APACMed
The voice of MedTech

Impact of Changes to Asia Pacific Markets under the In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746 (IVDR)

An Asia Pacific Medical Technology Association (APACMed) Position Paper on EU IVDR

Contents

Key Terms & Definition

MDR : Medical Devices Regulation, (EU) 2017/745

IVDR : In Vitro Diagnostic Medical Devices Regulations, (EU) 2017/746

DoA : Date of Application (DoA of MDR is May 2021; DoA of IVDR is May 2022)

IFU : Instructions for use

NB : Notified Body

'Making available on the market' means any supply of a device, other than an investigational device, for distribution, consumption or use on the **EU market**, whether in return for payment or free of charge (IVDR Article 2 definition 20).

'Placing on the market' means the first making available of a device, other than an investigational device, on the **EU market** (IVDR Article 2 definition 21).

'Putting into service' means the stage at which a device, other than an investigational device, has been made available to the final user as being ready for use for its intended purpose on the **EU market** for the first time (IVDR Article 2 definition 22).

Significant change[3] means a change that could reasonably be expected to affect safety and/or performance of a device.

Non-significant change[3] means a change that will not affect safety and/or performance of a device.

1 Introduction

i. What is EU *in vitro diagnostic* Medical Device Regulation

The new European *in vitro diagnostic* Medical Device Regulation, (EU) 2017/746 (IVDR), published in May 2017, introduces a major update to the regulatory framework in the European Union and will replace the existing *in vitro diagnostic* medical devices Directive (98/79/EC)(**IVDD**).

For more comprehensive information about the new regulation, please refer to the *Factsheet for Authorities in non-EU/EEA States on Medical Devices and in vitro Diagnostic Medical Devices* published by the European Commission.

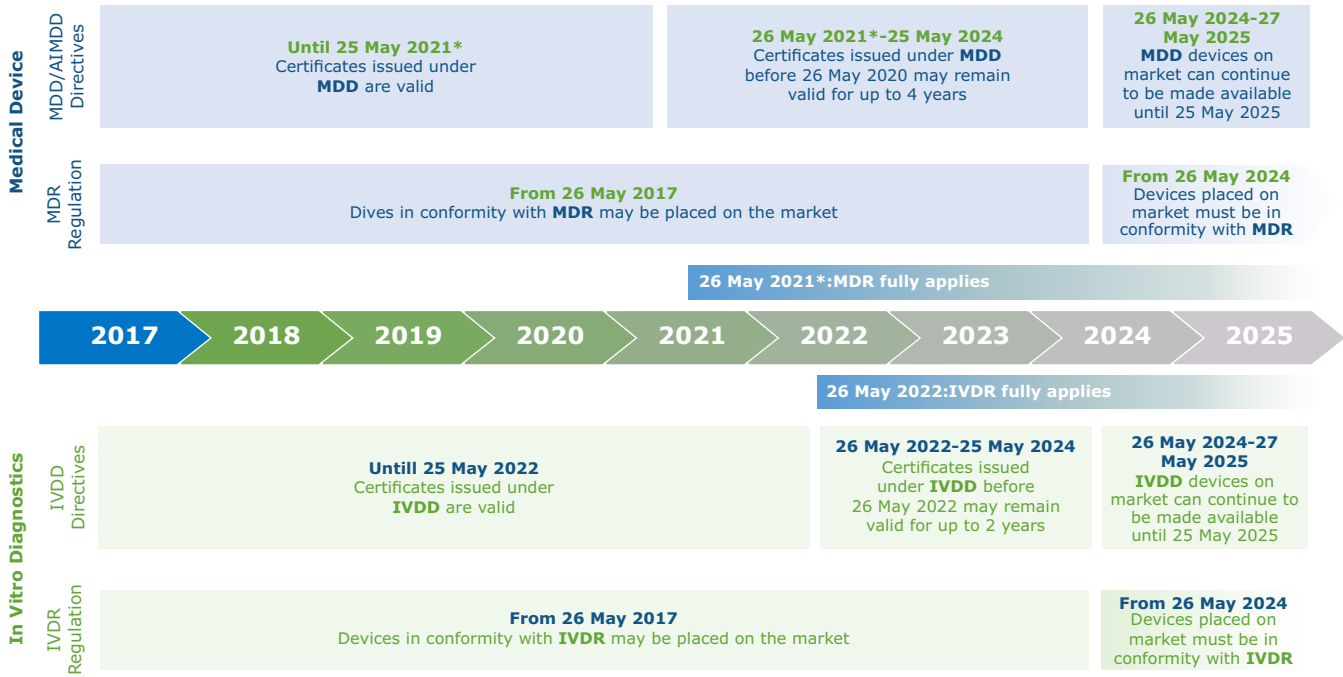
ii. Transition Period

While the European Commission published the new regulations for both medical devices (MDR) *and in vitro diagnostic* devices (IVDR) back in May 2017, MDR has a 4-year transition period (until May 2021, as the Data of Application of the MDR, with 1-year postponement due to COVID-19) and IVDR has a 5-year transition period (until May 2022, as the Date of Application of the IVDR).

