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PROPOSED REGULATORY FRAMEWORK FOR MODIFICATIONS TO ARTIFICIAL INTELLIGENCE/MACHINE LEARNING (AI/ML)-BASED SOFTWARE AS A MEDICAL DEVICE (SAMD) IN US

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ABSTRACT

Computer systems can learn and adapt by implementing human intelligence, which is known as artificial intelligence (AI). When it used in combination with medical software, it creates an artificial intelligence (AI)-based medical device that uses in data and algorithms to help with activities like diagnosis and treatment suggestions, potentially increasing the accuracy and effectiveness of medical care, and the use of Artificial Intelligence/Machine Learning (AI/ML) into medical devices, especially Software as a Medical Device (SaMD), this enclosed important concepts like AI/ML, medical devices, SaMD, 510(k) notifications, FDA, CDRH, PMA, TPLC, IMDRF, SPS, and ACP. Through launch the issues raised by AI/ML in SaMD, the structure required to strike a compromise between patient safety and innovation. The subject is to establish the SaMD Pre-Specifications (SPS) and Algorithm Change Protocol (ACP) as crucial elements for open changes, ongoing monitoring, and post-market surveillance. Primary goal is to extend the framework by providing guidance for change control plans using AI/ML methods, particularly those with software learning over time. The Premarket Approval

(PMA) pathway and the 510(k) procedure were covered, taking into account the Quality System Regulation and the IMDRF Quality Management System. Clinical evaluation ensures safety & effectiveness of medical devices. The approach also emphasized the need of using real-world data, sticking to an iterative update cycle, and adopting Good Machine Learning Practices. Basically, the suggested regulatory framework aimed to offer a structured strategy to deal with the difficulties of AI/ML-based SaMD alterations within the regulatory landscape while encouraging innovation and ensuring patient safety.

Keywords: AI / ML, Clinical Evaluation, Medical device, SaMD, 510k notification, FDA, CDRH, PMA, TPLC, IMDRF, SPS, ACP

INTRODUCTION:

The ability of automated systems or other technologies to perform tasks that traditionally require human intellect is referred as computational intelligence. They are capable of comprehension, learning, decision-making. and a method for computers to learn from examples is machine learning. Together, AI and machine learning (ML) make it possible for robots to carry out tasks that ordinarily demand for human intelligence. To educate the machine relationships between features and results, AI gathers data, extracts features, and trains data sets. The problem determines the algorithms to use, and the model is then trained, assessed, and inferred. Through repeated modifications, the model's performance is continuously enhanced. AI systems may adapt and learn from new data, enhancing performance over time. AI integration comprises ML models. Machines can now address difficult jobs like language translation, image recognition, and recommendation systems because to this combination. As technology develops, these systems become more sophisticated and are able to comprehend and learn from a variety of data kinds to carry out activities that were previously thought to be the purview of human intelligence. By making data collecting, integration, diagnosis, and imaging possible, AI and machine learning have transformed medical equipment. Personalized treatment, predictive analytics, remote monitoring, drug development, surgical help, natural language processing (NLP), genetic analysis, data protection, and continuous learning are all made possible by AI-powered devices that analyze medical images and look for irregularities. These developments have the potential to improve patient outcomes, increase the functionality of medical devices, and progress healthcare. Prior to the integration of AI and ML, the healthcare sector relied on conventional methods for data administration, medical diagnosis, and treatment. These systems were dependent on budget constraints,

surgical procedures, clinical research, imaging, treatment planning, data management, monitoring, and data security. Although the old system had some shortcomings in terms of accuracy, efficiency, and the use of enormous volumes of medical data, it was nevertheless somewhat effective. By automating data analysis, enabling individualized therapies, improving diagnostic accuracy, and transforming other aspects of healthcare, the introduction of AI and ML has completely changed the industry, Traditional medical equipment have a number of drawbacks and restrictions before implementing of AI/ML.

Limited Diagnostic Accuracy: Before the advent of AI and ML, the diagnostic accuracy of healthcare practitioners was mostly dependent on their particular expertise. Human error or a lack of access to detailed patient data could result in a misdiagnosis or a delayed diagnosis.

Manual Data Analysis: Medical data analysis required manual interpretation and took a lot of time. Examples include radiology results or patient records. Delays in choosing a course of treatment may result.

Lack of Personalization: Treatments were frequently generic and did not take into account the particular characteristics, such genetics and medical history, of each patient.

Data Accessibility and Sharing: It was challenging to access and distribute information among various healthcare facilities and providers since patient data was kept in physical files or simple electronic systems.

Dependency on Manual Procedures: Surgery was only performed with conventional instruments and the medical knowledge of the physician.

