



The voice of MedTech

Digital Health Regulation In India

Overview And Best Practices

A Position Paper by APACMed Digital Health
India CoE – Regulatory Working Group
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Introduction

The Asia-Pacific Medical Technology Association (APACMed) formally launched its Digital Health Committee in 2020. Given the rise in the adoption of Digital Health (DH) solutions in the region, especially as a result of the COVID-19 pandemic, the focus of the Committee is to seek greater harmonization around topics such as interoperability, cybersecurity, and regulation.

On the latter, in 2021, APACMed published two position papers - Digital Health Regulation in Asia-Pacific: Overview and Best Practices calling for the development and convergence of tailored, risk-based software regulatory frameworks across APAC countries¹ (<https://apacmed.org/digital-health-regulation-in-asia-pacific-overview-and-best-practices/>). The reports highlight that implementation of such frameworks will enable greater access to software innovation, better use of limited regulatory resources, and ultimately empower countries in the APAC region into the next generation of personalized healthcare with more informed decision-making and improved outcomes. Such an achievement will benefit regulators, software developers, and, most importantly, patients.

The original reports highlight the DH regulatory activities in leading markets in APAC like Australia, Japan, Singapore, Korea and China, identifying best practices and gaps and drawing comparisons to forward-thinking DH regulation from abroad such as in the United States.

Within this report, APACMed reviews India's regulatory approaches for software regulation alongside international best practices, reiterating the framework for fit-for-purpose regulation of DH solutions. The ultimate purpose of the paper is the same as that of the original papers: To provide regulators with recommendations that enable the implementation of a harmonized framework supporting the introduction of safe and effective DH solutions at a pace that matches the speed of innovation and benefits regulators, software developers and, most importantly, patients.

Thematic Best Practices in Regulation of SaMD: Assessment Areas of Focus

As in the original APACMed report, the following six key areas were used to assess the DH regulatory frameworks of India:

01 Software Qualification

Regulatory authorities should clearly articulate, through guidance or regulation, those software functions that do not qualify as a medical device. Approaches to software qualification should align with international best practices and ensure that software functions such as those used for administrative support of a healthcare facility, general wellness purposes, transferring and displaying information, clinical workflow, and non-device clinical decision support are not considered as medical devices.

02 Software Classification

Regulators should implement an approach to Software as a Medical Device (SaMD) classification that is SaMD-specific and takes into account the unique aspects of software products. Such an approach should be based on the International Medical Device Regulators Forum (IMDRF) SaMD framework described in its N12 guidance, "Software as a Medical Device: Possible Framework for Risk Categorization and Corresponding Considerations." SaMD classification should be based on two factors:

1. The state of the healthcare situation or condition that the SaMD is intended for; and
2. The significance of the information provided by the SaMD to the healthcare decision. Taking these two factors into account results in four categories of risk, as shown in Table 1².

State Of Healthcare Situation Or Condition	Significance Of The Information Provided By SaMD To The Healthcare Decision		
	Treat Or Diagnose	Drive Clinical Management	Inform Clinical Management
Critical	IV	III	II
Serious	III	II	I
Non-Serious	II	I	I

Table 1. IMDRF SaMD Risk Categorization Matrix²

03 Software with Multiple Functions

Software products with multiple functions may break down into a number of applications that include medical device and non-medical device functions. For such products, it is important that regulators have clearly articulated approaches by which they evaluate the intended use of each function independently, as the various functions may have medical or non-medical device functionality even when residing on the same platform. An example is Apple's ECG app that is intended to create, record, store, transfer, and display a single channel electrocardiogram (ECG) and determine the presence of atrial fibrillation or sinus rhythm. This product consists of the ECG app, the Apple watch, and the iPhone. In this example, the ECG app is a medical device function while the Apple Watch and iPhone are consumer products (non-medical device functions). Regulators should exercise oversight only over those functions with an intended purpose that fulfills the medical device definition.

04 Alternative Pathways for DH Regulation

Given the significant differences between SaMD and traditional medical devices (including In-Vitro Diagnostics, IVDs), regulators should consider alternative approaches to SaMD regulation that are tailored to their unique and iterative aspects. Such approaches may take a variety of forms and can include the use of recognition and reliance models, expedited review pathways, pre-certification type programs, conditional approvals and predetermined change control plans.