A reasonable transition period is needed as the new regulation requires the designation of Notified Bodies. The designation process for Notified Bodies took more than 18 months with more rigorous rules and new requirements and responsibilities. Since the process of designating Notified Bodies took up a significant part of the transition period, **there is very limited time for manufacturers to have all their products certified before the Date of Application[1].**

As highlighted by the European Commission in the Factsheet, "to avoid market disruption and allow a smooth transition from the Directives to the Regulations, several transitional provisions are in place. Some devices with certificates issued under the Directives may continue to be placed on the EU market until 27 May 2024 and made available until 27 May 2025".

Figure 1: EU MDR/IVDR Transition timeline for EU markets



*Extended by 1 year from May 2020 to May 2021 due to COVID-19 impact

It is important to note that, to transition into the new regulations, regulatory authorities (in EU and outside EU), Notified Bodies, and industry players, are likely to experience resource constraints, given the significant market share of impacted products, as well as the overlapped implementation timelines between MDR and IVDR (as illustrated in **Figure 1**). It is especially the case, after the 1-year postponement for MDR, announced by EU Parliament back in May 2020,when the regulation was initially slated to take effect.

Transition timeline for IVDR in EU markets is as follows:

26 May 2017- 25 May 2022: During this transition period, IVDs can be placed on the EU market following either the current Directive (IVDD) or the new IVD Regulation (IVDR).

26 May 2022 – 25 May 2024: Products which have been certified by a Notified Body under the IVD Directive (IVDD), may have (up to) an additional two years after 26 May 2022, during which they can continue to be placed on the EU market, i.e., up until 26 May 2024. IVDs that are not supervised by Notified Bodies under the Directive (IVDD) must comply with the new Regulation, from 26 May 2022 onwards, in order to be lawfully placed on the EU market.

26 May 2024 – 26 May 2025: Only IVDR-compliant Devices can be placed on the EU market and IVDD devices already placed on the EU market may be made available until 26 May 2025 and used according to its label. Therefore, **until May 2025, products certified under IVDD and products certified under IVDR will co-exist on the EU market**. Both will have **equal status** under the legislation, and **no discrimination** in public tenders may take place[1].

27 May 2025 onwards: No more IVDD products may be made available on the EU market. Devices that are in stock in health institutions in EU can still be used after May 2025 until they reach their expiration dates or end of life.

In Asia Pacific markets, it is very important to note that, during the transition period, we may receive products that are covered by the **IVDD** Notified Body Certificates or the **IVDR** Notified Body Certificates. Similarly, Certificate of Free Sale (CFS) which may be issued with the corresponding certificates under both the IVDD and the IVDR will be equally valid[2]. To avoid any unintended adverse impact on the supply of products, it is imperative that regulatory authorities in APAC markets recognise the equal status of both IVDD and IVDR versions of products, as well as the validity of the corresponding certificates, based on the transition timelines in EU markets.

iii. What has changed from the existing Directive

Major changes in IVDR compared to IVDD include:

- Risk classification of IVD devices;
- Role of Notified Bodies;
- Clarification of obligations of economic operators (manufacturers, authorized representatives, importers and distributors);
- Tightened requirements for Post-Market Surveillance and Vigilance;
- Tightened requirements for clinical evidence and conformity assessment;
- Introduction of a unique device identifier (UDI) for every IVD device;
- Increased transparency, with information on IVD devices and 'higher risk' performance studies being made public in the new European Database for Medical Devices (EUDAMED). As highlighted in the Factsheet, **as an exceptional case**, the existing Directive (IVDD) might still apply to some extent, in case EUDAMED is not fully functional by the Date of Application.

For IVDs, the biggest changes are the risk classification and the role of Notified Bodies. The IVDR classification rules assign each device to one of four risk categories, ranging from class A for lowest risk, to class D for highest risk (IVDR Article 47). As a result, around 85% of all IVDs will now need oversight from Notified Bodies, compared to 20% under the Directive (IVDD) [1].

As proposed by the European Commission in the Factsheet, "competent authorities in non-EU markets that export devices to the EU, are encouraged to make your manufacturers, national associations and chambers of commerce aware of the new rules, timelines and obligations under the new Regulations; refer them to the website of the European Commission for further information on the application of the Regulations or for guidance.

As an authority in non-EUmarkets that import devices from the EU, it is also recommended to inform your health institutions, procurement bodies, customs officers, and importers about the new requirements and the applicable timelines, and clarify the various transition provisions regarding, for example, the labelling requirements, so as to avoid disruptions on your market".

