The table below provides an assessment of the changes due to transition to the EU MDR. When reading this table, it is important to note that changes to regulatory documentation because of the EU MDR are likely to vary from product to product.

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 product is 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. intended users, 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 to EU member states only	None	None	No impact on use or patient safety

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
Declaration of Conformity	Additional information, including UDI, registration number of manufacturer and of European authorized representative (if already issued), etc. APAC country has their respective DoC formatting	None	None	No impact on use or patient safety
Classification	Changes to the classification rules in Annex VIII of the EU MDR may result in a higher risk class for some devices, leading to more stringent conformity assessment requirements APAC country has their respective classification rule to 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

Overview of Current Practices in APAC

This section provides an overview of the current change implementation practices in a couple of the markets in APAC.

Australia

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.

Often, sponsors submit for their ARTG inclusion leveraging conformity assessment certificates issued by a European notified body (or other comparable overseas regulator), and manufacturers need to maintain continuity of such certification while supply of the device continues within the Australian market.

When changes are made to the medical device such as design, manufacturing, and labelling, if the Australian sponsor has leveraged the conformity assessment certification issued by one of the European Notified Bodies (NBs) (or other comparable overseas regulator) to support their ARTG entries, the Australian regulations require that any substantial changes should be reported to the NBs for assessment and not the TGA. 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, changes to the functional description of the device or changes to device variants is a change notification required to the TGA for assessment and approval. Additionally, if the changes result in the reissue of a NB QMS certificate (or a new NB QMS Certificate) the sponsor shall update the certificate in the TGA's manufacturer's evidence database.

In conclusion, 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. 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

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. Such examples are:

- Technical changes to Class C and D medical devices
- Review Changes *(such as changes to indication of use, addition of new models, removal or revision of warnings, precautions and contraindications, modification of approved method of use, including change from 'professional use only' to 'home use')* for Class B medical devices
- Administrative changes that affect the Singapore Medical Device Register (SMDR) listing information
- Notification changes *(e.g. changes to delete or remove devices which are published on public SMDR listing, all other changes that are not administrative, technical or review changes)*

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.

According to HSA, "European Union (EU) is one of HSA's five reference regulatory agencies commonly referenced in abridged evaluation route for medical device registration. With EU's recent regulatory framework transition to Medical Devices Regulation (MDR) and IVD Regulation (IVDR), the related changes will impact existing registered medical devices, especially IFU and labels. This document serves to provide clarity on HSA's position on change notification applications related to EU MDR and IVDR updates". As stipulated in HSA's guideline, below are the 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

Further details can be found in the amended GN-219 on Change Notification as published by HSA.

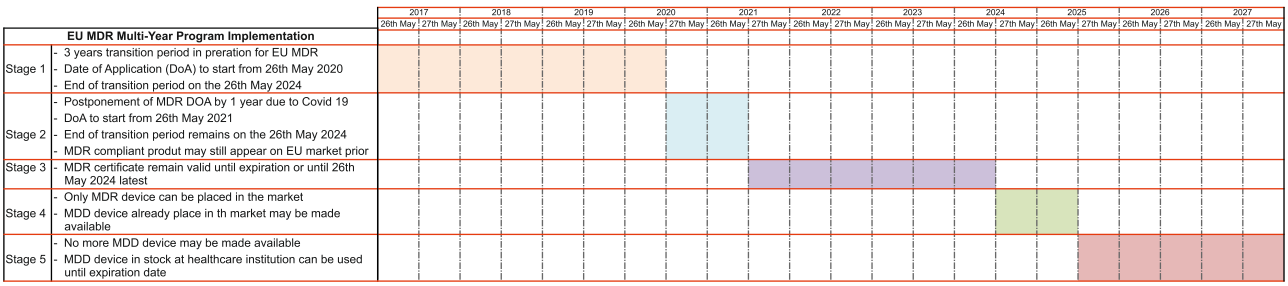
Recommendations

Timeline Recommendations

Based on the sheer volume of the number of submissions for change notifications due to the changes implemented by the EU MDR, the workload to the Regulators as well as to the importers/ license holders will be extremely burdensome. As such, we would like to provide the following recommendations, which take into consideration the following factors:

1. Timeline to implement the EU MDR and the transitional timeline for the CE certificates until expiry
2. Burden faced by manufacturers that have existing MDD compliant stocks upon the implementation of the EU MDR
3. Different importation jurisdictions by different countries

The EU MDR implementation is a multi-year program in the EU comprising of the following stages:



Based on the above transition plan in the EU, we would like to propose an implementation timeline for products impacted by the changes as a result of the EU MDR with specific focus on the following categories for Regulators' consideration:

1. New product registration submission
2. Registration under review by the authorities
3. Pre-market approved products
4. Products already placed in the market