05 Pre-Submission Consultation (PSC)

Regulators should have programs in place that encourage and support the use of PSCs to enable software developers (and device manufacturers in general) to discuss specific aspects of a future regulatory submission so as to ensure that statutory requirements will be fulfilled.

06 Framework for Artificial Intelligence / Machine Learning (AI/ML)

The use of AI/ML in the development and commercialization of DH solutions is becoming more widespread. Regulators should ensure that AI/ML-based SaMD products are regulated based on their intended use and not unnecessarily burdened with regulatory requirements simply because they leverage AI/ML. Further, regulators should implement novel approaches to the regulation of AI/ML-based SaMD products, particularly with respect to change management, that foster innovation and enable safe, effective AI/ML solutions and their modifications to reach patients and healthcare professionals in an expeditious manner.

It is also important to clarify the definitions put forth by IMDRF:

Software in a Medical Device (SiMD) - Necessary for a hardware medical device to achieve its intended purpose. SiMD is also referred to as “dependent” or “embedded” Software. Regulatory and clinical evaluation of SiMD occurs concurrently with the medical device / instrument itself.

Examples include:

- Software that powers the mechanics of a medical device or processes the information that is produced by a medical device
- Embedded software in an in-vitro diagnostics analyzer necessary for the analyzer to achieve its intended purpose.

Software as a Medical Device (SaMD) - IMDRF describes SaMD as software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device³. This means the software has its own intended use and may also be referred to as “independent” or “standalone” Software.

- Software as a Medical Device ranges from smartphone apps that calculate insulin doses based on a patient’s blood glucose levels to Computer-Aided Detection (CAD) software that performs image post-processing to help detect breast cancer.
- Software that calculates the risk of prostate cancer from ultrasound images, patient and laboratory parameters.



India – Digital Health Regulation Status, Best Practices, and Gaps

DH and its regulation are evolving quickly, with many countries in APAC establishing regulatory frameworks specific for DH solutions. However, these frameworks should converge with global approaches and include innovative pathways that enable timely delivery of safe and effective DH solutions to the market.

The table below provides a summary of the current regulatory status of India in relation to best practices for the regulation of DH solutions. The best practices have been introduced in the inaugural APACMed reports and are based on the six assessment areas described in the previous section¹. Following the table, we provide a detailed analysis of the DH regulatory approaches in India and identify any best practices and gaps.

	Qualification	Risk Classification	Software with Multiple Functions	Alternative Pathways for DH	Pre-Submission Consultation	Framework for AI/ML
Best Practices	Software must have an intended purpose that fulfils the definition of a medical device in order to qualify as a medical device.	IMDRF’s N12 guidance describes that the two key factors that should be taken into account when assessing the risk categorization of a SaMD product are: 1. State of the healthcare situation or condition that the SaMD is intended for. 2. The significance of the information that is provided by the SaMD to the healthcare decision.	For software products with multiple functions, regulatory authorities exercise oversight only over those functions with an intended purpose that fulfils the medical device definition.	Approaches to regulatory review that are tailored to the unique needs of DH solutions.	Opportunity to en-gage with regulatory authorities prior to premarket sub-mission review.	Risk-based guidance and/or framework suited to the unique regulatory challenges posed by AI/ML technologies.
India (CDSCO)						

Table 2. Comparing the APACMed DH regulation best practices for SaMD with the current state in India

- The best practices are not currently adopted
- Some guideline is currently available, however, further improvements are recommended
- Current regulatory framework encompasses the recommended best practices

Best Practice Theme 01 Qualification

Software qualification is the process by which regulators determine whether or not a software product meets the “medical device” definition and is thus regulated by health authorities. Software must have an intended use that fulfills the definition of a medical device in order to be considered as a medical device.

India

While the CDSCO does have a robust classification catalog for medical devices & IVDs, it does not have guidance that is specifically dedicated to determining whether a software product meets the “medical device” definition and is thus required to meet the existing associated requirements.

