Regulatory Framework for Digital Therapeutics (DTx) and Software as a Medical Device (SaMD): A Global Perspective

Asma Shaik[1], Syam Kumar Kanigiri[2], Beena Devi Maddi[3], Venkata Nagabhushanam Maddi[4]
Department of Pharmaceutical Regulatory Affairs, Hindu College of Pharmacy, Amaravati Road, Guntur-522002, A.P.

***Abstract*—The rise of digital health solutions has paved the way for Digital Therapeutics (DTx) and Software as a Medical Device (SaMD) to become essential parts of today's healthcare landscape. These innovative technologies deliver evidence-based therapeutic interventions, enhance patient outcomes, and provide fresh approaches to managing chronic illnesses. Yet, navigating the regulatory environment for DTx and SaMD can be quite tricky, as various regions have adopted different frameworks. This paper takes a closer look at the regulatory structures surrounding DTx and SaMD in major markets like the USFDA, EMA, PMDA, and CDSCO. We'll discuss key regulatory requirements, classification criteria, clinical evaluation methods, and strategies for post-market surveillance. The paper emphasizes the need for harmonization, improved cybersecurity measures, and more streamlined approval processes to ensure global compliance and safeguard patient safety. Additionally, this review examines regulatory guidelines and showcases six case studies of DTx/SaMD products that have successfully gained approval, aiming to extract best practices for both developers and regulators.**

***Index Terms*—Digital Therapeutics (DTx), EMA, Regulatory Framework, Software as a Medical Device (SaMD), USFDA**

I. INTRODUCTION

The incorporation of digital technologies into healthcare has transformed how medical care is delivered, especially through Digital Therapeutics (DTx) and Software as a Medical Device (SaMD). DTx refers to software solutions grounded in evidence that are designed to prevent, manage, or treat medical conditions, while SaMD encompasses standalone software intended for medical use, independent of hardware devices. Both DTx and SaMD are becoming increasingly important for managing chronic diseases, addressing mental health needs, and enabling remote patient monitoring. As these advancements continue to grow, the lack of a cohesive regulatory framework poses challenges for developers aiming to enter global markets. Grasping the regulatory requirements in key regions is vital for ensuring product safety, effectiveness, and compliance.

II.OBJECTIVES

• To clearly define and distinguish between Digital Therapeutics (DTx) and Software as a Medical Device (SaMD), highlighting their significance in today's healthcare landscape.
• To delve into the global regulatory environment surrounding DTx and SaMD, with a focus on major regions like the United States (FDA), European Union (EMA/MDR), Japan (PMDA), and India (CDSCO).
• To investigate the classification criteria and approval processes for DTx and SaMD as outlined by various regulatory bodies.
• To look into the hurdles that developers and regulators encounter when evaluating safety, efficacy, cybersecurity, data privacy, and real-world evidence for DTx and SaMD.
• To evaluate harmonization initiatives, such as those led by the International Medical Device Regulators Forum (IMDRF), and their influence on global standardization. Additionally, to showcase best practices and case studies from successful regulatory approvals of DTx and SaMD products.
• To consider the future of regulatory frameworks as they adapt to emerging technologies like AI/ML-

based SaMD, adaptive algorithms, and personalized digital health solutions.

III.METHODOLOGY

This narrative review was carried out by examining published regulatory guidelines, peer-reviewed articles, and public databases from agencies like the FDA, EMA, PMDA, and CDSCO. The search terms included "Digital Therapeutics regulation," "SaMD approval," and "DTx case studies." Resources were reviewed from January to March 2025, and only English-language sources were included.

IV. DEFINITION

a. Digital Therapeutics (DTx):

Digital Therapeutics are evidence-based therapeutic interventions driven by high-quality software programs to prevent, manage, or treat medical disorders or diseases. DTx solutions are used independently or alongside medications, devices, or other therapies to optimize patient outcomes [1].

Example: Mobile apps for managing type 2 diabetes, cognitive behavioural therapy for depression, or digital platforms for substance use disorder treatment.

b. Software as a Medical Device (SaMD):

According to the International Medical Device Regulators Forum (IMDRF), SaMD is defined as software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device [2].

Example: An AI-based app that analyses ECG data to detect arrhythmias, or a mobile app that calculates insulin dosage based on blood glucose readings.

