

Regulatory Challenges and Strategies for AI/ML (SaMD) Enabled Medical Device Data Submission

Authors: Shashikant Kumar & Mrityunjay Kumar

Presentation No. - SA07

Stream: Submission & Agency (SA)

PHUSE US Connect 2025, Orlando, Florida 16–19 March

Agenda

1. Introduction
2. Examples of SaMD
3. IEC 62304 Standard
 - a. Software Development Lifecycle Process
 - b. Software Safety Classification
4. Regulatory Challenges in AI/ML-Enabled SaMD
 - a. SaMD regulatory overview and framework
 - b. Strategies for AI/ML-Enabled SaMD Data Submission
5. Challenges and Considerations
6. Conclusion

Introduction

SaMD (Software as a Medical Device)

- Software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device [[source: IMDRF](#)]
- It performs functions such as diagnosis, monitoring, treatment, and disease prevention by analysing data from medical imaging, biosensors, wearables, and other health-related sources
- SaMD is transforming healthcare by improving diagnostics, patient management, and treatment outcomes

AI/ML enabled devices SaMD

- New and no new frameworks for data management and analysis which poses a challenge for regulatory bodies to establish guidelines on how AI-processed data should be handled
- AI/ML softwares may get updated on frequent intervals so guidance on version control becomes necessary

Regulatory Framework

- Action Plan was drafted by FDA in 2021
- EMA has no guidelines
- Risk of Harmonization between Regulatory bodies (RA)

Examples of SaMD

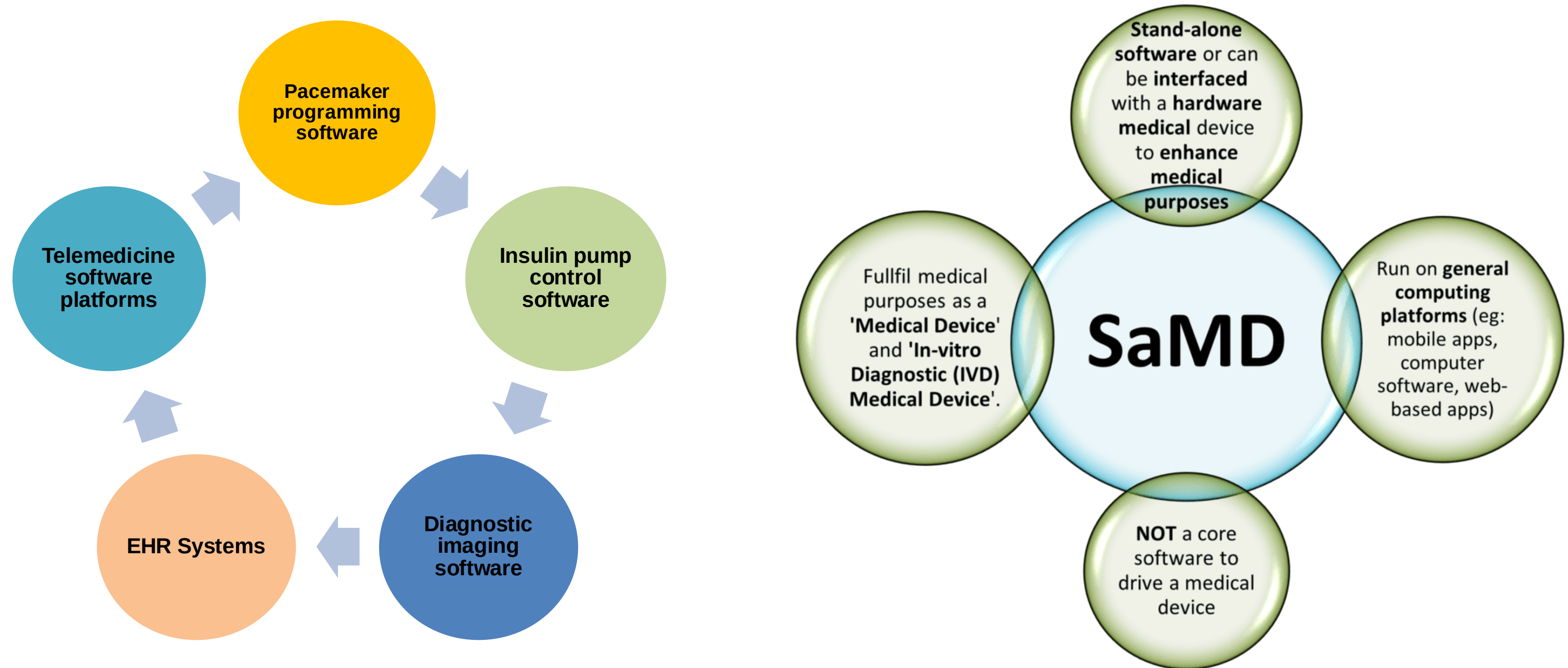


Figure 1: General requirements to be classified as a SaMD. Copyright 2021, Kvalito Consulting Group

Examples of SaMD contd.

Software as Medical Device (SaMD)	Not SaMD
Software that evaluates MRI images and makes diagnosis recommendations.	Software that controls an MRI machine (SiMD).
A mobile app that monitors a patient's heart rate or glucose levels and makes treatment recommendations to the patient and/or patient's doctor.	Software that allows a patient to control their insulin pump based on glucose readings (SiMD).
An application, based on machine learning algorithms, that reviews patient health data and makes treatment recommendations.	Software that securely stores patient health and treatment history (Digital Health Records or Medical Information System).