With implementation of mandatory phase from 1st Oct 2021 of Medical Device Amendment Rules-2020, Industry stakeholders could benefit from a cohesive, comprehensive guidance related to software qualification. Therefore, CDSCO is encouraged to publish guidance that clearly articulates its approach to software qualification and provide representative list of features and functionalities that either meet or don't meet the definition of SaMD which aligns with international best practices in which software must have an intended purpose that fulfills the definition of a medical device in order to qualify as a medical device.

Best Practice Theme 02 Risk Classification

Risk classification is a very important concept for medical devices and IVDs, as a device's risk class determines its premarket and post market regulatory requirements. For SaMD products, regulators should leverage IMDRF's N12 guidance² when making classification decisions and consider two key factors:

1. the state of the healthcare situation or condition that the SaMD is intended for; and
2. the significance of the information that is provided by the SaMD to the healthcare decision-making.

India

CDSCO employs the Global Harmonization Task Force (GHTF) system in its approach to medical device and in vitro diagnostics classification⁴. The approach is a four-class system based on potential risk to human health.

Class	Risk Level
A	Low Risk
B	Low Moderate Risk
C	Moderate High Risk
D	High Risk

Table 3. CDSCO Approach to Medical Device Classification and IVD Classification

In July 2021, CDSCO published a new classification list for medical devices and IVD products in order to clarify regulatory pathways and requirements⁵. Among the 24 medical device classifications, CDSCO has included software as a category for the first time. The category includes over 20 software types, such as data analysis software; secondary displays for glucose monitoring, insulin pump and other devices; and orthodontic and dental software. CDSCO has proposed three broad IVD classification categories: IVD analyzers (53 individual IVD types), IVD instruments (18 device types), and IVD software (nine device types).

While it is encouraging that CDSCO has focused efforts on the classification of SaMD products, the approaches employed do not appear to be based on IMDRF's SaMD Risk Categorization Framework². In particular, it appears that the CDSCO classification decision for most SaMD product groupings is only based on the “state of the healthcare situation or condition the SaMD is intended for,” while it should be based on both “state of the healthcare situation or condition the SaMD is intended for” and the “significance of the information provided by the SaMD to the healthcare decision” (according to IMDRF). For example, any SaMD product that has an intended use related to cancer is Class C regardless of whether the software is “informing,” “driving,” or “treating or diagnosing” the healthcare situation or condition. Thus, CDSCO's approach to SaMD classification is missing an important factor that is present in the IMDRF SaMD Risk Categorization Framework (“the significance of the information provided by the SaMD to the healthcare decision”). This factor is important to include in classification decisions, as a SaMD product that provides information to a healthcare provider intended to inform his/her treatment decision for a cancer patient has a much different risk than a SaMD product used to automatically diagnose cancer in a patient.

As such, CDSCO should consider an approach to SaMD classification that is based on the IMDRF SaMD Risk Categorization Framework². Specifically, such an approach should take into account the “state of the healthcare situation or condition the SaMD is intended for” and the “significance of the information provided by the SaMD to the healthcare decision” when making a classification decision. As CDSCO already uses a four-tiered medical device classification scheme, 1:1 mapping of the four risk categorizations described within the IMDRF SaMD Framework should be relatively straightforward.

Best Practice Theme 03 Software with Multiple Functions

Software products with multiple functions may break down into a significant number of applications that include medical device and non-medical device functions. In such instances, it is important that regulators appropriately qualify and evaluate the intended use of each module or function independently, as the various modules may have medical or non-medical device functionality, even while residing on the same platform.

Internationally, it has been recognized that, for software products with multiple functions, regulatory authorities should only have oversight over those functions with a medical device intended use. For example, in the EU, Medical Device Coordination Group (MDCG) 2019-11 guidance ("Guidance on the Qualification and Classification of Software in Regulation (EU) 2017/745 – MDR and Regulation (EU) 2017/746 – IVDR")⁶ states that, in a software product with multiple functions, medical device modules are subject to medical device regulatory requirements while non-medical device modules are not. In the US, a similar concept is included in the 21st Century Cures Act legislation⁷, stating that the Agency shall not regulate those functions which do not meet the definition of a medical device when software has multiple functions. The US FDA provides further thinking in its guidance on "Multiple Function Device Products," which is broader than just software⁸. In both the EU and US approaches, it is important that software developers clearly define the boundaries between medical device and non-medical device functions and assess the impact that non-medical device functions can have on medical device functions.