Benefits of AI in Medical Device:

- Using AI apps to manage the workflow helps enhance administrative procedures.
- AI-powered solutions make it simple to communicate information for each patient's care.
- The machine learning program will improve the patient ability to self-manage so that they can be observed and given recommendations for the best the treatment.
- As expensive physical labour is eliminated, it lowers the overall cost of operating the business. Patients receive better care more quickly.
- AI robots provide safer surgery procedures with more success and accuracy.
- It increases access to healthcare through providing the digital infrastructure needed for rapid symptom detection and build a productive healthcare ecosystem.
- By protecting their data, hospitals can avoid harm to their reputation

and assist in reducing risks to the safety of their patients.

- AI will speed up clinical judgment and increase the number of lives that can be saved.
- AI technologies are used to identify medication errors by analyzing previous data and comparing fresh prescription to it.
- Automated visual evaluation improves diagnosis accuracy while minimizing human error **[1]**.

The idea of using artificial intelligence (AI) throughout the pharmaceutical manufacturing process was just a hypothesis, but it eventually taking over as the market's new reality. and it is transforming manufacturing Process of pharmaceuticals by analyzing data and acting automatically to achieve goals. It is essential for digital conversion, utilizing machine learning techniques, with increasing regulatory requirements for data automation and management. AI/ML-based software focused on specific applications, promoting patient trust and safety. It is named as SaMD by FDA and IMDRF. AI and ML technologies can improve healthcare by gaining insights from massive data. Manufacturers of medical devices are embracing AI and ML to develop new products, improve performance and patient care. FDA develops AI/ML-based SaMD for individualized, safe, care and enforcing policies. Manufacturers prepare dossier applications with data requirements based on SaMD likewise the CDRH (Center for Devices and Radiological Health) recommends modifications in design for software cleared under 510(k) notification. The risk categorization approach for SaMD includes four categories: I, II, III, and IV, with lowest risk being class I and high risk being IIa, IIb, and III. AI algorithms have improved, offering cheaper and faster processing capabilities. They help regulatory agencies improve decision-making, operational procedures, and identify regular guidelines. Regulatory intelligence will become essential for businesses, allowing inspection, tracking, competitor problems, and forecasting approval dates. The objective of the study is to develop the proposed regulatory framework further, such as by issuing draft guidelines on a preset change control plan by AI/ML techniques (for software learning over time).

This article will be devoted to studying:

Medical device software" has several uses in various fields of healthcare. These software programs offer resources for data analysis, patient management, diagnosis, and other functions. Listed below are a few applications of medical device software.

Electrocardiography (ECG/EKG) Software: Software used to record and

analyze electrocardiograms (ECGs) aids in the diagnosis of heart disorders such as arrhythmias, heart attacks, and irregular heart rate.

Diagnostic Accuracy: Diagnostic accuracy was primarily reliant on the knowledge of individual healthcare experts in the absence of AI and ML. Human error or a lack of access to thorough patient data could result in a misdiagnosis or a delayed diagnosis.

Electronic Health Records (EHR) Systems: Healthcare providers may easily access patient data, medical histories, and treatment plans thanks to EHR software, which saves and manages patient medical records digitally.

Radiology and Imaging Software: Medical picture interpretation, structure visualization, and ailment diagnosis are all made easier by specialized software.

Emergency Medical Response Systems: Software helps transfer cardiac data from accident scenes to hospitals, enabling medical staff to go ready to treat patients right away when they arrive.

SaMD: A program known as a Software as a Medical Device (SaMD) can be used in place with actual equipment to diagnose, treat, monitor, prevent, or mitigate medical issues. It improves medical decisions and patient care by operating on platforms like computers, mobile devices, wearables, or cloud services.

The software of the medical device gathers and examines data to find problems, give healthcare information, show outcomes, protect data, and learn from data acquired. Additionally, it warns of crises so that sufferers can receive help right away.

1. Mobile Medical App for Skin Lesion Dermatologists can manage clinical circumstances in complex healthcare settings with the use of AI/ML MMA, which uses smartphone camera images to give dermatologists specific information on the features of skin lesions.
2. FDA approves the marketing of a device that uses artificial intelligence to identify specific diabetes-related eye issues.
3. FDA authorizes First Cardiac Ultrasound Software With Robotics Advice for Sale.

Medical device software has been transformed by AI and ML, improving clinical decision support, predictive analytics, personalized treatment plans, real-time monitoring, drug discovery and development, surgical assistance, telemedicine, remote monitoring, data security and privacy, regulatory compliance, research and patient engagement. These technological advancements have enhanced patient outcomes, healthcare delivery, and medical innovation. Data privacy, legal compliance, and comprehensive validation

remain problems, Medical device software has become smarter and more effective thanks to AI and ML.

Modification procedure following initial inspection by accredited SPS and ACP:

Modifications must conform to a systematic and controlled procedure after an initial review with established Pre-Specifications and Algorithm Change Protocol, or SPS and ACP, respectively in order to ensure that the changes are correctly planned, tested, and integrated while reducing risks, Similar to the recommendations for software modifications, the proposed framework for AI/ML SaMD modifications requires manufacturers to record change histories and files for future reference.