SaMD Model

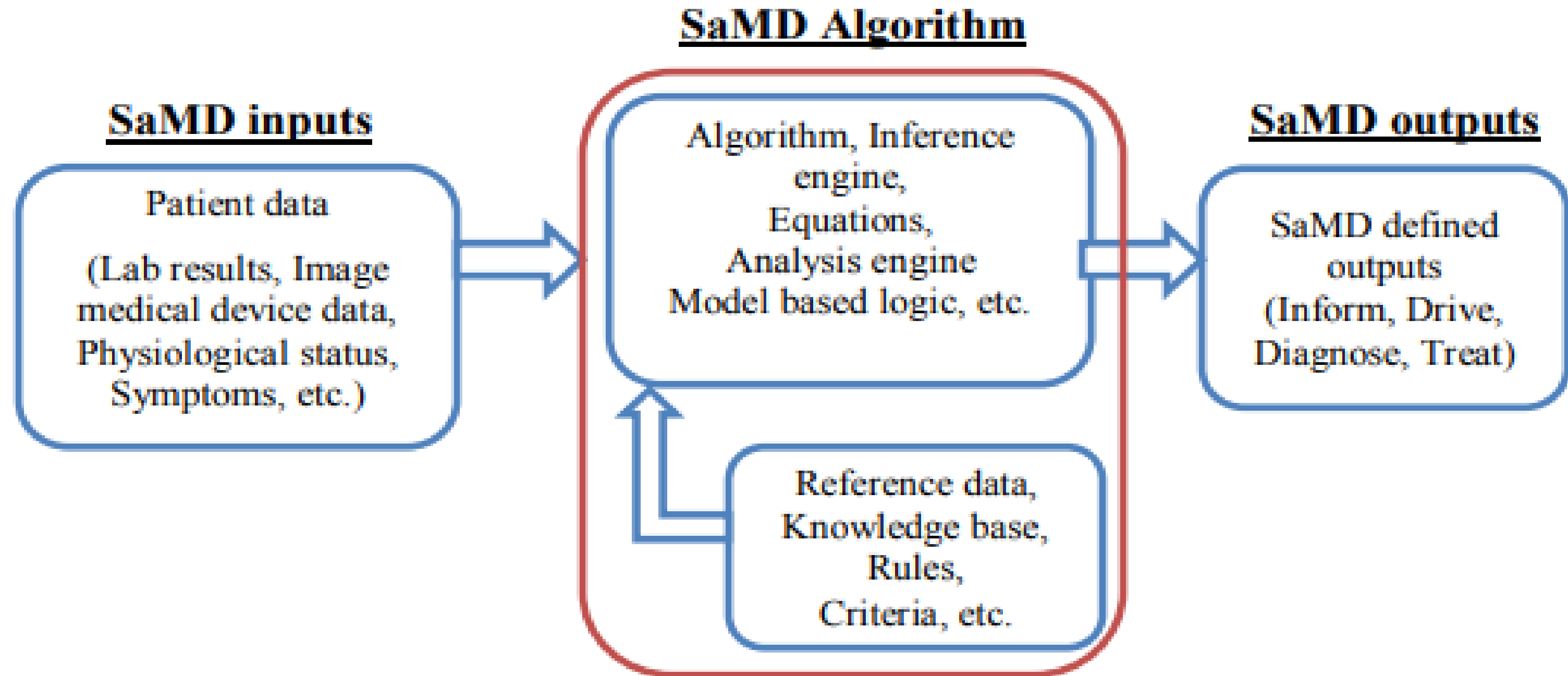
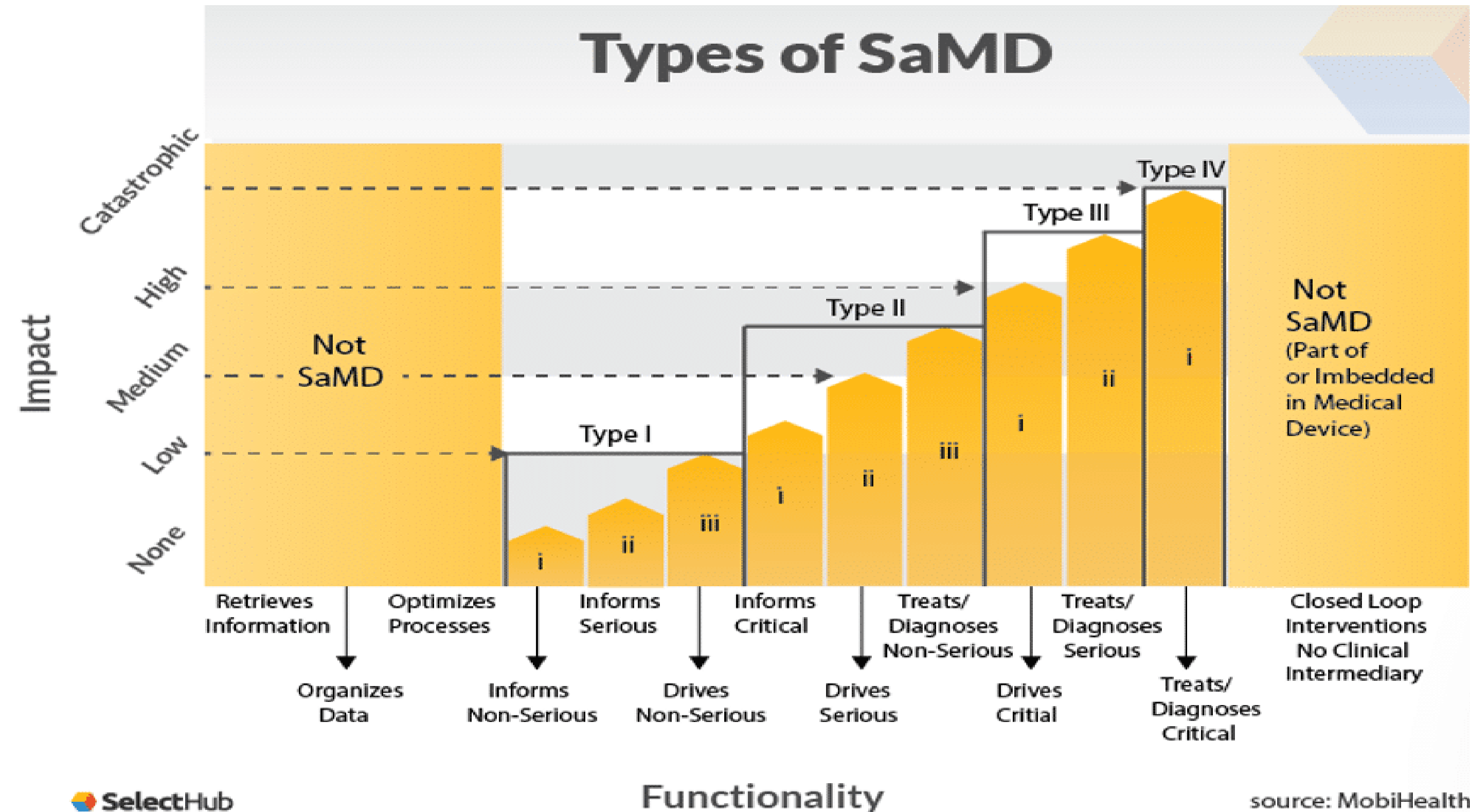