Table: 1. Key Differences Between DTx and SaMD:

Feature	Digital Therapeutics (DTx)	Software as a Medical Device (SaMD)
Purpose	Treat or manage medical conditions through software therapy	Diagnose, monitor, or treat using software as a tool
Regulatory Category	Subset of SaMD (if used for medical purposes)	Broader category that includes all types of medical software
Evidence Requirement	Must be clinically validated with trials (like drugs)	Also needs evidence, but can vary depending on risk classification
Examples	CBT app for insomnia, digital asthma therapy	AI diagnostics, insulin dosing apps
Therapeutic Functionality	Provides therapeutic effect directly	Supports diagnosis or therapy decisions

V.ROLES IN MODERN HEALTHCARE

• Personalized and Scalable Care: DTx and SaMD facilitate tailored treatment plans and remote care delivery, particularly beneficial for managing chronic diseases.

• Bridging Gaps in Healthcare Access: These tools provide therapeutic support to underserved communities and rural areas through mobile or web-based platforms [3].

• Data-Driven Insights: They gather and analyze real-time data, enabling clinicians to monitor adherence, effectiveness, and side effects more efficiently.

•Cost-Effectiveness:

Reduces reliance on in-person consultations and long-term hospitalization by offering continuous digital interventions.

•Integration with Traditional Therapy: Often used in combination with pharmacotherapy to improve treatment adherence and outcomes (e.g., digital CBT alongside antidepressants) [4].

VI. CLASSIFICATION CRITERIA AND REGULATORY APPROVAL PATHWAYS FOR DTX AND SAMD ACROSS KEY GLOBAL AUTHORITIES

Digital Therapeutics (DTx) and Software as a Medical Device (SaMD) represent a transformative shift in healthcare delivery by offering software-driven clinical interventions. However, their safe and effective integration into healthcare systems depends

heavily on well-defined regulatory frameworks. Regulatory authorities globally have developed classification systems and approval pathways based on the risk profile, intended use, and clinical functionality of these software solutions.

A. Classification Criteria Overview

Regulatory classification of DTx and SaMD is typically risk-based, focusing on the potential impact of the software on patient health and the significance of its role in clinical decision-making. Key determinants include:

- Intended medical purpose (diagnosis, treatment, prevention, etc.)
- Degree of human oversight required
- Condition severity (non-serious, serious, or critical)
- Level of autonomy or AI integration

Most jurisdictions classify software as Class I (low risk) to Class III (high risk), with increasing regulatory controls at higher classes.

B. Regulatory Framework in Key Regions

1.United States – Food and Drug Administration (FDA)[5]

- Regulated under the *Federal Food, Drug, and Cosmetic Act (FD&C Act).*
- Oversight by the *Centre for Devices and Radiological Health (CDRH).*
- Classification based on *risk and functionality:*

Class I: Low-risk (e.g., fitness/wellness trackers)
Class II: Moderate-risk requiring special controls (e.g., insulin dose calculators)
Class III: High-risk devices needing *Premarket Approval (PMA)* (e.g., AI diagnostic tools)
Approval Pathways:
510(k): Substantial equivalence to a legally marketed device.
De Novo: For novel, moderate-risk devices without a predicate.
2. PMA: For high-risk, Class III devices.
Pre-Certification Program (Pre-Cert): A now-retired pilot initiative that aimed to streamline regulation by focusing on the developer's excellence rather than individual product reviews. It introduced a lifecycle-based approach particularly relevant for DTx developers.

3.European Union – European Medicines Agency (EMA) and MDR [6]

SaMD and DTx are governed by the Medical Device Regulation (MDR) – EU 2017/745.
Classification follows a *risk-tiered structure:*
Class I: Low-risk (e.g., symptom checker apps)
Class IIa/IIb: Moderate-risk (e.g., clinical decision support tools)
Class III: High-risk (e.g., ICU monitoring algorithms)
Requires *CE Marking* after successful *conformity assessment* by a Notified Body.
Strong emphasis on *clinical evaluation, post-market surveillance,* and cybersecurity for software.

4.Japan – Pharmaceuticals and Medical Devices Agency (PMDA) [7]

Regulated under the *Pharmaceuticals and Medical Devices Act (PMD Act).*
SaMD classification based on:

- Risk level
- Medical purpose
- Required clinical evidence

PMDA approval requires *robust clinical data and review by the Ministry of Health, Labour and Welfare (MHLW)* for moderate- to high-risk products.
Japan has approved multiple DTx solutions, including those for nicotine dependence and mental health.

5.India – Central Drugs Standard Control Organization (CDSCO) [8]

Governed under the *Medical Devices Rules, 2017*.
SaMD that fulfills a *medical purpose* is classified as a medical device and requires:
Registration and licensing
Compliance with risk-based categorization (Class A to D)
The *Ministry of Health and Family Welfare (MoHFW),* in collaboration with CDSCO, is formulating emerging guidelines for DTx, focusing on digital health, telemedicine, and AI-integrated platforms.
Clinical validation, cybersecurity, and patient privacy are areas of ongoing regulatory refinement.