SPS: This are early specifications created before the full and final set of specifications for a product or software were referred to as "pre-specifications" in most cases. As a place to start for further development and improvement, these early specs provided an overview of the fundamental needs, features, and functionalities. Prior to engaging in extensive planning and implementation in aligning their understanding and expectations.

ACP: In order to maintain desired performance, accuracy, and safety levels, algorithmic system modifications must follow a set of protocols known as the algorithm Change Protocol. It involves determining the impact, testing new algorithms, managing hazards.

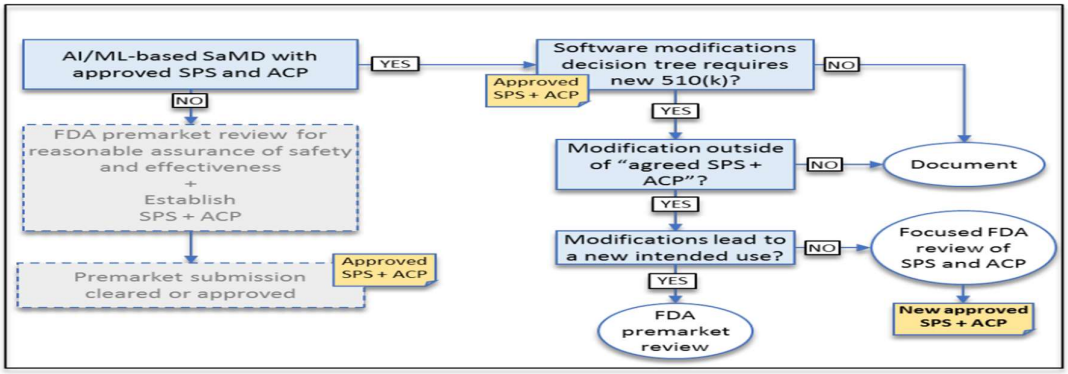

Figure 1: SaMD with SPS and ACP modifications that were previously approved

Pre-Specifications and the Protocol for Algorithm Change allow for adjustments to previously authorized medical software that has already received the regulatory green light.

Approved software refers to a computer program that has been determined to be safe for use in medicine. Pre-Specifications, a strategy in place to direct adjustments, is followed by an algorithm change protocol. Making the software safer or more efficient is the aim. If significant, regulatory approval is obtained from organizations like the FDA. Changes that have been approved are

implemented carefully in accordance with the methodology, evaluated, and monitored to guarantee their efficacy.

If software changes prolong SaMD endorsement, manufacturers must submit fresh premarket applications **[2]**.

Table 1: Difference between Traditional Device World and Evolving Digital Health Device World

Traditional Device World	Evolving Digital Health Device World
Product Development Timeline -Months to years+ -Less frequent modification	**Weeks to months (incremental, iterative) and potentially frequent modifications**
Postmarket Data -Limited availability and access to real world Data (S22, PAS, MDRs, MedSun)	**Potential for high availability and access to rich real-world data (benefits and risks)**
FDA Premarket Program Volume -Stable(~3,500 510(k) submissions/2200pre submissions)	**Potential for exponential increase in volume of submissions**

Table 2: AI/ML-Permitted Medical Devices

S. No.	Data of Decision	Submission Number	Device	Panel	Primary Product Code
1	07/29/22	K213760	ABMD Software	Heart Lung Corporation	Radiology
2	07/29/22	K220961	Deep Learning Image Reconstruction	GE Healthcare Japan Corporation	Radiology

The strength and density of your bones are determined through a medical test called Automated Bone Mineral Density (BMD). It aids medical professionals in determining whether or not you are at danger of fractures (broken bones).