Figure 9 - SaMD Basic Programming Model

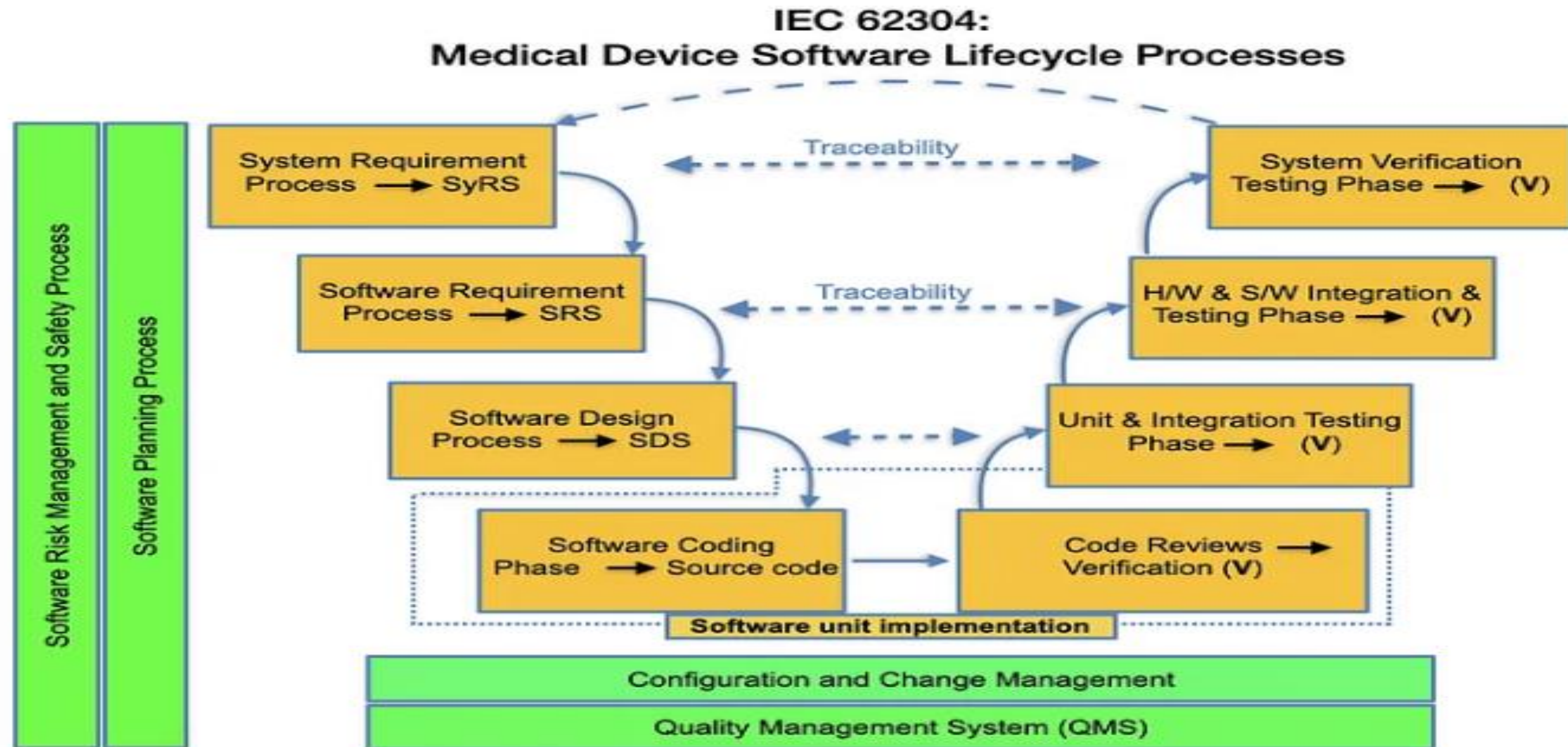
Source: IMDRF

SaMD Categories



IEC 62304 Standard

a. Software Development Lifecycle Process



Summary illustration of IEC 62304

IEC 62304 Standard

b. Software Safety Classification

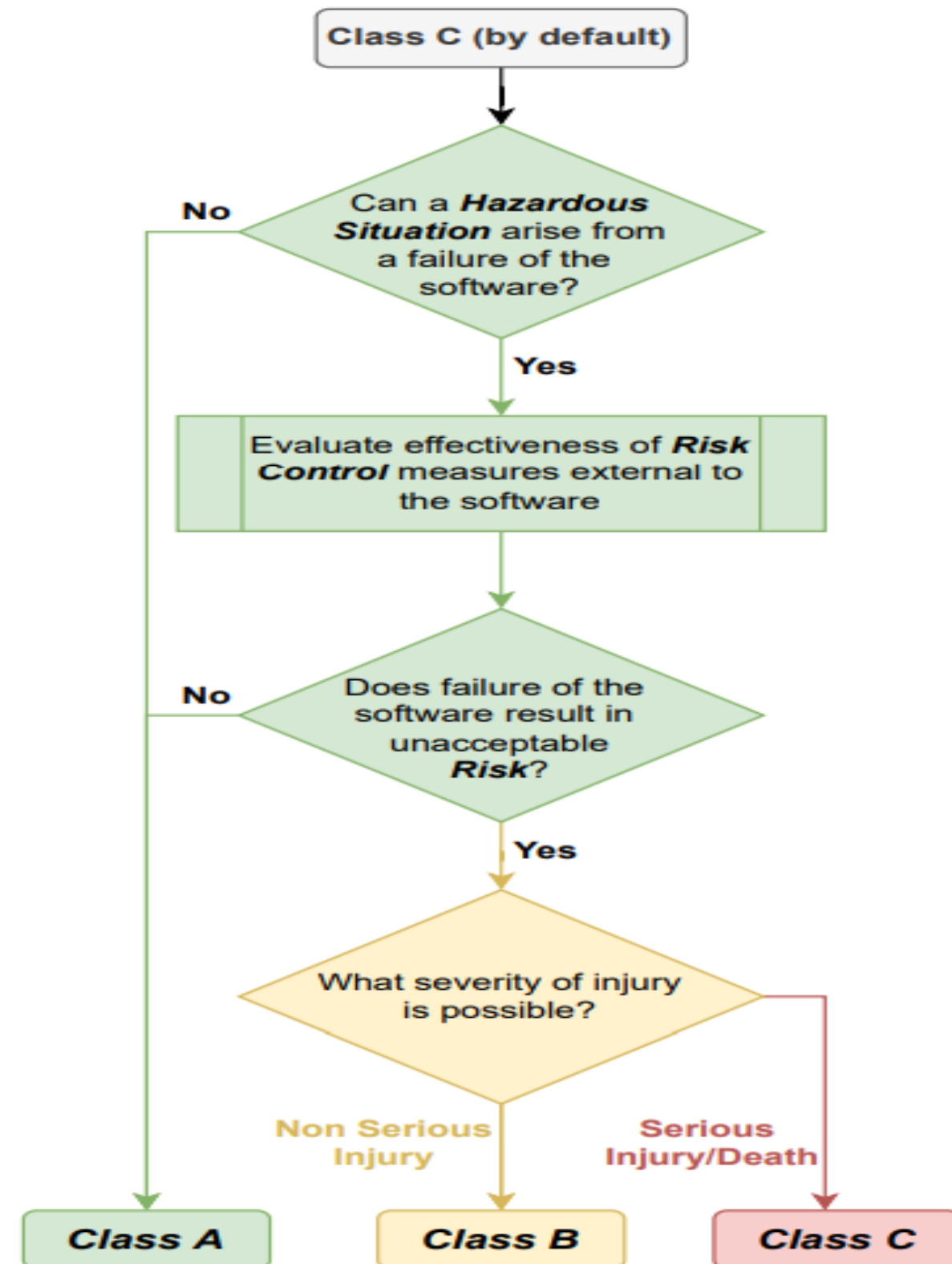


Table 1. Medical device classification according to FDA and MDR.

Risk	FDA Class	MDR Class	Example
Low	Class I	Class I	Bandages
Moderate	Class II	Class IIa	X-ray-Machines
Moderate to High	Class II/III	Class IIb	Defibrillators
High	Class III	Class III	Pacemakers

Figure 2. Software safety classification according to IEC62304

Regulatory Challenges

a. SaMD regulatory overview and framework

Why does SaMD have independent regulatory considerations?

Over the past decade, the IMDRF, FDA, and other regulatory bodies have worked to better align regulations with the quickly evolving capabilities and nature of digital devices since SaMD generate unique opportunities and considerations.

Because SaMD software typically runs on publicly available hardware:

1. SaMD software must not only be designed to work on specific platforms (usually multiple) but must also be tested and updated frequently as new hardware and operating systems become available.
2. Agile software development methodologies can provide an environment in which fast product feedback loops are supported within the required regulatory framework.