To APACMed's knowledge, CDSCO is yet to describe regulatory approaches to software products with multiple functions. Regulators are encouraged to leverage international best practices and publish guidance on this topic to ensure that, for software products with multiple functions, regulatory oversight is exercised only over those functions with an intended purpose that fulfils the medical device definition.

Best Practice Theme 04 Alternative Pathways for DH

Given the significant differences between SaMD versus traditional medical devices and IVDs, some health authorities have developed alternative SaMD regulatory approaches tailored to their unique and iterative aspects. Such approaches take a variety of forms, such as the use of:

- **Recognition and reliance models**
 - **Recognition:** The acceptance of the regulatory decision of another regulator or trusted institution. Recognition should be based on evidence of conformity that the regulatory requirements of the reference regulatory authority are sufficient to meet the regulatory requirements of the relying authority.

- **Reliance:** The act whereby the regulatory authority in one jurisdiction may take into account and give significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative agency in reaching its own decision. The relying authority remains independent, responsible and accountable regarding the decisions taken, even when it relies on the decisions and information of others.
- **Expedited Regulatory Pathways:** Registration pathways that speed the review and approval of a product. The review and approval can be accelerated by the reliance on or recognition of prior reviews by stringent regulatory authorities
- **Abridged Regulatory Review Pathways:** Relies on assessments of data that have been already reviewed and approved by reference regulatory agencies / stringent regulatory authorities but includes an abridged independent review of a certain part of the dossier relevant to use under local conditions.

- **Implementation of expedited review pathways**

Regulatory pathways that are designed to provide a faster pre-market decision than traditional regulatory pathways.

- **Development of pre-certification type programs**

Certain organizations may create regulator trust by demonstrating quality in their software development and maintenance practices, leading to a streamlined pre-market review process with increased post-market commitments.

- **Predetermined change control plans**

Incorporation of predetermined change control plans during premarket review to support the rapid implementation of software modifications post-deployment.

India

To APACMed's knowledge, CDSCO is yet to describe alternative regulatory approaches for software described above.

CDSCO should particularly consider reliance mechanisms, since furnishing approval status of the product in GHTF countries is already a part of the pre-market review process in India.

- A product that is approved by at least one of CDSCO's reference regulatory agencies (US FDA, Health Canada, EU Notified Bodies, MHLW Japan and TGA Australia) should be provided an expedited review route or an abridged evaluation route.
- Predicate device and clinical study requirements should also be waived if the product is approved by CDSCO's reference regulatory agencies.

An example of a comparable regulatory authority that has implemented recognition and reliance approaches is HSA Singapore. Specifically, HSA has implemented SaMD - Immediate Class B Registration (IBR) and Immediate Class C Registration (ICR) Evaluation Routes for products that fulfil the following criteria:

- Products can be eligible if approved by at least 1 of HSA's independent reference regulatory agencies.
- There can be no safety issues globally associated with the use of the product in the last 3 years or since market introduction of the product globally.
- There can be no rejection/withdrawal of the medical device from any of the independent reference regulatory agencies due to quality, performance or safety issues.

CDSCO has demonstrated regulatory agility via global cooperation during the COVID-19 pandemic. This has enabled timely access to several vaccines for COVID-19 while maintaining rigorous standards for assessing safety and efficacy. Such an approach should be applied in the future to the regulation of digital health solutions by increasing reliance on decisions from international regulators to support CDSCO's own regulatory decisions. This will contribute to the development of mutual reliance frameworks that will reduce regulatory burden on manufacturers of SaMD solutions.

CDSCO is also encouraged to consider more innovative approaches to change management for DH products. Specifically, CDSCO should implement predetermined change control plans, similar to the approaches that have been developed by US FDA and Japan's PMDA/MHLW¹. In such a concept, a software developer would gain alignment with CDSCO during an initial premarket submission on the scope of future software changes and how the risks associated with those changes would be controlled using a predetermined change control plan. Once the initial product is launched and the predetermined change control plan approved, the software developer could then make changes according to the predetermined change control plan without lengthy premarket reviews required. Such an approach greatly facilitates the iterative nature of DH products and ensures that patients and healthcare professionals receive innovative and timely updates in a safe and effective manner.

