SOFTWARE AS A MEDICAL DEVICE (SAMD) KEY DEFINITIONS

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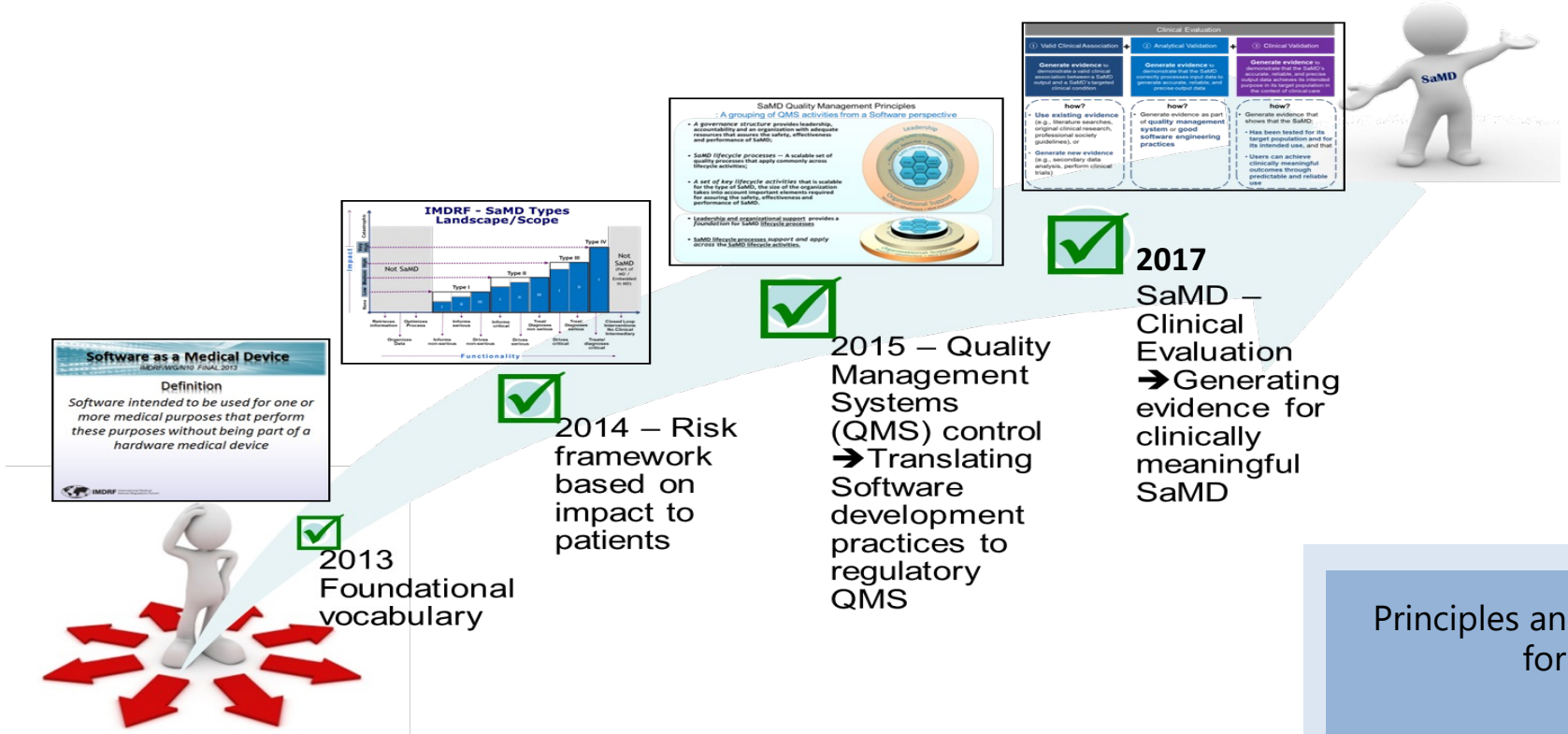
Overview

- IMDRF SaMD
- FDA Policy / Guidances / Regulatory Framework
- Digital Health Technology
- Resources

The International Medical Device Regulatory Forum (IMDRF) has issued a series of document related to SaMD



Principles and Practices for Software Bill of Materials for Medical Device Cybersecurity
Started July 2022

Additional Work

[Machine Learning-enabled Medical Devices: Key Terms and Definitions]
Published May 2022

[Principles and Practices for Medical Device Cybersecurity]
Published April 2020

It has been almost 10 years since IMDRF defined SaMD

Published in December 2013*, the term "Software as a Medical Device" (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.

NOTES:

- SaMD is a medical device and includes in-vitro diagnostic (IVD) medical device.
- SaMD is capable of running on general purpose (non-medical purpose) computing platforms
- "without being part of" means software not necessary for a hardware medical device to achieve its intended medical purpose;
- Software does not meet the definition of SaMD if its intended purpose is to drive a hardware medical device.
- SaMD may be used in combination (e.g., as a module) with other products including medical devices;
- SaMD may be interfaced with other medical devices, including hardware medical devices and other SaMD software, as well as general purpose software
- Mobile apps that meet the definition above are considered SaMD.