2 Impact Assessments

IVDR will bring about several changes to the information provided with IVD devices and their regulatory documentation. It is important to note that, not all changes will apply to all IVDs. Therefore, changes to regulatory documentation due to the IVDR, are likely to vary from product to product

As highlighted in the MedTech Europe Paper[2], "**Most of these changes will simply mean that additional information is available for existing devices. This in no way changes the use, effectiveness, performance or safety profile of the devices and as such should have no particular impact on registrations.** The regulatory documentation around a device will be updated - this can include changes to Notified Body certificates, free sales certificates, and declarations of conformity. The update of the regulatory documentation does not necessarily impact the device characteristics, i.e. changes to the regulatory documentation do not imply changes to the composition of the ingredients or the manufacturing processes unless otherwise indicated."

i. Assessment of changes to product information due to IVDR transition

With reference to the MedTech Europe Paper[2], we have summarized in **Table 1** below the assessment of expected changes to product information due to IVDR transition.

Table 1: Assessment of changes to product information due to IVDR transition

Type of information	Type of change	Does it change the risk/benefit profile of the device?	Does it change the use of the device?	Does it affect product quality and/or performance?
Labels	Additional information, including UDI, notified body number, new symbols (self- test, near-patient testing, single use), etc.	No	No	No
IFU	Additional information, including notified body number, clarification (intended use, intended user, existing available performance data), etc.	No	No, except for changes specified in **the row below**	No

Type of information	Type of change	Does it change the risk/benefit profile of device?	Does it change the use of the device?	Does it affect product quality and/ or the performance?
Intended purpose change and/ or new performance data	Intended purpose might be amended for some IVD products, some of which will have new performance data from studies and/or literature	Maybe	Maybe	Needs to be assessed on case by case basis
Notified Body Certificates	Additional information, including UDI, notified body number, product classification, etc. A notified body certificate is a new document for many IVDs	No	No	No
Declaration of Conformity (DoC)	Additional information, including UDI, notified body number, product classification, registration number of manufacturer and of European authorized representative (if already issued), etc. **(Some APAC markets have their respective format for DoC)**	No	No	No
Classification	IVDR adopts new IVD classification based on IMDRF classification (class A, B, C, D) which will be reported on CE certificates and CE Declarations of Conformity. **(Some APAC markets have their respective in-market classification rules)**	No	No	No
Certificate of Free Sale (CFS)	Additional information, including Basic UDI, notified body certificate number. Possible new layout for the CFS as IVDR foresees the possibility to adopt a model format.	No	No	No

In summary, most of the changes caused by IVDR, will **NOT** change the risk/benefit profile, the quality and performance, or use of the products. As such, no impact on patient safety is foreseen due to such changes. Only for a minority of cases, changes to intended purpose will be expected during the transition, which needs to be assessed on a case-by-case basis.

Hence, **APACMed highly recommends that regulatory authorities in Asia Pacific to take a risk-based approach when assessing changes caused by IVDR, and consider formulating special measures to cater for such changes, in view of the large volume of products impacted by MDR and IVDR and minimal impact on patient safety foreseen in most cases.**

Additionally, it is worth noting that other than changes listed in the **Table 1**, some products will **expect legal manufacturer changes** and/or **catalogue number changes** during the IVDR transition period. Although these changes are not directly mandated by IVDR, but rather the manufacturers' decisions, **APACMed recommends regulatory authorities in our region to also apply a risk-based approach when assessing such changes, based on the rationale of changes and potential risks for patient safety.** It is very critical to ensure a smooth transition by enabling stakeholder conversions, given the very tight timeline and the potential negative impact on patient access, should there be any supply disruptions.

ii. Assessment of the magnitude of number of products impacted by IVDR transition

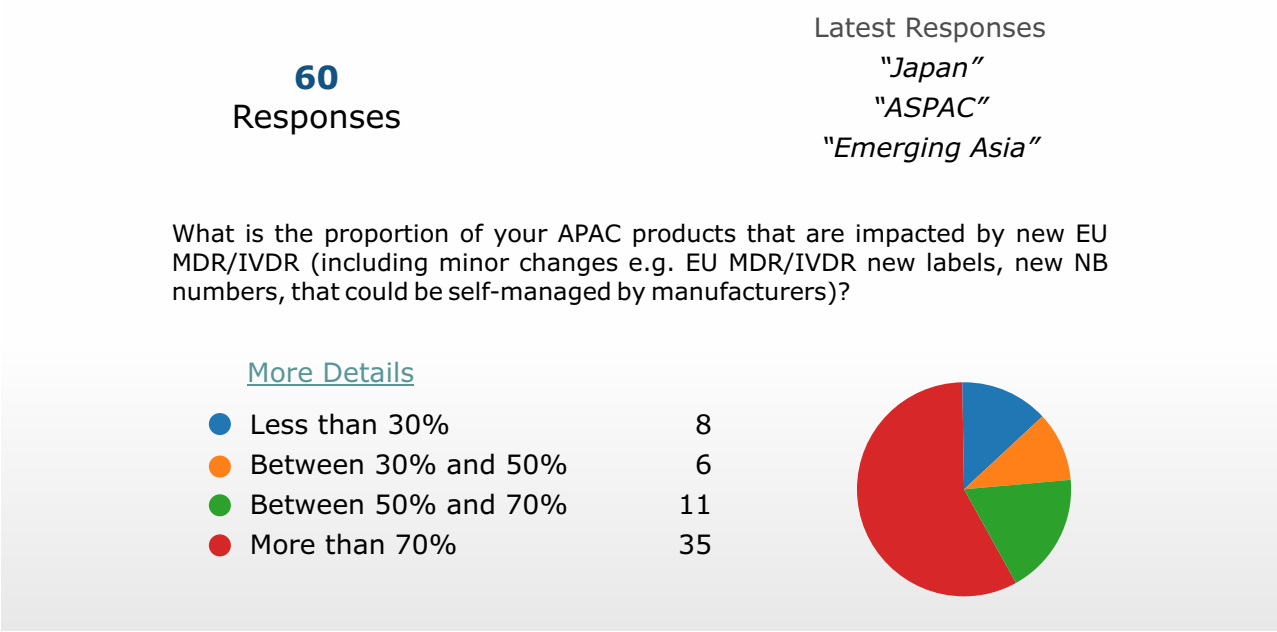
As mentioned above, the EU regulations on medical devices (MDR) and *in vitro diagnostic* devices (IVDR) are going through a largely overlapped transition timeline. The sheer number of products going through the changes might not just pose challenges to the EU regulators and Notified Bodies, but also may cause submission "**traffic jam**" in the non-EU markets due to the change management requirements in the importing markets.