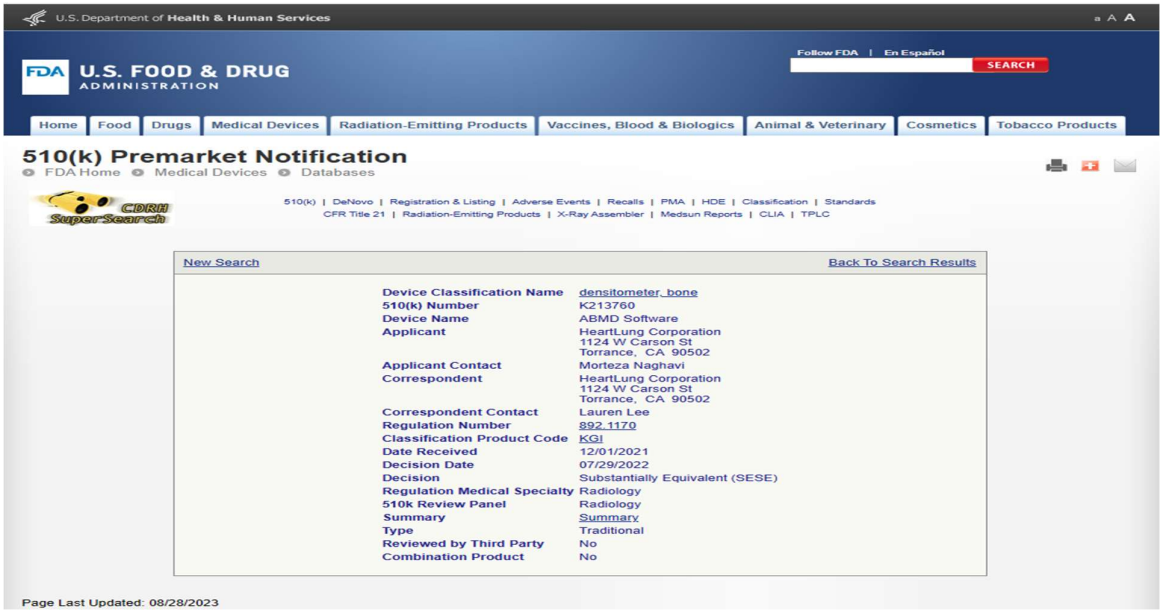

Figure 2: Overview of 510K Notification

To assess the bone density of an area of the body, such as the hip or spine, a machine uses ultrasound or X-rays. Doctors must do this rapid, painless test to check for strong

bones and avoid fractures, especially in elderly patients or those at risk for osteoporosis.

RESULTS & DISCUSSIONS:

A regulatory framework for AI/ML-based medical device improvements has been laid out by FDA to balancing patient safety and innovative solutions, intended to ensure, secure and beneficial modifications.

The TPLC regulatory framework for AI/ML-based SaMD to ensures the creation of high-quality software, testing, and product performance monitoring. This approach ensures efficacy and safety throughout businesses and products, ensuring customer and stakeholder safety, Medical devices require AI software, particularly machine learning (ML), to gain insightful data.

Machine learning (ML)-enhanced medical equipment capabilities have gained attention, with FDA approving more devices in the past decade. The FDA expects this trend to continue. A change control plan outlines modifications and methodologies to minimize patient risks.

Quality assurance specialists analyze and update SOPs for regulatory changes, using AI for faster, cheaper, and less human error-prone processes, allowing quality functions to focus on corrective and preventative actions.

Pre-Market Notification (or) 510K:

In order to determine whether a software upgrade to a medical device may require the submission of a new premarket notification (510(k)), the guidance is meant to help industry and Agency staff. It is not intended to change how the FDA currently thinks about when a submission is necessary for devices that have received 510(k) clearance or other devices that are subject to 510(k) regulations. The advice makes an effort to provide predictability, consistency, and transparency in the decision-making process for software changes.

The need for medical gadgets that incorporate ML functionality has increased recently. Over the past ten years, the FDA has assessed and approved an increasing number of medical devices containing ML that have been legitimately marketed (via 510(k) clearance, granted De Novo requests, or approved PMA).

Premarket Approval (PMA): The PMA regulatory pathway is the toughest one available for medical devices, including software-based ones that make use of intelligent technology. It is necessary for devices that are regarded as high-risk and do not have any predicate devices that are essentially equivalent on the market. The U.S. Food and Drug Administration (FDA) conducts a thorough evaluation as part of the PMA process to determine the device's effectiveness and safety. Clinical data, rigorous testing, and meticulous

documentation are frequently needed for this process. Manufacturers must ensure that their products meet the strictest standards for safety, effectiveness, and morality before they are released onto the market.