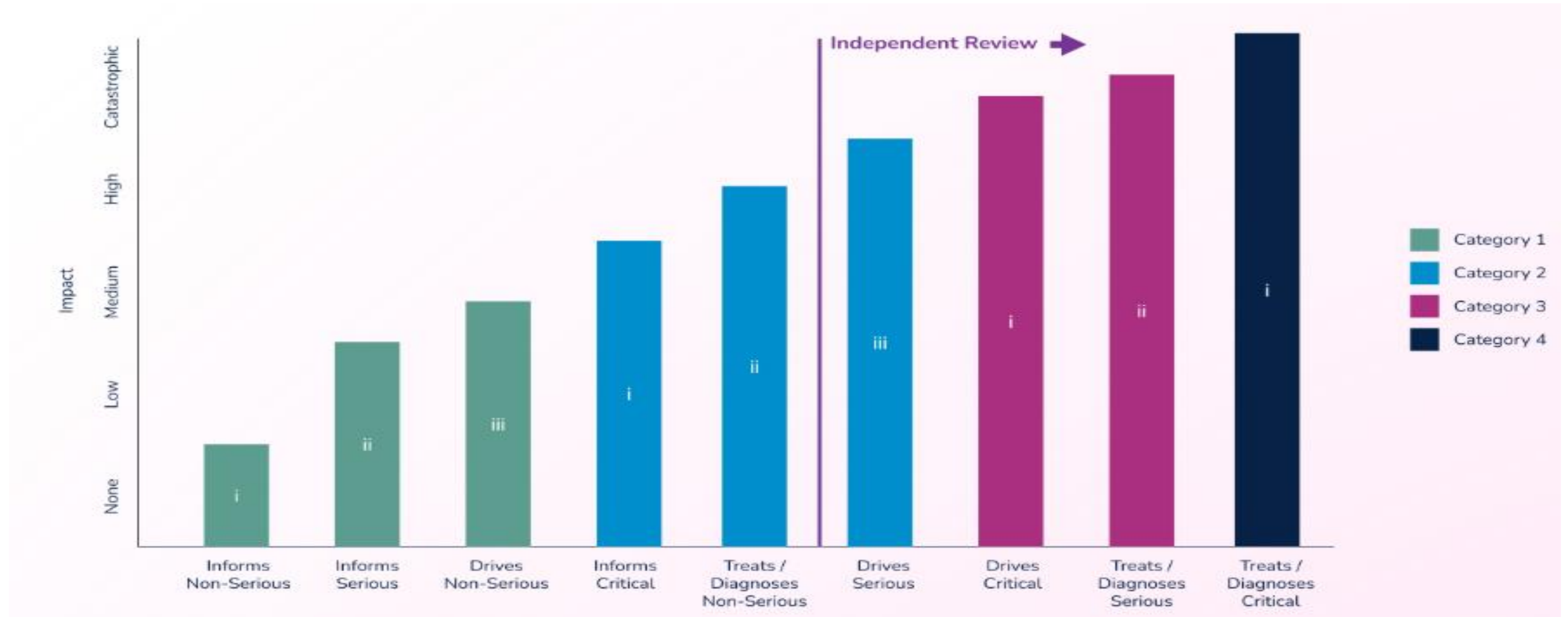
Regulatory Challenges

a. SaMD regulatory overview and framework contd..

Because SaMD software can be made readily available to the public, or specific patient groups, using their own devices:

1. SaMD software can generate faster user/patient feedback - both for medical professionals and for the device manufacturer. Given this environment, regulatory bodies generally want to enable the market to safely take advantage of new innovations as quickly as possible.
2. Product testing needs to consider the unique and varied environments in which the software may be used, potentially in environments the product is not intended for. The software developer cannot control updates to operating systems or internet browsers, other software that may be running on a user's device, or the ability for the user to potentially share software or data with others.
3. The advantages of quickly delivering product fixes and updates need to be measured against potentially introducing new, possibly misunderstood or unwanted features, to all users at once.