To better understand the magnitude of number of products (in Asia Pacific markets) impacted by the new EU regulations, APACMed has done a survey among its members (manufacturers that are either manufacturing in or supplying to the EU market).

According to the survey result (as shown in **Figure 2** below), **more than 50% respondents responded that over 70% of their APAC portfolio (products sold in APAC markets) are impacted by the new EU regulations (MDR and/or IVDR); and over 75% of respondents reported that at least 50% of their APAC portfolio are impacted.**

This number included those **minor changes** or **non-significant changes** (such as new labels or new Notified Body numbers), which have no impact on product safety/performance or patient safety, hence are not reportable or not regulated in many markets. **Hence, for these markets, submission "traffic jam" is much less likely to occur, compared to those markets that regulate all minor changes or non-significant changes, or even invest regulatory resources in reviewing and approving for such changes.**

Figure 2: APACMed survey among members about EU MDR/IVDR impact scale



iii. Assessment of the current regulatory measures for IVDR changes and impact to patient access

Based on our observations, APACMed members have summarised the current regulatory set-up for handling IVDR changes in **Table 2** below. As explained earlier, most changes caused by IVDR or accompanying the IVDR transition will **NOT** affect safety and/or performance of a device. Therefore, according to the AHWP/GHWP definition[3], we have categorized these changes as **non-significant changes**, while at the same time acknowledging that different jurisdictions in the Asia Pacific regions have their respective terms and definitions for such "changes" (e.g. minor changes, administrative changes, etc.)

The same applies to the terms for "regulatory measures". For the ease of discussion and comparison, we tried to use the more generally acceptable terms, such as "change notification" and"change registration", while acknowledging that some markets might use other terms (e.g. change submission, amendment registration, post-approval change, etc.)

It is worth highlighting that, even when different jurisdictions use the **same terminology** to define the regulatory measurers for change management, they may define and/or implement it in **highly divergent manners**. Take "**change notification**" as an example, in most markets, "change notification" does not require "approval"and can be implemented immediately after submission by the manufacturers. However, some markets require the manufacturers to wait for "approval" before implementation for change notifications. And several other markets, although they do not require manufacturers to wait for approval before implementation, still invest resources in review and approval of such notification items.

Based on the analysis of the current regulatory landscape in Asia Pacific markets (as summarized in **Table 2** below), we observed that, for the same type of changes that might be caused by the same reasons during IVDR transition, **regulatory measures vary from no action required or exemption, to change notification, to change registration, and even new registration. Consequently, the regulatory timelines vary from 0 month to 12-18 months.**

Table 2: The Divergent Regulatory Measures in Asia Pacific Markets for non-significant changes caused by IVDR, and legal manufacturer changes and catalogue number changes happening during IVDR transition

Asia Pacific Markets	Non-significant changes caused by EU IVDR		Other Non-significant changes happening during EU IVDR transition	
	Regulatory measures	**If bundling or supplement is allowed**	**Legal manufacturer change**	**Catalogue/ Material/ Part number change**
Australia	No action required (for a majority of change types that does not impact devices of a Kind)	N/A	Where it leads to a new registration (up to 6 months) (experiential in 2021)	No action required with no product name change and insignificant functionality change
Cambodia	Change notification	No	New registration (8-12 months)	New registration (8-12 months)
China	Class I: Change notification; Class II & III: Change registration (Administrative or License change) (1- 6 months)	No	Class I: self-modification or Change notification; Class II & III: Change registration (Administration change) (30 days)	No action required for pure material number change. In case of combining with other changes, then change registration is required
India	Change notification	No	Post-approval changes (submission required within 1 month from implementation; full dossier submission required in 6 months)	No action required
Indonesia	Change notification (requiring approval)	Yes (group of 5-10 products with limitation based on terms and conditions such as same changes and same product risk class); the bundling criteria/ limitation is	Change registration or Change notification (requirement approval)	Change registration or new registration (3-6 months)