Table 2: Comparative Table: Regulatory Classification Framework

Aspect	USFDA	EMA	PMDA	CDSCO
Classification	Class I-III	Class I-III	Class I-III	Class A-D
Approval Pathways	510(k), De Novo, PMA	CE Marking	PMD Act	Medical Device Rules
Clinical Evidence Requirement	High	Moderate to High	High	Emerging Guidelines

VII. KEY REGULATORY CONSIDERATIONS

- Classification Criteria: DTx and SaMD are categorized based on intended use, risk level, and the impact they have on patients.
- Clinical Evaluation: Regulatory agencies stress the importance of clinical trial data to to prove the product safety and effectiveness.
- Cybersecurity Requirements: It's crucial to maintain data integrity, protect patient privacy, and guard against cyber threats.
- Post-Market Surveillance: Developers need to set up strong monitoring systems for reporting adverse events and managing software updates.
- Interoperability and Data Integrity: Regulatory bodies promote the use of interoperable platforms to ensure secure data sharing.

VIII. CHALLENGES IN HARMONIZATION [9]

- Diverse Regulatory Definitions: Varying definitions of SaMD and DTx create ambiguity.
- Inconsistent Approval Timelines: Different review timelines delay global market entry.
- Data Security Risks: Protecting sensitive patient data during digital interventions remains a major concern.

IX. PROPOSED HARMONIZATION STRATEGIES

- Adoption of ICH Guidelines: Aligning DTx and SaMD regulations with international standards to streamline global approvals [10].
- Common Risk Classification Framework: Implementing a globally accepted risk-based model for classification.
- Centralized Digital Repository: Creating a global database for approved DTx and SaMD products for better accessibility and information sharing.
- Emphasis on Real-World Evidence (RWE): Encouraging regulators to integrate RWE in decision-making to accelerate approvals.

X.BEST PRACTICES AND CASE STUDIES FROM SUCCESSFUL REGULATORY APPROVALS OF DTX AND SAMD PRODUCTS

As Digital Therapeutics (DTx) and Software as a Medical Device (SaMD) continue to transform modern healthcare, regulatory success stories highlight valuable *best practices* in development, clinical validation, and engagement with regulatory authorities. These case studies demonstrate how rigorous design, robust evidence generation, and proactive compliance can lead to successful market entry.

1. Best Practices in Regulatory Approval of DTx and SaMD

a. Early and Continuous Regulatory Engagement

Initiating pre-submission meetings with regulatory bodies (e.g., FDA Q-Sub program) allows developers to align early on with regulatory expectations.

Continuous feedback loops during development reduce delays during formal submission.

b. Risk-Based Product Development

Aligning with global frameworks such as the IMDRF SaMD Risk Categorization Framework ensures appropriate classification and regulatory planning.

Products are designed with built-in risk mitigation strategies including user validation, cybersecurity protocols, and fail-safe mechanisms.

c. Robust Clinical Evidence Generation

Conducting *randomized controlled trials (RCTs*) or real-world evidence (RWE) studies to demonstrate safety, efficacy, and patient outcomes.

DTx products often require the same clinical rigor as pharmaceutical products, particularly when used as standalone treatments.

d. Regulatory-Grade Software Development Lifecycle (SDLC) [11]

Implementing *Good Software Engineering Practices (GSEP),* including usability testing, validation, version control, and documentation.

Adhering to IEC 62304 (Medical device software lifecycle processes) enhances credibility during regulatory review [12].

e. Strong Post-Market Surveillance Plans

Developing mechanisms for real-time monitoring, adverse event reporting, and patient feedback integration.

Continuous learning algorithms must have controlled update pathways and FDA's adaptive AI/ML change protocols.

2. Case Studies of Successful Approvals

A. reSET® and reSET-O® – Pear Therapeutics (USA)[13]

Type: Prescription Digital Therapeutics (PDT)

Use: Treatment of substance use disorder and opioid use disorder

Approval: FDA 510(k) clearance (Class II device)

Best Practices:

Clinical trials demonstrated significant improvements in abstinence and treatment retention.

Developed in partnership with behavioural health providers.

Includes real-time data tracking and clinician dashboards.

B. Welldoc's BlueStar® – Digital Diabetes Management (USA)[14]

Type: FDA-cleared SaMD

Use: Type 2 Diabetes management

Approval: FDA Class II clearance

Best Practices:

First mobile prescription therapy for diabetes with clinical data published in peer-reviewed journals.