Implementation of novel regulatory approaches would facilitate the rapid introduction of safe and effective DH solutions in India for the patient population and create a regulatory-enabling environment that fosters the development of leading-edge technologies.

Best Practice Theme 05 Pre-Submission Consultation (PSC)

PSC is an opportunity to discuss specific aspects of a future regulatory submission with regulatory bodies to ensure that statutory requirements will be fulfilled (for example, consultation for a clinical trial design supporting a novel claim). Under the PSC scheme, regulatory agencies allow manufacturers or sponsors of DH solutions to seek innovation support during a pre-submission phase in order to expedite patient access to the solution in a safe and effective manner. Manufacturers or sponsors can consult the regulatory authority on requirements during the DH solution development phase, and seek feedback on dossier completeness before submission. For novel DH solutions, which do not fit naturally into current regulatory systems, PSC is crucial to expedite registration and facilitate early patient access.

CDSCO is yet to roll out a formal PSC mechanism, and we recommend that they establish such a program for all medical devices, including DH solutions.

Best Practice Theme 06 Frameworks for AI/ML

As AI/ML-enabled DH solutions become more prevalent, it is important that regulators implement novel regulatory approaches, particularly with respect to change management, that foster innovation and enable safe and effective AI/ML solutions and their modifications to reach patients and healthcare professionals in an expeditious manner.

India

To APACMed's knowledge, CDSCO is yet to describe regulatory approaches for software / SaMD systems based on AI/ML.

Overview of Digital Health Regulation in Asia-Pacific: IMDRF Countries

Please refer to our original position papers to read in detail about the regulatory controls in the 5 markets. A snapshot of their regulatory controls is in the table below.

	Qualification	Risk Classification	Software with Multiple Functions	Alternative Pathways for DH	Pre-Submission Consultation	Framework for AI/ML
Best Practices	Software must have an intended purpose that fulfils the definition of a medical device in order to qualify as a medical device.	IMDRF's N12 guidance describes that the two key factors that should be taken into account when assessing the risk categorization of a SaMD product are: 1. State of the healthcare situation or condition that the SaMD is intended for. 2. The significance of the information that is provided by the SaMD to the healthcare decision.	For software products with multiple functions, regulatory authorities exercise oversight only over those functions with an intended purpose that fulfils the medical device definition.	Approaches to regulatory review that are tailored to the unique needs of DH products.	Opportunity to engage with regulatory authorities prior to premarket submission review.	Guidance and/or framework describing the regulation of AI/ML technologies.
Australia (TGA)						
Japan (PMDA)						
Singapore (HSA)						
Korea (MFDS)						
China (NMPA)						

- The best practices are not currently adopted
- Some guideline is currently available, however, further improvements are recommended
- Current regulatory framework encompasses the recommended best practices

Overview of Digital Health Regulations in the USA

Over the last several years, the US FDA, Health Canada and EU have been very active in shaping the DH regulatory landscape. In this section, we highlight best practices and gaps associated with these regulatory authorities.

Regulatory Agency	Best Practice & Gaps	Qualification	Risk Classification	Software with Multiple Functions	Alternative Pathways for DH	Pre-submission Consultation	Framework for AI/ML
US FDA	Best Practice	Section 3060 of the 21st Century Cures Act removes five software functions from the "device" definition, including low-risk clinical decision support software. ⁷	The US FDA Software Precertification Pilot Program proposes an approach to risk classification that relies on IMDRF's N12 SaMD Risk Categorization Framework. ⁹	Per Section 3060 of the 21st Century Cures Act, for a SW device with multiple functions, the US FDA only has regulatory oversight over those functions with a medical device intended use. ⁷	The US FDA is exploring alternative approaches to software regulation, such as the implementation of a Software Precertification Program and unique approaches to the regulation of AI/ML-based SaMD products. ⁹	The US FDA has a Pre-Submission Program whereby software developers and manufacturers can seek guidance prior to regulatory submissions.	In its 2019 AI Discussion Paper, the US FDA has outlined innovative regulatory approaches to the regulation of AI/ML-based products. ¹⁰
	Gaps	The US FDA currently defines "non-device clinical decision support software" very narrowly, and there is currently no clear guidance on this topic.	Currently, the US FDA has not created a classification system unique to SaMD products and instead relies on its existing medical device classification system. This approach does not take into account the "significance of information provided by SaMD to the healthcare decision" and leads to the up classification of lower risk software products.	N/A	The Software Precertification Program is several years away from implementation . The Agency should work to implement unique approaches to DH regulation, such as streamlined premarket reviews and widespread implementation of predetermined change controls plans, in the short term to enable DH innovation.	N/A	As with Alternative Pathways, the US FDA should consider more widespread implementation in the short term of the concepts it has described within its Discussion Paper on AI/ML. ¹⁰