Categories	Recommendations	Proposed Timeline
New Product Registration Submission	• Countries should accept submission with either MDD or MDR certificates • Only submission with MDR certificates is allowed	26 May 2020 - 26 May 2024 27 May 2024 onwards
Registration Under Review by Authorities	• Not mandatory for amendment or update to MDR certificates with submission under review • Authorities to allow company to update submission with changes related to MDR certificates if company is ready • Authorities to approve products with either MDD or MDR certificates	26 May 2020 - 26 May 2024
	• Authorities to allow company to update submission with changes related to MDR certificates if company is ready • Authorities to approve products with either MDD or MDR certificates	27 May 2024 - 26 May 2025
	• Only submission with MDR certificates is allowed	27 May 2025 onwards
Pre-Market Approved Products	• Allow flexibility to submit MDR-related administrative updates as and when company is ready by allowing consolidated single submission • Non-MDR related changes shall require amendment to submission as per local guidance	26 May 2020 - 26 May 2024
	• Allow company to submit MDR-related administrative updates in consolidated single submission • Non-MDR related changes shall require amendment to submission as per local guidance	27 May 2024 - 26 May 2026
	• Only products with MDR certificates should be allowed	27 May 2026 onwards

Categories	Recommendations	Proposed Timeline
Products Already Placed in the Market	• Products with either MDD or MDR certificates can be placed in the market	26 May 2020 - 26 May 2026
	• Only products with MDR certificates can be placed in the market • Countries may decide to continue allowing importation of products with MDD certificates without CE Mark (this will be dependent on country-specific requirements) • Products with MDD certificates already with end users' to be allowed in the market until the end of life	27 May 2026 onwards