Asia Pacific Markets	Non-significant changes caused by EU IVDR		Other Non-significant changes happening during EU IVDR transition	
	Regulatory measures	**If bundling or supplement is allowed**	**Legal manufacturer change**	**Catalogue/ Material/ Part number change**
		extremely challenging for manufacturers, given the large number of product submission		
Japan	No action required	N/A	No action required	No action required
Korea	No action required for administrative changes; Minor change submission for other non-significant changes	No for bundling; but for supplement, MFDS recently started simultaneous multiple change applications	New KGMP is required and all related licenses need to be updated	Minor change submission
Malaysia	Change notification (requiring approval but can be implemented immediately after submission)	Yes (per submission cluster)	Change notification (requiring approval but can be implemented immediately after submission)	Change registration (4-6 months)
Myanmar	No action required	N/A	New registration required (4-6 months)	New registration required (4-6 months)
Philippines	Change registration (3-6 months, admin)	Yes (for simple changes of the same kind)	Change registration (3-6 months, admin)	New registration (12-18 months)
Singapore	Exemption (for most IVDR-introduced changes) or notification	Yes (for same risk classifications)	Change registration (30 days)	Change registration (30 days)
Sri Lanka	Change notification	No	New registration (12-18 months)	Change notification (2-3 months)
Taiwan	No action required	N/A	No action required	New registration (9-12 months for Class 2&3)
Thailand	No action required (except for alcohol & HIV products, for which notification is required)	No	New registration (200, 250, 300 days for class A, B&C, D)	New registration (200, 250, 300 days for Class A, B&C, D)
Vietnam	Change notification for Class A	Yes, IVDR changes can be supplemented into the Decree 169 CSDT submission for Class B, C, D	New registration (for Class B,C,D: before Jan 2022: 6-8 months; after Jan 2022: 15-18 months)	New registration (for Class B,C,D: before Jan 2022: 6-8 months; after Jan 2022: 15-18 months)

Note: Some markets are excluded from this analysis because the regulation is not enforced yet (e.g. Bangladesh, Hong Kong, Laos, New Zealand, Pakistan, etc.). Green box for good practices and Orange box for burdensome practices according to APACMed members' assessment.

To summarize, given the sheer number of products transitioning into MDR and IVDR during a relatively short and overlapped time period, there is significant concern from APACMed members that **the peak of administrative work** may lead to a "**traffic jam**" at the authority side, when many companies notify changes or submit change registration (and even new registration) for a large number of changes caused by MDR and IVDR during the same time period.

Since the majority of changes to product information are only minor changes or non-significant changes with no impact on the product itself or patient safety, **APACMed highly recommends that regulatory authorities re-evaluate their current regulatory mechanism for change management, based on risk-based principles and best practices in the region, and consider providing special measures for MDR/IVDR triggered-changes to avoid submission "traffic jam", to avoid supply risks for patient access to life-saving medical technologies.**

The situation is even more concerning for some markets, where the transition period is very short with less flexibility. APACMed has summarized our observations in **Table 3** below.

Table 3: A glimpse of the transition mechanism for change implementation (not specifically for MDR/IVDR triggered changes)in Asia Pacific markets

Transition measures & timeline		
	Whether IVDD products can be imported after IVDR change approval by respective jurisdication (based on current regulatory mechanism)	**How long can IVDD products (already imported) be sold after IVDR change approval by respective jurisdiction (based on current regulatory mechanism)**
Australia	Yes	Till the product expiry date
Cambodia	Yes	Till the product expiry date
China	Yes, as long as the manufacturing date of the IVDD version is before the date of the IVDR change approval granted by the local regulatory authority	Till the product expiry date
India	Yes, can import IVDD version till the IVDR conversion time, as per stated in the change submission	Till the product expiry date
Indonesia	**No**	**Maximum 3 months, depending on MoH approved transition period on a case by case basis**
Japan	N/A	N/A
Korea	No	Till the product expiry date
Malaysia	Yes	**Not defined by Authority**
Myanmar	Yes	Till the product expiry date
Pakistan	Yes	Till the product expiry date
Philippines	Yes, as long as the products will be used up **within 6 months** from approval date of IVDR change	**Within 6 months** after IVDR change approval

Transition measures & timeline		
	Whether IVDD products can be imported after IVDR change approval (based on current regulatory mechanism)	**How long can IVDD products (already imported) be sold after IVDR change approval (based on current regulatory mechanism)**
Singapore	Yes	Till the product expiry date
Sri Lanka	Yes, can import IVDD till the IVDR conversion time, as per stated in the change submission	Till the product expiry date
Taiwan	**No**	Till the product expiry date
Thailand	Yes, as long as the IVDD license in Thailand is still valid	Till the IVDD license expires
Vietnam	Yes, as long as the IVDD license in Vietnam is still valid	Till the IVDD license expires

In addition to the above-mentioned challenges and complexity, it is worth noting that during the MDR/IVDR transition period, several Asia Pacific markets are either establishing their own **new regulations for MDs and IVDs, or upgrading their local regulatory framework**, such as China, India, Hong Kong, Korea, Pakistan, Philippines, Taiwan, Thailand, and Vietnam, etc. Due to this reason, industry players in these markets will have to follow "**dual transition**" measures and timelines. Resource constraints from both sides are also more likely, hence a close dialogue between the government and industry stakeholders will be very helpful to explore more efficient and effective mechanisms.