Overview of Digital Health Regulations in Canada

Regulatory Agency	Best Practice & Gaps	Qualification	Risk Classification	Software with Multiple Functions	Alternative Pathways for DH	Pre-submission Consultation	Framework for AI/ML
Health Canada	Best Practice	Health Canada guidance describes those software products that are regulated as SaMD as well as information on classification of SaMD. ¹⁰	Health Canada has attempted to map the IMDRF N12 SaMD Risk Categorization Framework to its existing medical device classification system. ¹⁰	N/A	Health Canada is actively engaged in work sharing, information sharing and regulatory convergence activities through international activities like MDSAP. Implement recognition and reliance models, making use of regulatory assessments from comparable overseas regulators when conducting DH regulatory decision-making	Health Canada has pre-submission consultation plan where manufacturer can discuss and seek guidance on regulatory pathways and submission strategy	Health Canada is exploring regulatory approaches to adaptive machine learning enabled devices through its Advanced Therapeutic Pathway
	Gaps	Similar to US FDA, Health Canada defines "non-device clinical decision support software" narrowly, and the non-device clinical decision support software "signal" and "pattern" criterion are difficult to understand and limiting.	Health Canada's mapping approach is not well aligned with IMDRF principles and not very risk-based. For example, SaMD that informs a non-serious condition can have the same risk as software that treats or diagnoses a serious condition. Health Canada has attempted to retrospectively fit its existing classification scheme to IMDRF for SaMD classification rather than use IMDRF as a foundation for SaMD classification.	To APACMed's knowledge, Health Canada has published no guidance related to software products with multiple functions.	Health Canada should work to evolve novel regulatory approaches for digital health products that foster their iterative and innovative aspects, particularly with respect to change management.	N/A	To APACMed's knowledge, Health Canada has not published any guidance related to classification or regulatory approaches to AI-based DH solutions

Overview of Digital Health Regulations in the EU

Regulatory Agency	Best Practice & Gaps	Qualification	Risk Classification	Software with Multiple Functions	Alternative Pathways for DH	Pre-submission Consultation	Framework for AI/ML
EU	Best Practice	The EU has issued a guidance document with flowcharts and examples to support the determination of when software is and is not medical device software (MDSW) ⁶	The EU classification criteria (classification rules) are set out in Annex VIII of the Medical Devices Regulation (EU) 2017/745 (MDR) and In vitro Diagnostic Medical Devices Regulation (EU) 2017/746 (IVDR). ¹²	The MDCG 2019-11 Guidance describes an approach to the regulation of software products with multiple functions whereby only those functions with a medical device intended purpose are subject to medical device regulatory requirements. ⁶	N/A	N/A	N/A
	Gaps	The published guidance does not consider software qualification in relation to certain types of software, such as non-device clinical decision support software. Determining when a SaMD is a medical device or an in vitro diagnostic device is unclear and challenging within the existing EU regulatory structure.	The MDR and IVDR approaches to SaMD classification do not leverage IMDRF principles and are not risk-based. MDR and IVDR implementing and classification rules (including MDR Classification Rule 11) essentially require all SaMD to undergo conformity assessment by a notified body, regardless of risk. This does not align well with the risk-based approach described by IMDRF, particularly with respect to when independent review is "less important" and "more important."	N/A	There are currently no alternative regulatory pathways in the EU that enable speed of innovation while supporting safety and effectiveness for DH solutions.	With the implementation of the new Regulations, Notified Bodies are less willing to have informal consultations with device manufacturers, leading to greater regulatory uncertainty.	The European Commission published in spring, 2021 a proposed AI Act that, if implemented, will establish horizontal regulatory requirements for all products that leverage AI, including medical devices. The majority of the requirements in this proposed AI Act duplicate (and in some instances conflict) with existing device regulatory requirements. This will create additional challenges for AI-based medical device developers working to navigate an already complex regulatory landscape and will stifle innovation in the EU.