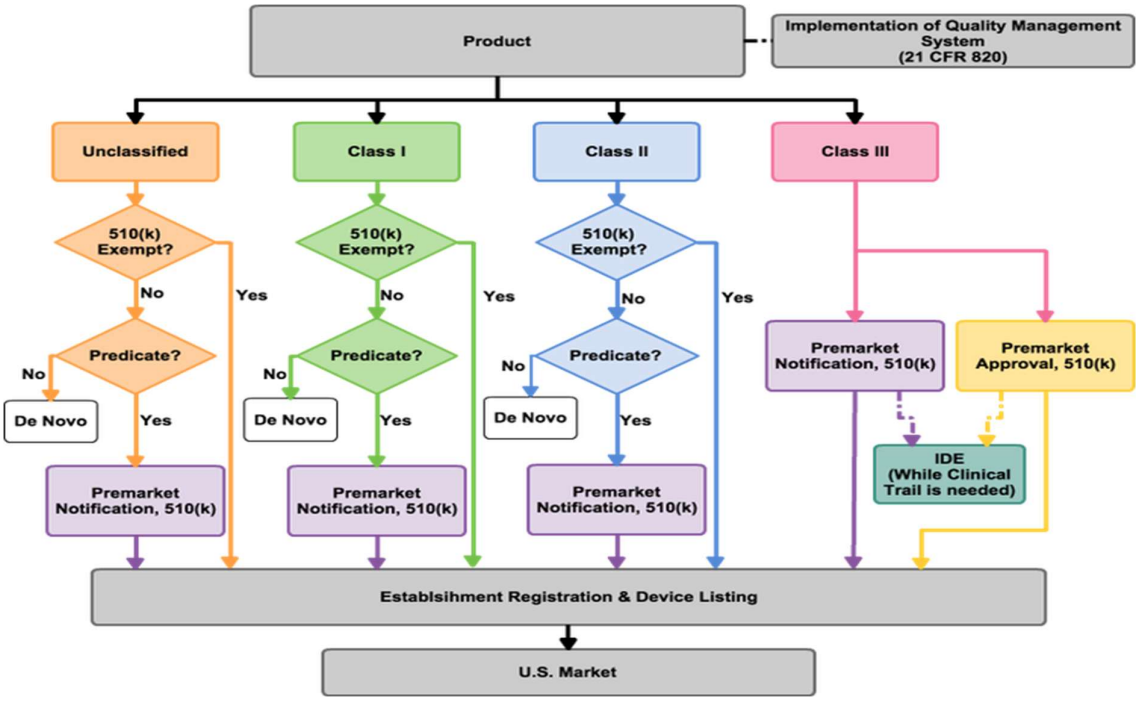

Figure 3: Pathway of Premarket Notification and Premarket Approval

Quality system regulation and 510(k) procedure:

21 CFR Part 820, the Quality System Directive, is critical in ensuring the safety and effectiveness of modifications to a legally marketed item. Changes to device design and production must be reviewed and approved by manufacturers, documented in the device master record, and validated if they cannot be verified. Manufacturers are required under the QS regulation show that the new device complies to the design change. standards and to retain records for FDA investigators. In other situations, a new 510(k) may not be required, and compliance with the QS standard can reasonably ensure the safety and efficacy of the modified device.

Under the Quality System guideline in 21 CFR Part 820, software modifications such as bug fixes, hot fixes, patches, and code changes are analyzed **[3]**.

Types of Common Software Changes:

Infrastructure, Architecture, Core Algorithm, Reengineering and Refactoring.[4]

In order to help producers and regulators understand and execute medical device quality management systems, the IMDRF SaMD framework focuses on clinical and technology issues, scalable lifecycle support, and usage processes.

Figure 4: Overview of SaMD Quality Principles

With an emphasis on therapeutic and technical issues, scalable lifecycle support, and usage processes, the IMDRF SaMD framework assists manufacturers and regulators in comprehending and implementing the medical device quality management systems **[5]**.

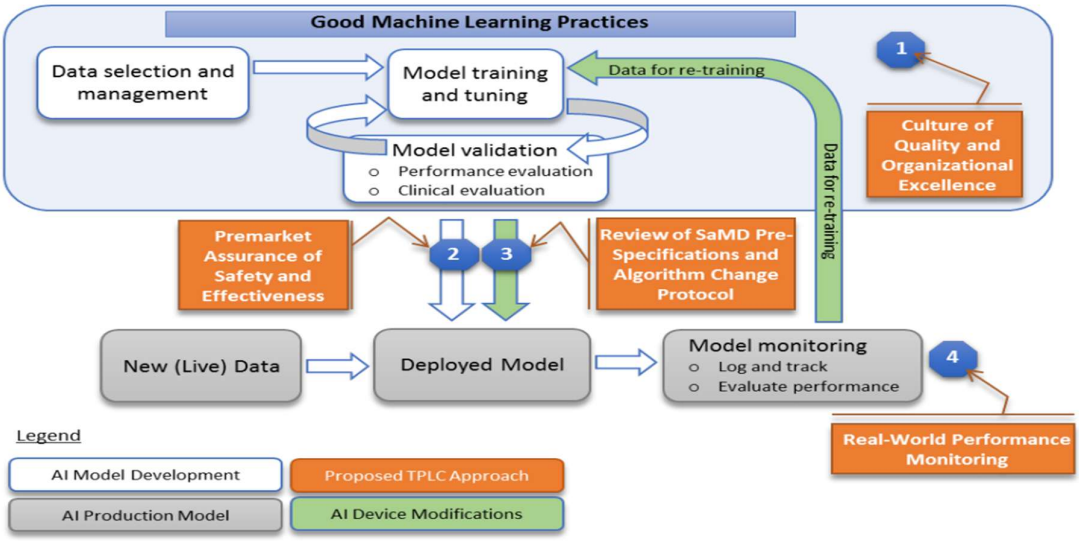

Figure 5: Clear stricture for quality systems on good machine learning techniques and Overlay of FDA's TPLC approach on AI/ML workflow

The FDA implemented a TPLC methodology for AI and ML to ensure their safe and accurate application in healthcare. This additional layer of rules ensured a sequential procedure for security and efficacy, offering an additional safety check for the application of AI and ML in healthcare **[6]**.