Therefore, **APACMed recommends that for markets with new upcoming regulations or in the midst of local regulatory upgrade, regulatory authorities will take the IVDR transition scenarios and timelines into consideration while designing/implementing their local transition measures.** A close conversation with local and regional industry trade associations is highly recommended as ensuring patient access is the shared global for both parties when exploring the regulatory flexibility for managing such unique and complex situation.

Lastly, the **COVID-19 pandemic** has been draining regulatory resources worldwide in the past year and also likely for the next 1-2 years to come due to the sheer volume of novel products and accumulative innovation for COVID-19 prevention, diagnosis and treatment. Therefore, **highly efficient usage of regulatory resources on a risk-calibrated basis is paramount to** ensure the supply continuity and well-beings for the population of APAC markets.

3 Current Best Practices from two Asia Pacific Markets

In this section, we would like to share some best practices from our region in change management and in special considerations to deal with the EU MDR/IVDR-triggered changes as well as the impact on our market supply.

AUSTRALIA

The Australian medical device regulatory framework has been in place since 2002, with the *in vitro diagnostic* medical device regulatory framework added in 2010. The regulations allow various submission routes for approval and inclusion onto the Australian Register Therapeutic Goods (ARTG), including conformity assessment through the Therapeutic Goods Administration (TGA) or leveraging the approval of a comparable overseas regulator including EU notified bodies and the Medical Device Single Audit Program (MDSAP).

When considering the IVDR change impact on supply of goods in Australia, it should be seen from the Australian Regulations perspective. The change type of any current product must be considered against what is required for continued compliance with the Australian Labelling requirements (Essential Principle 13 (EP13)[4] from Schedule 1 of the Therapeutics Goods (Medical Device) Regulations 2002), Inclusion requirements (classification and intended use), and Manufacturer's Evidence requirements.

We expect a large portion of products to have little or no impact to their Australian regulatory status, where they are already supplied as low-mid risk IVDs, as many were audited under Regulation 5.3 having no EU Certification basis in the past. For IVDs that are included in the ARTG on the basis of overseas-issued certification (i.e. Conformity assessment (CA) documents issued by comparable overseas regulators or high risk EU Notified Body CA Certificates), it is likely that only changes (significant in nature) to the intended use, intended user, or performance reporting of the test may trigger actions required of the Australian Sponsor. Manufacturers should always consider Australian specific legislation when determining if there is a need to undertake regulatory action.

To that end the likely impacts noting the common IVDR change types previously mentioned are:

- If the new IVDR label and instructions for use text continue to cover EP13 requirements, particularly EP13.3 #29, then there is no impact even where additions or layout changes might have occurred for that same label or IFU to meet IVDR requirements. This applies to all Classes of device, including locally conformity assessed, mandatory audit and low risk devices
- If the IVDR class does not match that of the current Australian Classification. At this time there is no immediate impact as the Australian regulations take precedence; where new claims have been introduced during the IFU re-write for IVDR, this might cause a change in Classification in Australia

- The Manufacturer's QMS and where applicable Design evidence submitted as the basis of approval of Licenses in Australia may be minimally impacted by the IVDR Certification, again this depends on what is the current license base:
    - IVDD Cert - a small list of product types might have been based upon IVDD Certification. For these, the IVDR CE Certification would simply be added to the online Manufacturer's Evidence as a matter of Notification
    - Australian TGA Conformity Assessment (CA) - this evidence base is separate from IVDR, however often the audit carried out to obtain a TGA CA Certificate will leverage EU CE Notified Body (NB) reports. Thus, the new IVDR CE certificate is expected to reduce the time for assessments where the NB has already approved a change
    - MDSAP - allows access to 5 jurisdictions; however first-time Product Applications of Class 2-3 are audited for performance assessment. Following that changes from IVDR for a current product will be considered like any change of any product in this group. Change audits would focus on Products under Regulation 5.3 (Class 3, Point of care, Self-test, Companion diagnostic and so on), where the change impacts IVD intended purpose/functionality and were greater than simple layout or EU specific additions in IFU's as described above. Whilst changes to lower risk IVDs that are not subject to Regulation 5.3 can be managed by the Manufacturer's QMS and local Sponsor records. Equally this same principle applies to the addition of same Kinds of devices to a current ARTG entry for Inclusions/Entries support by MDSAP based evidence. Refer to https://www.tga.gov.au/medical-device-single-audit-program-mdsap
    - ISO 13485 QMS (non-MDSAP) - this base is rarer in Australia as the list of acceptable Auditing bodies reduces in time and therefore we expect a similar IVDR impact for these products as MDSAP listed above

A large portion of imported product is affected in some manner by the European implementation of IVDR. The Therapeutic Goods Administration (TGA) is expected to update guidance for Australian sponsors in Q2 of 2021 to provide clarification on processing of changes to ARTG entries that are required as a result of IVDR implementation. Guidance will also be made available on notification and application for substantial changes to conformity assessment certificates issued by the TGA.