Integrated with electronic health records (EHRs) and met HIPAA standards.

Involved continuous FDA interaction during premarket submission.

C. Sleepio® – Big Health (UK/USA) [15]

Type: DTx for Insomnia

Use: Cognitive Behavioral Therapy for Insomnia (CBT-I)

Approval: FDA De Novo Classification in 2022

Best Practices:

Clinical evidence from six randomized controlled trials.

Provided a software-only therapy with no human intervention.

Gained adoption in UK's NHS Digital Health Framework.

D. CureApp SC® – CureApp (Japan) [16]

Type: DTx for smoking cessation

Approval: PMDA/MHLW approval as a Class II device

Best Practices:

First DTx product approved in Japan.

Includes doctor-facing dashboard and AI-driven patient coaching.

Approval required clinical data and collaboration with healthcare providers.

E. Kaia Health – Musculoskeletal Therapy (EU/US)

Type: SaMD and DTx hybrid

Use: Back pain therapy with physical exercises and coaching

Approvals: CE-marked in Europe, FDA 510(k) in the U.S.

Best Practices:

AI-based personalization of therapy programs.

Collected large-scale real-world data and patient-reported outcomes.

F. Cardio track – AI-Based Cardiac Diagnostic Platform (India) [17]

Type: Software as a Medical Device (SaMD) – Class B

AI-powered cardiac diagnostic solution integrated with handheld ECG hardware.

Use: Enables early detection of arrhythmias and cardiac conditions through AI-based ECG

Approval:

Applied for CDSCO registration as Class B SaMD

Operates under Indian Medical Device Rules (IMDR), 2017

Data processing aligns with basic privacy and safety standards; evolving toward formal SaMD compliance

Best Practices:

Cloud-based ECG storage and AI analytics enable rapid, remote specialist consultation

Portable design facilitates use in rural clinics and PHCs

Real-time alerts and diagnostic support improve cardiac triage and referral efficiency

Partnered with PHCs in Karnataka and Tamil Nadu to improve early cardiac care access
Demonstrates integration of hardware + AI software in a low-resource setting.

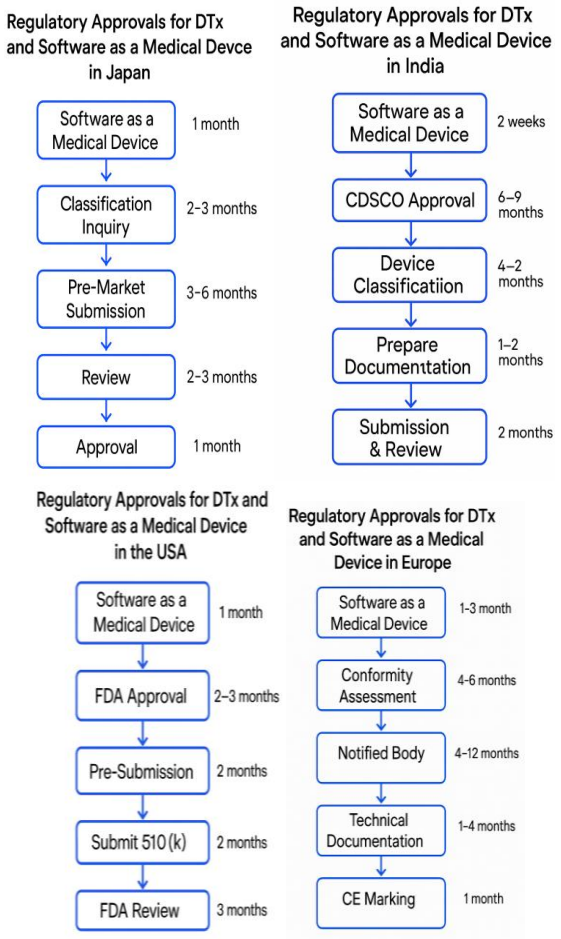

Figure 1. Regulatory approval flow charts for DTx and software as a medical device

XI. DISCUSSION

While many countries have adopted risk-based classification systems and rigorous clinical validation standards, the lack of harmonization leads to redundant testing and regulatory delays. Regulatory science must evolve to accommodate AI/ML-powered adaptive algorithms, which challenge traditional clinical trial models. Furthermore, India's regulatory approach, while progressing, needs clearer guidelines and implementation support for startups and developers. The inclusion of real-world evidence and global pilot initiatives like the IMDRF SaMD WG should be scaled for effective international convergence.