SaMD within the FDA and MDR Regulatory Framework



source: www.rimsys.io

Pathway for Continuous Learning Leveraging Real World Performance Data

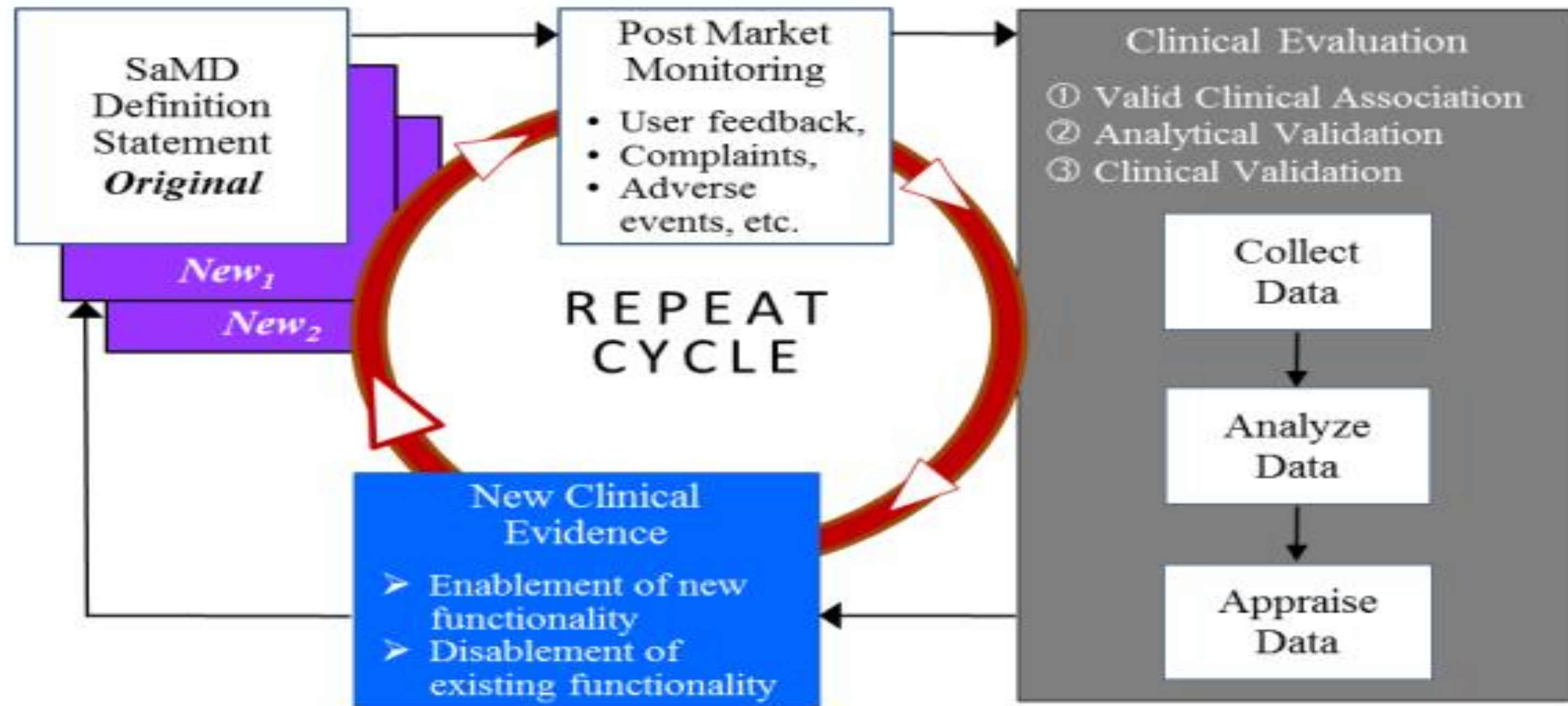
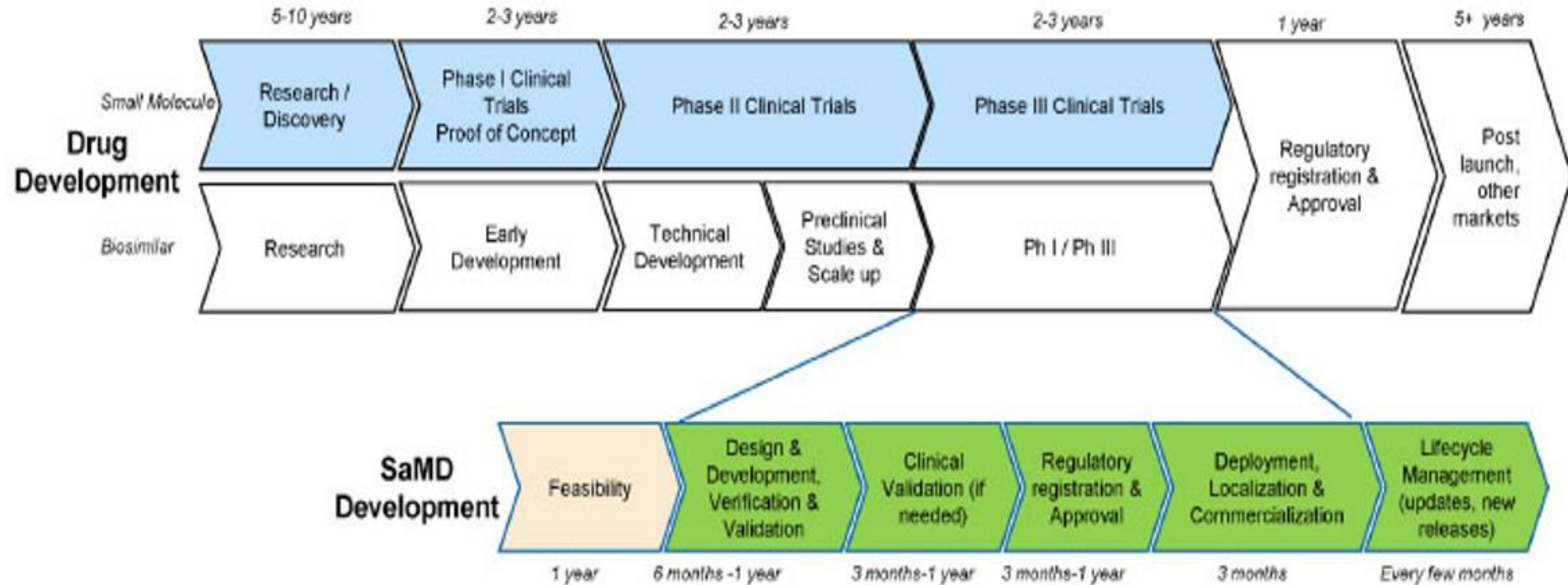


Figure 14 - Pathway for Continuous Learning - Use of Real World SaMD Performance Data in Ongoing SaMD Clinical Evaluation