* *IMDRF/SaMD WG/N10FINAL: 2013: Software as a Medical Device (SaMD): Key Definitions*

There are 5 key points to remember about SaMD

1. SaMD is a medical device and includes an in-vitro diagnostic (IVD)
2. SaMD can run on general purpose (non-medical purpose) computing platforms without being part of a hardware medical device to achieve its intended medical purpose
3. SaMD can be used in combination with other products including medical devices
4. SaMD can interface with other medical devices, including hardware medical devices, other SaMD software, and general-purpose software
5. Mobile apps that meet the definition above are SaMD

It is also important to know when Software is not SaMD

≠ SaMD

Software embedded in a medical device to "drive or control" that device

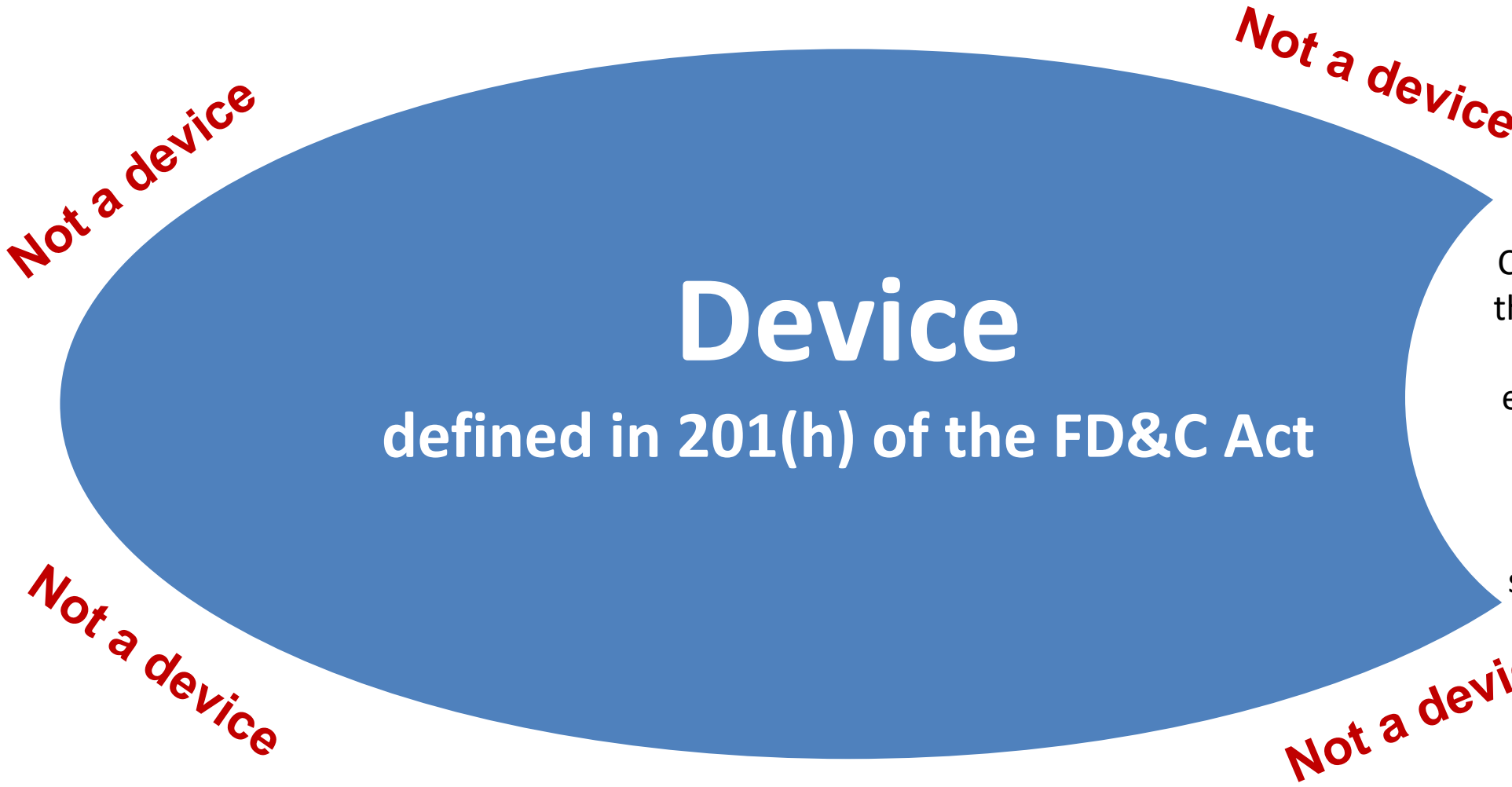
≠ SaMD

Software which is an accessory to a medical device or in vitro diagnostic medical device