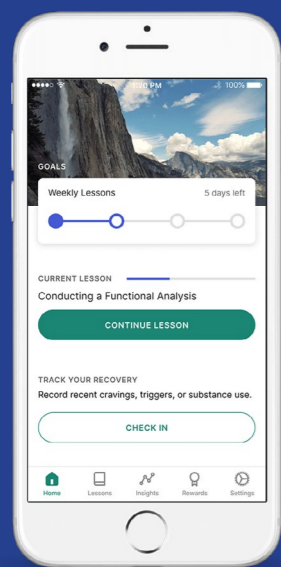
Use Cases – Digital Therapeutics (DTx)

In this section we focus on digital therapeutic (DTx) solutions which are a subset of SaMD. The definition of DTx by Digital Therapeutics Alliance - Digital therapeutics (DTx) deliver evidence-based therapeutic interventions that are driven by high quality software programs to prevent, manage, or treat a medical disorder or disease¹³. They are reviewed and cleared or certified by regulatory bodies as required to support product claims regarding risk, efficacy, and intended use. In this section, we will identify the key success factors for approval of a DTx.

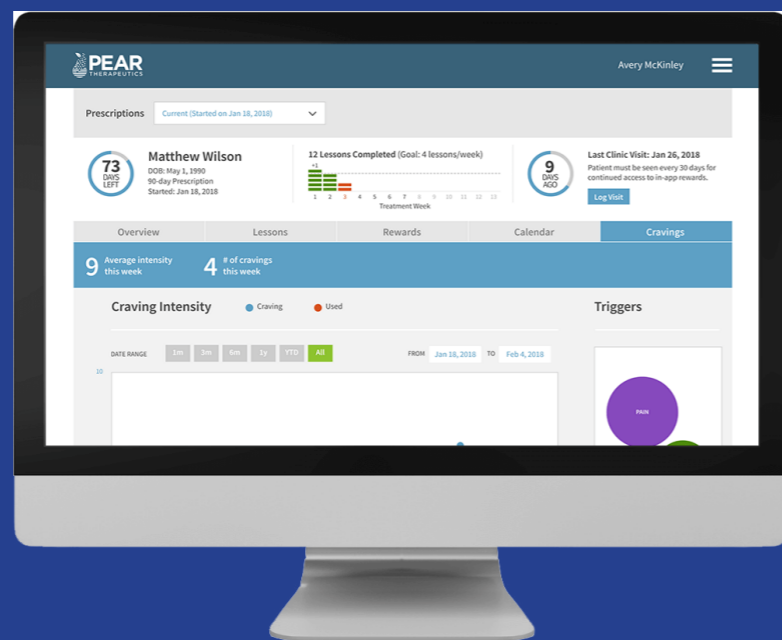
reSET[®], Pear Therapeutics

Pear Therapeutics discovers, develops, and delivers clinically-validated software-based therapeutics to provide better outcomes for patients, smarter engagement and tracking tools for clinicians, and cost-effective solutions for payers. Pear has a pipeline of products and product candidates across therapeutic areas, including severe psychiatric and neurologic conditions.

reSET[®] comprises a patient application and a clinician dashboard intended to deliver cognitive behavior therapy (CBT) to patients with SUD. It consists of several therapy lessons (modules) and, after the lessons, patients undergo fluency learning. The clinician can use the dashboard to view the therapy lessons that the patient has completed, as well as patient-reported substance use, cravings, and triggers.