Of interest is the changing landscape in Australia. In recent years a review of Medicines and Medical Devices (MMDR) occurred in Australia; a program of reforms is currently underway, which includes a recommendation to align with EU MDR and/or IVDR requirements wherever practical and/or possible. It is anticipated this will assist in harmonising differences between existing Australian requirements and the IVDR. Any such changes which impact Australian legislative requirements for IVDs will include relevant stakeholder consultation and engagement, which will allow adequate time for manufacturers to transition to new Australian regulatory requirements.

SINGAPORE

Established in 2010, the Health Sciences Authority (HSA) Medical Device Regulatory Framework 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, involving changes that affect safety, quality and efficacy of Class C and D medical devices

- Review changes, including changes to indication of use, addition of new models, removal or revision of warnings, precautions, contraindications, adverse events and modification of approved method of use, for Class B medical devices
- Administrative changes, for updates to the Singapore Medical Device Register (SMDR) listing information
- Notification changes (e.g. changes to delete or remove device which are published on the SMDR, all other changes that are not administrative, technical or review changes)

Specific low risk labelling changes, such as changes to layout, color, font sizes, addition of languages, addition of UDI information to labels with no change to existing device identifier, 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*[5] 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/ IVDR which can be implemented without seeking approval from HSA:

- Closed list of 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 adverse events and side effects (GMD and IVD) => Change type 5E, Change Notification
- Changes to IFU, covering only addition or clarification of performance data, which directly mirrors pre-clinical or clinical studies previously submitted to HSA => Change type 5E, Change Notification

Further details can be found in the *Change Notification applications arising from the EU MDR/IVDR related changes to registered medical devices*[5] document as published by HSA. This document is to be read in conjunction with GN-21: Guidance on Change Notification for Registered Medical Devices.

4 Recommendations on regulatory measures and transition timelines for handling IVDR-triggered changes in Asia Pacific markets

APACMed members share with regulators the ultimate goal to ensure patient safety and a continuous supply of critical products to healthcare systems worldwide. In addition to the recommendations detailed in the sections above, we have summarized in **Table 4** below our detailed recommendations on regulatory measures and timelines.

Table 4: Recommendations on regulatory measures and timelines for IVDR-triggered changes in Asia Pacific markets

<table>
<tr><th></th><th>Non-significant changes caused by EU IVDR</th><th>Other Non-significant changes happening during EU IVDR transition (legal manufacturer change and catalogue number change)</th><th>Changes to intended purpose and/ or new data</th></tr>
<tr><td>Patient/ user risk assessment</td><td>None</td><td>None</td><td>Varies based on the new data/ Intended Purpose</td></tr>
<tr><td>Recommended principles for regulatory procedure</td><td>Exemption of submission is preferred; change notification (with immediate implementation) should be sufficient</td><td>Change registration should be sufficient (instead of new registration)</td><td></td></tr>
<tr><td>Bundling & Supplement</td><td colspan="2">Bundling submission of similar changes for different products, as well as combination of multiple changes for the same product should be allowed; supplement submission into ongoing reviews should be allowed esp. for newly regulated markets. Existing submission family/group/cluster should not become the barrier for such bundling/combination measures</td><td rowspan="3">Follow applicable procedure in the market with due regard to ensuring a smooth transition for patient access</td></tr>
<tr><td>Approval Timeline</td><td>Immediate implementation should be allowed given no change to the product or use of product, and no risk to patient safety</td><td>A shortened approval timeline is preferred (via fast track or special arrangement for IVDR), given no change to the product or the use of the product, as well as minimal risk for patient safety</td></tr>
<tr><td>Transition measures</td><td colspan="2">For non-significant changes, IVDD/IVDR conversion should be managed by the manufacturers themselves by properly documenting change implementations in the QMS records</td></tr>
<tr><td>Transition timeline</td><td colspan="3">Sufficient transition timeline should be allowed, cautioning possibility of delays & unreadiness from EU side, esp. high risk products that are critical for local markets (e.g. blood screening products)</td></tr>
</table>

We highly respect that markets may have existing regulatory frameworks for managing product information changes. However, given the special situation arising from EU MDR/IVDR that might risk the essential supplies for our patients in the region, **APACMed recommends regulatory authorities explore and practise fully or partially, the regulatory agility elements wherever possible, including regulatory reliance, risk-calibrated methodology, flexibility, and mostly importantly having open dialogues with industry stakeholders and end users.**