SaMD Clinical Evaluation:

Assessing and examining clinical data for medical devices to verify their performance, effectiveness, and safety.

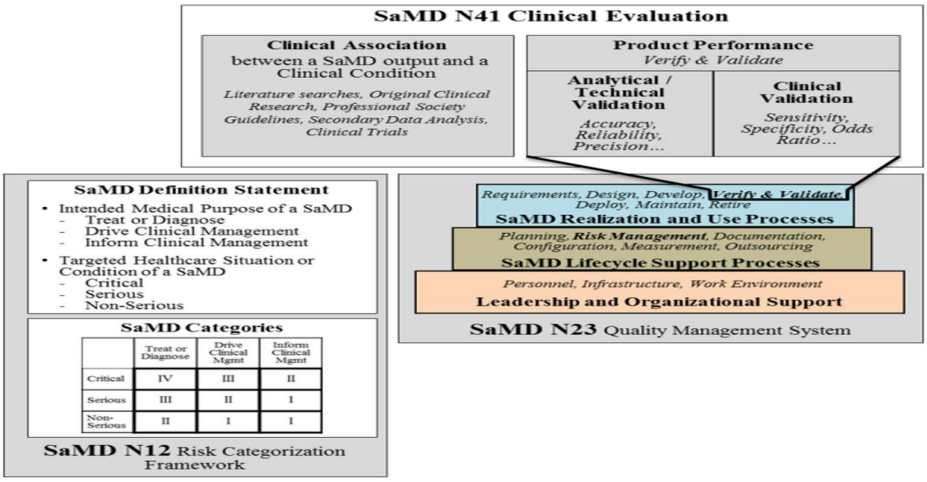

Figure 6: SaMD Landscape

To determine the functionality and patient usage of medical software, data collection is necessary to determine its efficacy and safety. To make sure the data is secure and efficient, experts examine it. To verify its safety, regulators or medical authorities examine the analysis. Based on the analysis and assessment, decisions are made about whether the software may be utilized for medical reasons or if any modifications are required or not.

Table 3: Flowchart for the SaMD Clinical Evaluation Process

Valid Clinical Association	Analytical Validation	Clinical Validation
Is there a valid clinical association between your SaMD output and your SaMD's targeted clinical Condition?	**Does your SaMD correctly process input data to generate accurate, reliable and precise output data?**	**Does use of your SaMD's accurate, reliable and precise output data achieve your intended purpose in your target population in the context of clinical care?**

Clinical Assessment Process for SaMD:

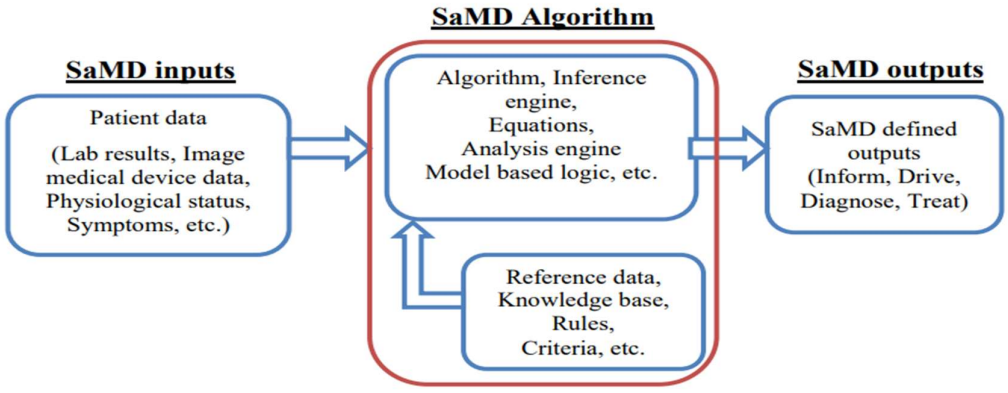

Figure 7: SaMD Basic Programming Model

When a product arrives on the market, SaMD producers use continuous lifecycle operations to assess its performance, accuracy, specificity, sensitivity,

dependability, constraints, and usage range. In order to understand customer requirements and keep track of safety, efficacy, and performance, they gather real-world performance data after the product has been launched. This information supports future functionality expansions, satisfies user needs, and enhances the efficiency of the device while also identifying and fixing problems.

Real-world performance data should be used by medical software developers to analyze user behavior and track technical and analytical performance for upcoming applications.