Patient-Facing Application



Clinician-Facing Application

reSET[®] is intended to provide cognitive behavioral therapy, as an adjunct to a contingency management system, for patients 18 years of age and older who are currently enrolled in outpatient treatment under the supervision of a clinician. reSET[®] is indicated for a 12 week (90 days) prescription-only treatment for patients with SUD, who are not currently on opioid replacement therapy, who do not abuse alcohol solely, or who do not abuse opioids as their primary substance of abuse. It is intended to:

- Increase abstinence from a patient's substances of abuse during treatment, and
- Increase retention in the outpatient treatment program.¹⁴

Pear went through the regulatory approval process for a digital therapeutic (DTx) solution and was the first company to receive US FDA clearance (DEN160018) for a prescription digital therapeutic (PDT)– reSET[®]¹⁵. In June 2020, the Health Sciences Authority (HSA) in Singapore approved reSET[®] (DE0504590) as a prescription only treatment to adults with substance use disorder (SUD)¹⁶. It was the first time Singapore had authorized a PDT, and it is the first country after the USA to approve Pear Therapeutics' solution.

The Digital Therapeutics Alliance concurs any organization claiming producing digital therapeutics must adhere to these foundational principles to ensure safety and effectiveness:

- Incorporate design, manufacture, and quality best practices
- Apply product deployment, management, and maintenance best practices
- Robust clinical data must be generated to demonstrate the safety and effectiveness of the DTx and to support the intended use claims.
- Make claims appropriate to clinical evaluation and regulatory status
- Be reviewed and cleared or certified by regulatory bodies as required to support product claims of risk, efficacy, and intended use
- Ensure appropriate product labelling for the end user capturing intended use claims, supporting appropriate clinical use, warnings etc

As CDSCO moves forward in regulating SaMD and DTx solutions there are some key considerations in order to become a leading regulatory agency in this space:

- Contribute to global convergence and harmonization by ensuring consistency with the IMDRF N12 risk categorization framework.
- Commitment to work sharing, recognition and reliance - There is increasing international focus on work-sharing, reliance, and recognition as methods to both address capacity gaps within regulatory authorities and to strengthen regulatory expertise. CDSCO can consider these mechanisms when regulating SaMD and DTx solutions.
- Consider leveraging real world data for regulatory decision making - SaMD and DTx solutions have a huge potential for generating post-market evidence as real world data through product use. This data can be clinical data, safety data, and complaint data.

Best Practices Framework

APACMed is encouraged by the efforts undertaken by APAC regulators to advance DH regulatory frameworks across the region. Based on a comprehensive assessment of the considerations described within this paper, we outline below an actionable path forward that CDSCO should apply when implementing fit-for-purpose, risk-based DH regulatory frameworks. Implementation of these actions will enable safe, effective, and timely delivery of innovative DH solutions that will benefit patients and healthcare professionals.

01

Fundamental Building Blocks for a Software-Focused Regulatory Framework

- Implement a clearly described approach to **software qualification (determining when software is a SaMD)** that aligns with international best practices and whereby the regulator only has oversight over those software functions with a medical device intended use.
- **Establish a classification method specific to SaMD that is based on IMDRF's N12 SaMD Risk Categorization Framework** and specifically takes into account the "state of healthcare situation" and "significance of information provided by the SaMD" in the classification decision.
- For software products with multiple functions, **implement policies by which regulators only exercise regulatory oversight over those functions with a medical device intended use.**

02

Pathways to Support Rapid Regulatory Review of SaMD Products and Their Modifications

- Implement **recognition and reliance models**, making use of regulatory assessments from comparable overseas regulators when conducting DH regulatory decision-making.
- Introduce **streamlined regulatory / abridged evaluation pathways for the introduction of SaMD products and their modifications**, such as through the development of expedited review pathways that can be leveraged by all SaMD developers and the endorsement of predetermined change control plans.
- Implement **risk-based regulatory approaches that enable the innovative and iterative aspects of AI-based SaMD solutions.**

03

Collaboration and Convergence Opportunities in the APAC Region

- Support DH regulatory global convergence through the **recognition and adoption of internationally recognized guidance documents and standards**, such as those developed by IMDRF and ISO.
- Foster greater collaboration with software developers through **pre-submission consultations.**
- **Partner with industry through industry associations, private-public consortia, and other fora** to share best practices and evolve the DH regulatory landscape.



About The Asia Pacific Medical Technology Association (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 several 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



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