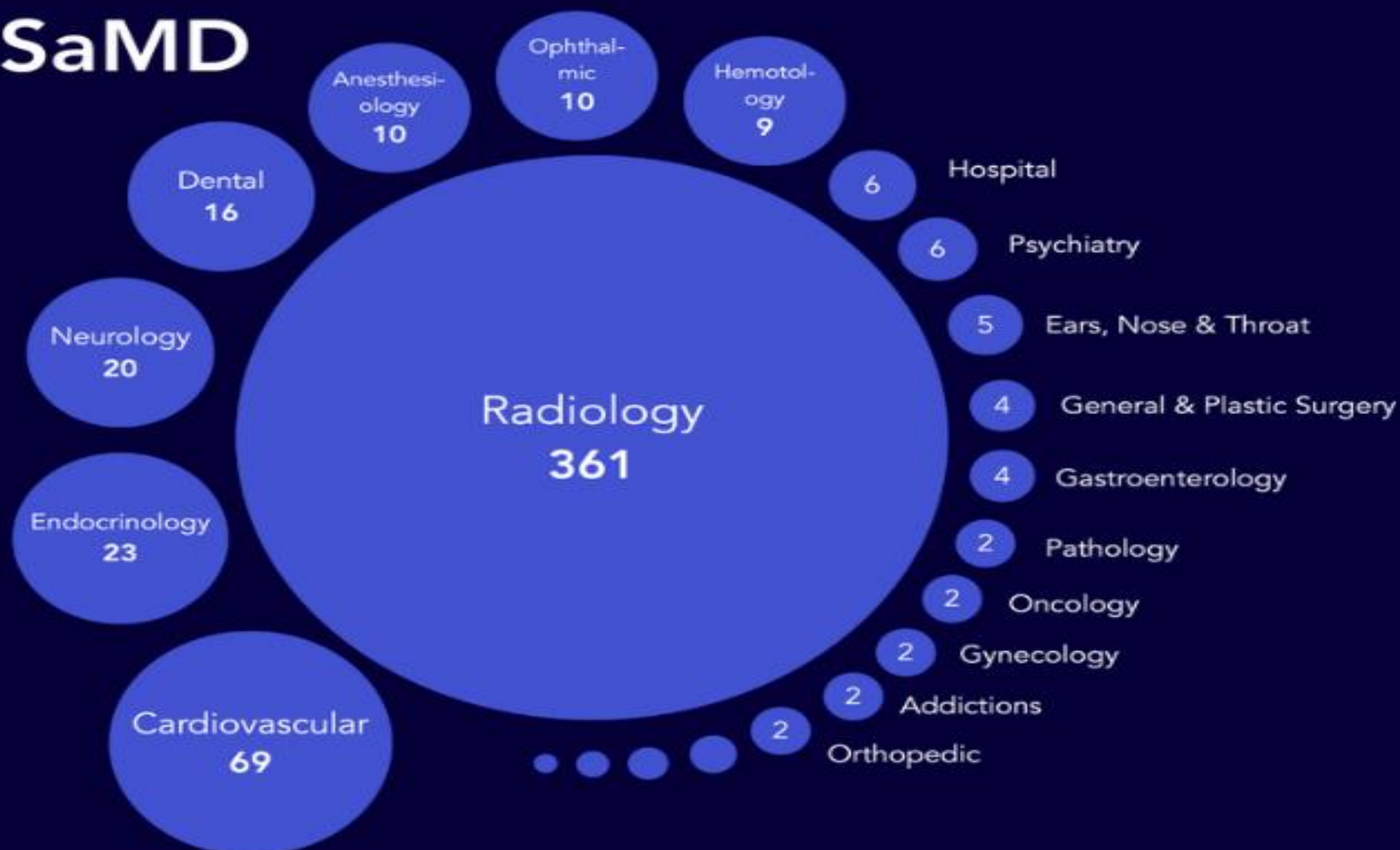
Source: IMDRF/SaMD WG/N41FINAL:2017

Drug Development vs SaMD Development



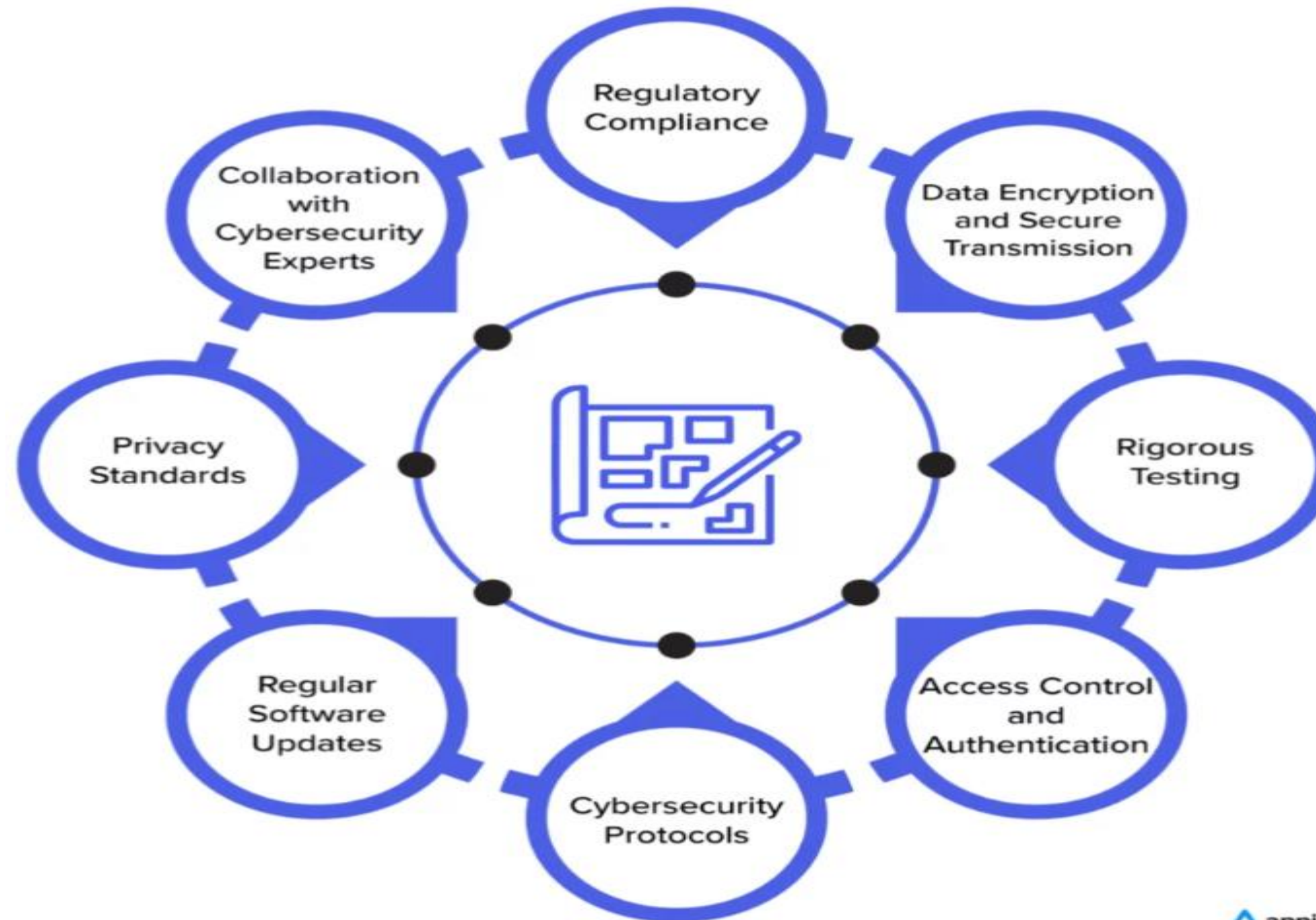
FDA Cleared SaMD

The First 500 FDA-Cleared SaMD



Safety and Security of SaMD

Ways to ensure safety and security of SaMD



Regulatory Challenges in AI/ML-Enabled SaMD

b. Strategies for AI/ML-Enabled SaMD Data Submission



Model interpretability techniques (e.g., SHAP, LIME) for regulatory approval

To gain regulatory approval, AI/ML-based SaMD must provide transparent and interpretable decision-making based on data that clinicians, regulators, and patients can understand.

Techniques	Description	Use Case in SaMD	Regulatory Relevance
SHAP (Shapley Additive Explanations)	Quantifies the contribution of each feature to a model’s prediction. Uses cooperative game theory principles.	Identifying key biomarkers influencing AI-driven disease risk scores.	Aligns with FDA Good Machine Learning Practices (GMLP) for AI transparency.
LIME (Local Interpretable Model-agnostic Explanations)	Generates local surrogate models to approximate black-box model behaviour.	Explaining AI-assisted radiology or tumor detection predictions.	Supports SaMD Risk Categorization Framework (IMDRF) by providing case-specific justifications.
Integrated Gradients	Measures feature importance in deep learning models by computing gradients.	Deep learning models for medical imaging and ECG/EEG analysis.	Aligns with EU AI Act and FDA SaMD Regulatory Framework.
Decision Trees & Rule-Based Models	Uses hierarchical tree structures to make human-readable predictions.	Clinical decision support systems (CDSS) for AI-driven diagnostics.	Preferred for low-risk AI/ML models in medical decision-making.

Regulatory Challenges in AI/ML-Enabled SaMD

b. Strategies for AI/ML-Enabled SaMD Data Submission



A structured Failure Mode and Effects Analysis (FMEA) or ISO 14971-based Risk Assessment helps in systematically identifying risks in AI/ML models

Risk Type	Potential Issues	Mitigation Strategies
Data-Related Risks	Bias, missing data, low-quality inputs	Use diverse, high-quality, representative datasets
Algorithmic Risks	Overfitting, lack of generalization	Validate with independent datasets, real-world data