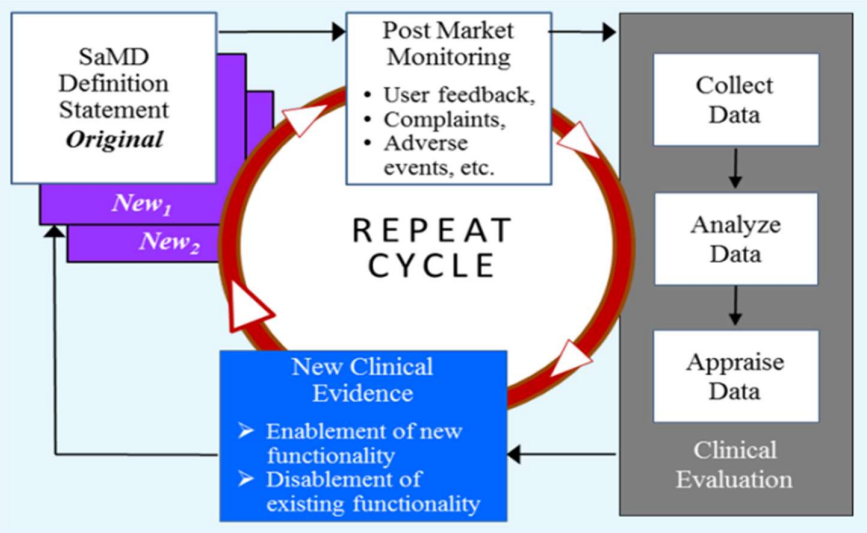

Figure 8: Methodology for Continuous Learning by Using Performance Data from the Real World

By connecting people and objects, SaMD manufacturers can keep an eye on performance, efficacy, and safety. They can develop their functionality and intended usage by gathering and studying data on post-market use. This information consists of end-user feedback, performance studies, clinical evidence, and safety data. Based on clinical data, this knowledge may result in modifications to the SaMD defining statement.

Factors to Consider When Using Real World Performance Data for Continuous Learning:

- The SaMD should make it easier to collect post-market data so that new or existing functionality can be enabled or disabled.
- Use SaMD's capabilities for clinical evidence and enforce minimally burdensome processes instead of requiring end users to participate in the manufacturer's data collecting.
- The risk categorization may vary as a result of continuous clinical evaluation, necessitating a modification to the SaMD defining statement.

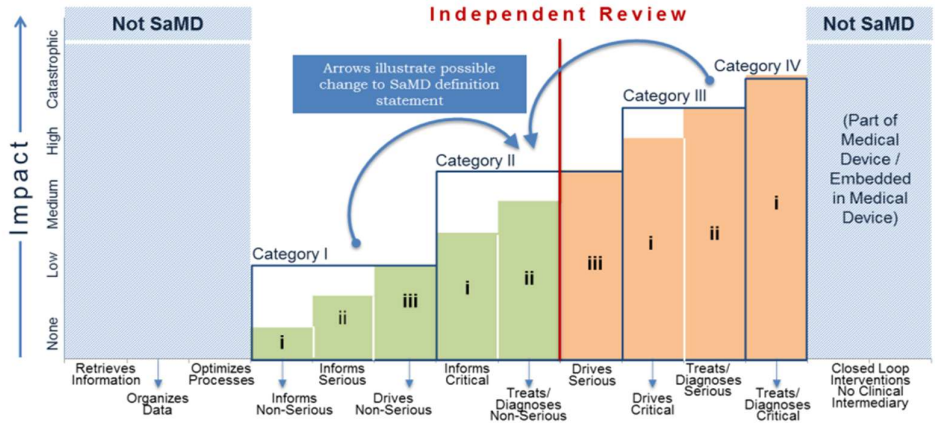

Figure 9: Change to SaMD category from continuous learning

- Manufacturer must take into account post-market data, real-world performance data, and clinical evaluations when changing the SaMD criteria.
- SaMD creators need to take independent evaluation recommendations for category adjustment and ongoing learning into consideration.
- Continuous learning refers to post-market data gathering, not machine learning software, after launch.
- The safety, effectiveness, performance, advantages, and risks of SaMD should be evaluated by manufacturing companies, who should also address any restrictions and labeling revisions **[7]**.

GMLP = Good Machine Learning Practices:

AI/ML-based algorithm design, development, training, and testing procedures that support in the production and assessment of high-quality ML/AI-based algorithms.

Based on elements from the quality management system, software dependability, machine learning, and data analysis.