5 Conclusion

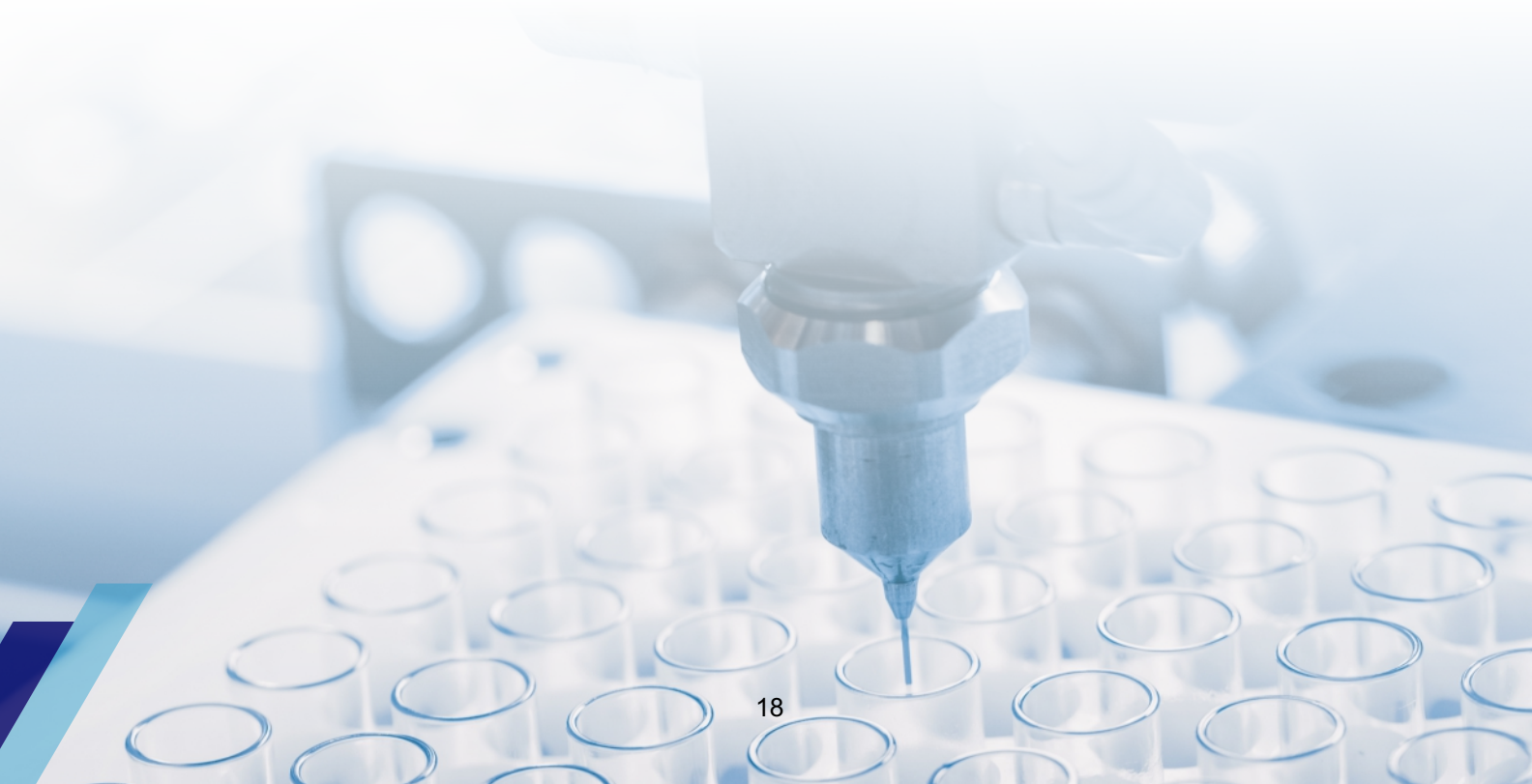
To avoid market disruption and allow a smooth transition from IVDD to IVDR, several transitional provisions are put in place by the EU Commission; but delays for critical infrastructures for IVDR implementation have been observed along the way, especially for the high-risk products and products requiring new infrastructures, such as the companion diagnostics.

We deeply appreciate and commend the strong efforts made by the government agencies in Asia Pacific in managing the COVID-19 crisis in an agile and efficient manner, establishing and upgrading the legal and regulatory frameworks for medical technologies, and ensuring business continuity and patient safety.

As such, the request is for regulatory authorities in our region to simplify the regulatory framework for changes triggered by IVDR and ensure proper transition measures, to adopt risk-based approach and practice regulatory agility, and to leverage the best practices from other countries. This will not only reduce the burden ("traffic jam") faced by the authorities to review and evaluate such a large amount of change submissions but will also avoid any medical supply disruptions during the global pandemic.

It is vital to ensure all key stakeholders in the Asia Pacific markets are well informed about the new EU regulations, as well as any transition measures granted by the EU authorities and by our national authorities. Key stakeholders include (but are not limited to) national trade associations, chambers of commerce, manufacturers, health institutions, procurement bodies, customs officers and importers.

APACMed and its member associations/companies are committed to working with regulatory authorities and other key stakeholders, to ensure a smooth transition in light of IVDR as well as new regulations in the markets, to ensure patient access to essential in-vitro diagnostic medical devices during the pandemic and beyond.



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Acknowledgment

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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.

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