Model Transparency	Black-box AI decision-making	Implement explainable AI (XAI) methods
Human-AI Interaction Risks	Over-reliance, automation bias	Design for human oversight and intervention
Security & Privacy Risks	Data breaches, adversarial attacks	Use encryption, adversarial robustness techniques
Regulatory Risks	Non-compliance with global standards	Align with ISO 13485, FDA, EU MDR, IMDRF

Risk Assessment Framework for AI/ML-Based SaMD

Regulatory Body	Guidance
US FDA	AI/ML-Based SaMD Risk Management (PCCP, Total Product Lifecycle)
IMDRF	SaMD Risk Categorization Framework
ISO 14971	Medical Device Risk Management
EU MDR	AI Risk Classification under Medical Device Regulation
Health Canada, MHRA	AI Transparency and Explainability

Regulatory Guidelines for a Risk-Based AI/ML Approach

Challenges and Considerations

1. Data Privacy and Security

Regulatory bodies require that the use of RWE in AI submissions complies with data privacy regulations (e.g., GDPR, HIPAA). Manufacturers must ensure that patient data is anonymized and protected.

2. Validation of RWD Sources

Regulatory authorities often require evidence that the RWD sources (e.g., EHRs, registries) used for the submission is validated and reliable. Manufacturers should demonstrate that these sources accurately represent the clinical environment in which the AI device will be used.

3. Understanding of RWE Limitations

RWE is not as controlled as clinical trial data, so its use must be carefully considered, with an understanding of potential biases or confounders in the data. The submission must address how these limitations are mitigated.

Conclusion

The regulatory landscape for AI/ML-enabled Software as a Medical Device (SaMD) presents significant challenges due to the complexity and continuous learning nature of AI/ML models.

As the regulations for SaMD become clearer, the emergence of various types of SaMD is inevitable. This latest technology extends beyond traditional medical care not only for medical personnel, and more importantly, it provides a reliable and accredited platform for engaging e-patients.

Medical care is never easy, but by working together and staying connected, we can make wonders.



THANK YOU