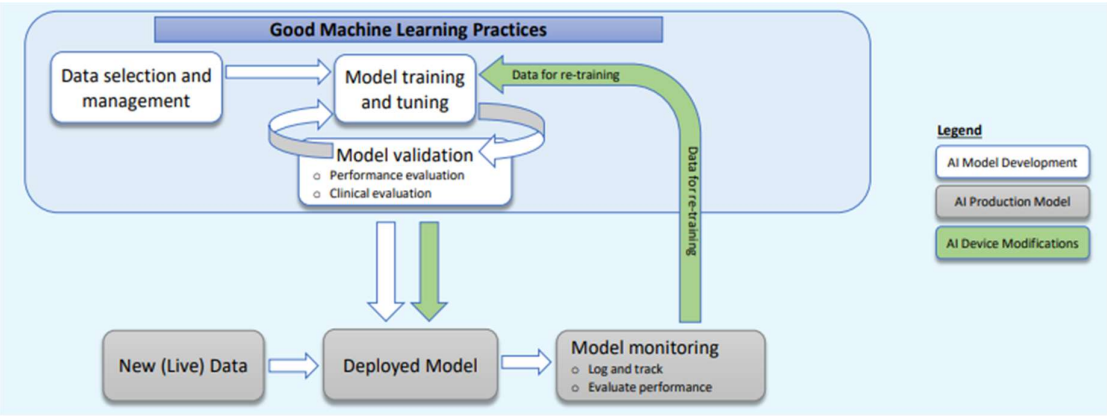

Figure 10: Overview of AI/ML Workflow on Good Machine Learning Practices

The AI/ML workflow includes a step-by-step method for making predictions and judgments. Accurate, equitable, and problem-free outcomes are guaranteed by good processes or regulations. These guidelines direct the system's operations and guarantee its success.

The FDA examines AI-powered medical device regulation and suggests a creative framework employing cGMP and TPLC to lessen the burden of regulation, improve safety, and advance the industry.

A new TPLC strategy is necessary for quick product improvement and efficient protections for continuing, autonomous, and adaptable devices because the current medical device regulatory framework does not allow adaptive AI/ML technology.

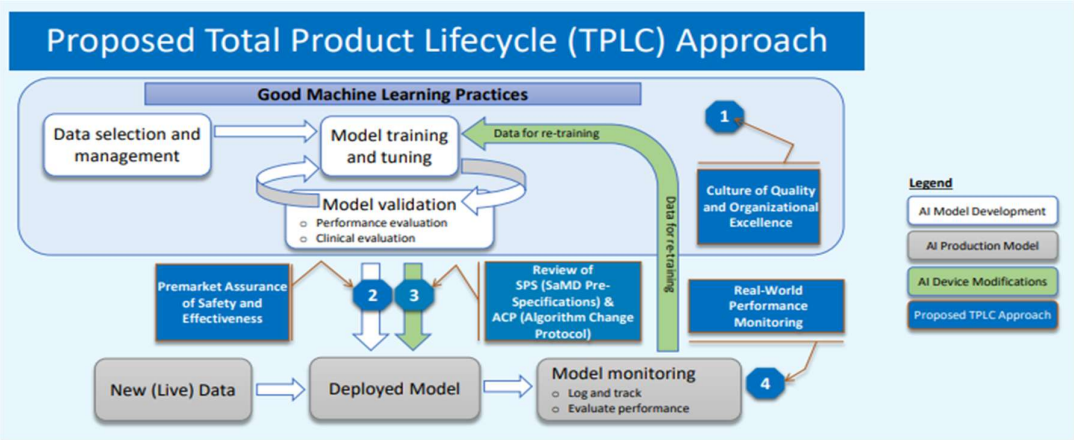

Figure 11: Overlay of TPLC Approach with Good Machine Learning Practices

In the Digital Health Software Precertification Program, the TPLC approach assesses the software lifecycle, through proposed TPLC strategy to allow the FDA regulation of AI/ML SaMD, ensuring continuous enhancement while maintaining patient safety. It includes algorithm change protocols, validation processes, and real-world performance monitoring. This framework helps manufacturers maintain safety and effectiveness, benefiting patients and clinicians.

TPLC Approach offers a clear road map for using machine learning techniques, and Good Machine Learning Practices allow correct and secure application

Challenges:

The strategic use of AI to healthcare presents ethical concerns like hygiene, informed consent & Data privacy and legal challenges like effectiveness & Liability, Cybersecurity, Intellectual property law in medical device applications. and this technologies are crucial for patient care. The rapid accelerated use of AI technologies in healthcare requires attention to safety and effectiveness. Prioritizing these concerns is essential for successful implementation.

The role of AI as a medical tool in the future:

AI application in healthcare is growing rapidly, and the majority of businesses and hospitals have already begun to see its benefits. There is no question that AI will completely transform the healthcare sector. AI repeatedly demonstrate reliability, accuracy, and intelligence through data and experience-based learning as it takes on all the future difficulties **[8]**.

SUMMARY & CONCLUSION:

Targeting to achieve a balance between stimulating innovation and assuring patient safety, the suggested regulatory structure for changes to Medical device software based on AI/ML in the US was designed. For the dynamic nature of AI/ML technologies, it offered a risk-based approach, change processes, and real-world performance monitoring. In addition, it was a proactive step toward regulating future AI/ML medical solutions & also addressed the particular difficulties presented by these technologies by promoting stakeholder participation, including risk assessment, and emphasizing ongoing performance review.

To retain efficacy and public confidence, it was dependent on ongoing modification, stakeholder involvement, and compliance with international standards intended for success.

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