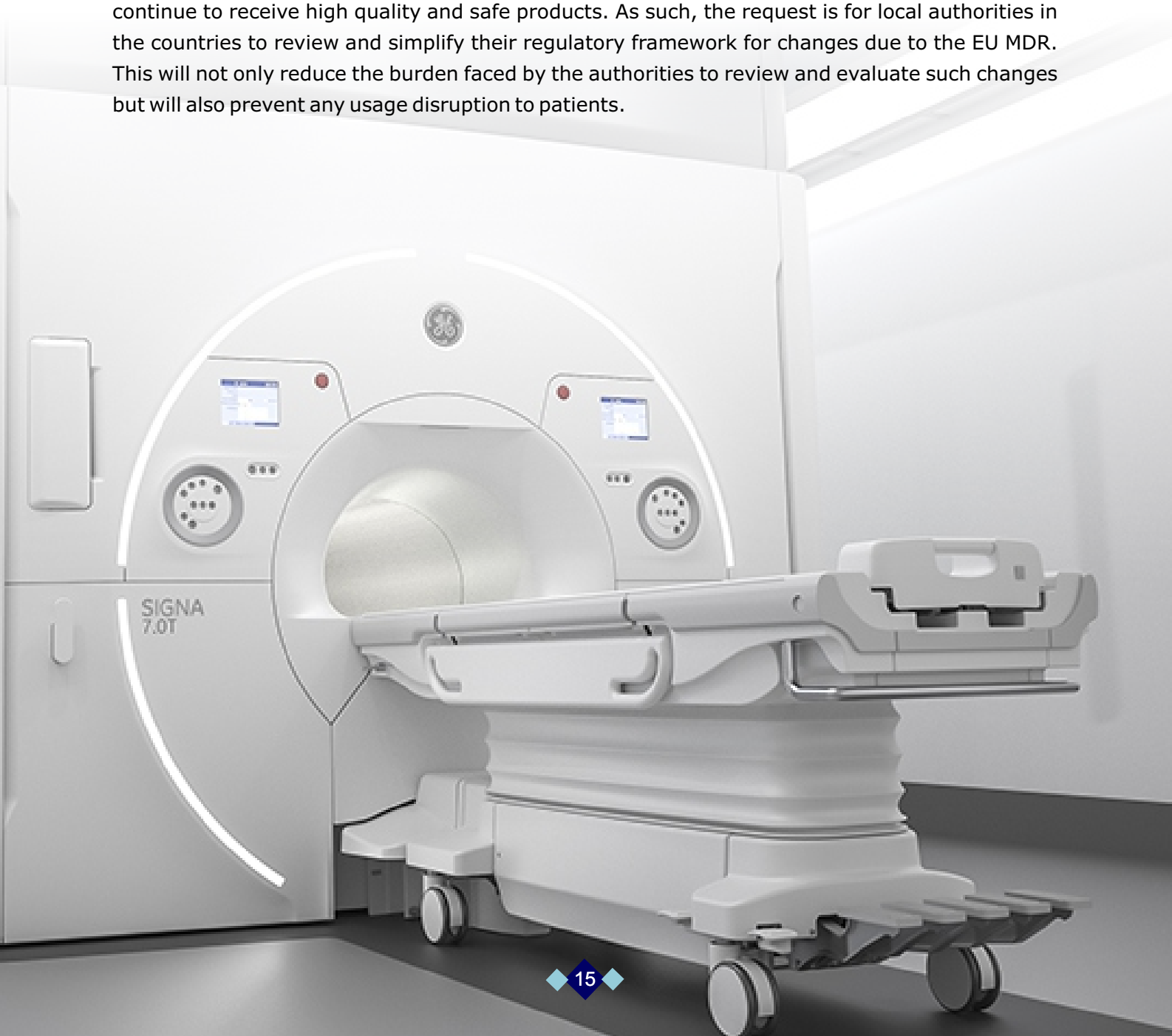
Evaluation Recommendations

Due to the significant workload as a result of the transition to the EU MDR, and based on some the best practices by Regulatory Authorities referenced earlier, APACMed would like the Regulators to consider the following recommendations for the management of changes as a result of the implementation of the EU MDR:

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

Conclusion

The new European Medical Device Regulation will create a robust, transparent, and sustainable regulatory framework, recognized internationally, which further improves clinical safety and creates fair market access for manufacturers. The implementation of this new regulation requires changes, both major and minor, that impact not only the manufacturers but also all the respective stakeholders including Regulators as well as importers. To avoid market disruption and allow a smooth transition from the Directives to the Regulations, several transitional provisions are put in place. As we translate this impact to the non-European countries where EU approved products are also supplied, the aim is to also ensure that there is no market disruption and that patients will continue to receive high quality and safe products. As such, the request is for local authorities in the countries to review and simplify their regulatory framework for changes due to the EU MDR. This will not only reduce the burden faced by the authorities to review and evaluate such changes but will also prevent any usage disruption to patients.



References

1. Regulation (EU) 2020/561 of the European Parliament and of the Council of 23 April 2020 amending Regulation (EU) 2017/745 on medical devices. EUR-Lex Website. https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1587712862624&uri=CELEX:32020R0561. Accessed on June 24, 2020.
2. Impact of changes under the new EU Medical Device Regulations (EU) 2017/745 to international registrations. MedTech Europe, 26 May 2020
3. Factsheet for authorities in non-EU/ EEA States on Medical Devices and in vitro Diagnostics Medical Devices (Jan 21, 2019). EU Commission Website.

   https://ec.europa.eu/docsroom/documents/33863. Accessed on June 24, 2020.
4. Spread the word. EU Commission Website. https://ec.europa.eu/growth/sectors/medical-devices/new-regulations/spread-word_de. Accessed on June 24, 2020.
5. The transition to a new regulatory framework for medical devices in the European Union. MedTech Europe Website. https://www.medtecheurope.org/resource-library/the-transition-to-a-new-regulatory-framework-for-medical-devices-in-the-european-union/. Accessed on June 24, 2020.
6. Transition timelines from the Directives to the Medical Device Regulation. EC Europe Website.

   https://ec.europa.eu/health/sites/health/files/md_newregulations/docs/timeline_mdr_en.pdf. Accessed on Sept 11, 2020
7. Factsheet for Authorities in non-EU/EEA States on medical devices and in vitro diagnostic medical devices. EC Europe Website. https://ec.europa.eu/docsroom/documents/33863. Accessed on Sept 11, 2020
8. Factsheet for manufacturers of medical devices. EC Europe Website. https://ec.europa.eu/health/sites/health/files/md_newregulations/docs/md_manufacturers_factsheet_en.pdf. Accessed on Sept 11, 2020
9. https://www.hsa.gov.sg/docs/default-source/hprg-mdb/change-notifications-arising-from-the-eu-mdrivdr-related-changes-(oct---pub).pdf

About APACMed

Founded in 2014, the Asia Pacific Medical Technology Association (APACMed) is the only regional association to provide a unified voice for the medical technology industry in Asia Pacific, representing both multinational corporations as well as small and medium enterprises, together with local industry associations across the region.

Headquartered in Singapore, APACMed's mission is patient-centric, and we strive to continuously improve the standards of care for patients through innovative collaborations among stakeholders to jointly shape the future of healthcare in Asia Pacific. We are committed to working with governments and other stakeholders to facilitate patient access to innovative and life-saving medical technologies, supporting strong and thriving healthcare systems across the region, and promoting a robust and sustainable regional ecosystem that encourages investment, trade, and innovation.

APACMed Corporate Members

Contacts

Harjit Gill
Chief Executive Officer
APACMed
hgill@apacmed.org

Anirudh Sen
Regulatory Affairs
APACMed
anirudh_sen@apacmed.org

Asia Pacific Medical Technology Association (APACMed)2 Science Park Drive,
Ascent Tower A, #02-07, Science Park I, S118222, Singapore