XII. FUTURE OUTLOOK

The rapid advancement of DTx and SaMD requires continuous regulatory evolution to balance innovation with patient safety. Regulatory bodies must collaborate to establish consistent guidelines that foster innovation while ensuring medical device efficacy. With improved harmonization and risk-based approaches, the adoption of DTx and SaMD will continue to grow globally, improving healthcare outcomes.

XIII. CONCLUSION

The regulatory landscape for Digital Therapeutics (DTx) and Software as a Medical Device (SaMD) is evolving rapidly to accommodate advancements in digital healthcare. By adopting harmonized standards, emphasizing data security, and streamlining clinical evaluation processes, regulatory agencies can improve global accessibility to these technologies. Ensuring compliance with established frameworks will drive innovation while safeguarding patient safety.

REFERENCES

[1] Digital Therapeutics Alliance, "Digital Therapeutics: Delivering High Quality Evidence-Based Therapeutic Interventions to Patients," [Online]. Available: https://dtxalliance.org/wp-content/uploads/2020/03/DTA_DTx-Definition-and-Core-Principles.pdf. [Accessed: Mar. 20, 2025].

[2] International Medical Device Regulators Forum (IMDRF), "Software as a Medical Device (SaMD): Key Definitions," [Online]. Available: https://www.imdrf.org/documents/software-medical-device-key-definitions. [Accessed: Mar. 20, 2025].

[3] World Health Organization (WHO), "Digital Health Interventions for Improved Healthcare Delivery," [Online]. Available: https://www.who.int. [Accessed: Mar. 20, 2025].

[4] European Medicines Agency (EMA), "Guideline on Clinical Evaluation of SaMD," [Online].

Available: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-evaluation-medical-devices_en.pdf. [Accessed: Mar. 20, 2025].

[5] U.S. Food and Drug Administration (FDA), "Policy for Device Software Functions and Mobile Medical Applications," [Online]. Available: https://www.fda.gov/media/80958/download. [Accessed: Mar. 20, 2025].

[6] European Medicines Agency (EMA), "MDR 2017/745 – Regulation for SaMD," [Online]. Available: https://www.ema.europa.eu. [Accessed: Mar. 20, 2025].

[7] Pharmaceuticals and Medical Devices Agency (PMDA), "Regulation of SaMD under the PMD Act," [Online]. Available: https://www.pmda.go.jp. [Accessed: Mar. 20, 2025].

[8] Central Drugs Standard Control Organization (CDSCO), "Medical Devices Rules, 2017," [Online]. Available: https://cdsco.gov.in. [Accessed: Mar. 20, 2025].

[9] Global Digital Health Partnership (GDHP), "Roadmap for SaMD Regulation and Harmonization," 2022. [Online]. Available: https://www.gdhp.org/publications/roadmap-samd-harmonization. [Accessed: Mar. 20, 2025].

[10] International Council for Harmonisation (ICH), "Reflection Paper on International Harmonisation of Real-World Evidence and Digital Health Technologies," 2023. [Online]. Available: https://www.ich.org/page/reflection-papers. [Accessed: Mar. 20, 2025].

[11] U.S. Food and Drug Administration (FDA), "Marketing Submission Recommendations for a Software Pre-Specification and Predetermined Change Control Plan," 2023. [Online]. Available: https://www.fda.gov/media/166683/download. [Accessed: Mar. 20, 2025].

[12] International Electrotechnical Commission, "IEC 62304: Medical Device Software – Software Life Cycle Processes," [Online]. Available: https://webstore.iec.ch/publication/22273. [Accessed: Mar. 20, 2025].

[13] Pear Therapeutics, "FDA Grants Class II Clearance to reSET® and reSET-O®," Press Release, 2021. [Online]. Available: https://peartherapeutics.com. [Accessed: Mar. 20, 2025].

[14] Welldoc, "BlueStar®: First Digital Therapeutic for Type 2 Diabetes with FDA Clearance," [Online]. Available: https://www.welldoc.com. [Accessed: Mar. 20, 2025].

[15] Big Health, "Sleepio Receives FDA De Novo Classification," [Online]. Available: https://www.bighealth.com/newsroom/sleepio-de-novo. [Accessed: Mar. 20, 2025].

[16] CureApp Inc., "Japan Approves First Prescription Digital Therapeutic for Smoking Cessation," [Online]. Available: https://www.cureapp.co.jp/en/news. [Accessed: Mar. 20, [21]

[17] Uber Diagnostics, "CardioTrack: AI-Powered ECG Diagnostic Platform," [Online]. Available: https://www.cardio.track. [Accessed: Mar. 20, 2025]. 2025].