Test Your Knowledge

Software that programs MRI magnets to turn	≠ SaMD
Software that helps radiologists and clinicians find and diagnose a cardiovascular condition by analyzing MRI scans	SaMD
Software used in a closed-loop control of a pacemaker	≠ SaMD
Software which retrieves information and performs a further action on that information to inform and/or help (directly or via a clinician) to treat or diagnose	SaMD

The US FDA has harmonized SaMD definition with IMDRF while taking in consideration US legislation



21st Century Cures amended the definition of "device" to exclude certain **software functions** pursuant to section 520(o)

Changes resulting from 21st Century Cures Act helped clarify how to interpret SaMD definition

December 13, 2016, the Cures Act amended the definition of "device" in the Federal Food, Drug, and Cosmetic Act to **exclude certain software functions**, pursuant to section 520(o), intended for...

- **Certain software functions intended for administrative support of a health care facility;**
- **Certain software functions intended for maintaining or encouraging a healthy lifestyle with no reference to any disease or condition;**
- **Certain software functions intended to serve as electronic patient records;**
- **Certain software functions intended for transferring, storing, converting formats, or displaying data and results;**
- **Certain software functions that are intended for clinical decision support.**

Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/changes-existing-medical-software-policies-resulting-section-3060-21st-century-cures-act

The U.S. has defined certain terms to help with further clarity

Function	A distinct purpose of a product
Device Function	A function that meets the definition of a device under section 201(h)(1) of the FD&C Act
Device Software Function	Software function that meets the device definition in section 201(h) of the FD&C Act.
Other Function	A function that: – does not meet the definition of a device; – meets the definition of device, but is not subject to premarket review (e.g., 510(k)-exempt); or – meets the definition of device, but for which FDA has expressed its intention not to enforce compliance with applicable regulatory controls.
Device Function-Under-Review	A function for which FDA is conducting a premarket review
Multiple Function Device Product	A product that contains at least one device function and at least one other function.

Function could be the intended use or a subset of the intended use of the product.

Examples

A product with an intended use to analyze data has one function: analysis.

A product with an intended use to store, transfer, and analyze data has three functions: (1) storage, (2) transfer, and (3) analysis.

Final rule clarifies that intended use can be based on different sources of evidence

- Final rule amended 21 CFR 801.4 (effective September 1, 2021)
- **Provides more clarity and direction regarding the types of evidence relevant to determining a product's intended use**, such as:
  - Express Claims and Representations
  - Implied Claims
  - Circumstances of the Sale or Distribution
  - Design or Composition
  - **Any relevant source of evidence may be considered**
- Better reflects the Agency's current practices in evaluating whether a product is intended for use as a device

Despite legislation and attempts to clarify what is, or what is not a SaMD, we still get questions on what is the right regulatory pathway

Examples of Software Function Regulatory Approach

Not a Device

Software functions that are intended for individuals to log, record, track, evaluate, or make decisions or behavioral suggestions related to developing or maintaining general fitness, health or wellness, with no reference to a disease or condition

Intention to Exercise Enforcement Discretion

Software functions that provide periodic educational information, reminders, or motivational guidance to smokers trying to quit, patients recovering from addiction, or pregnant women

Focus of FDA's Oversight

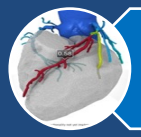
Software functions that use a sensor or lead that is connected to a mobile platform to measure and display the electrical signal produced by the heart (electrocardiograph or ECG)

Increasing Risk

Advancement in technology over the past decades have led to advancements in Digital Health Solutions

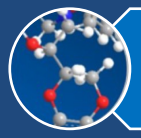
Healthy living | Prevention | Diagnosis | Treatment Recovery | Home care | Management

Convergence of computing power, connectivity, sensors, and software used in healthcare.


Used as a medical product


Incorporated into a medical product (include a pharmacologic product)


Used to develop a medical product


Used to study a medical product


Used as a companion or adjunct to a medical product, including diagnostics and therapeutics.

*Definition from FDA-NIH BEST Glossary. Available at https://www.ncbi.nlm.nih.gov/books/NBK338448/

Poised for growth, SaMD promises innovation for providers and patients

Healthy Living	Prevention	Diagnosis	Treatment	Recovery	Home Care	Management

Moving health care from the clinic to the patient

Understanding behavior and physiology in the real world

Leveraging computing power, sensors, connectivity, and software

Wearables: Vital signs monitors ; Sleep Apnea Monitors (PSG); Neurological Monitors; Activity Trackers/ Actigraphy

Software Solutions: Software as a Medical Device (Diagnostic and Therapeutic, CADx, CADe); General Wellness Apps

Tele-care: Activity monitoring; Remote medication management; Video Consultation

Healthcare Analytics: Public Health analytics; Care delivery analytics

Services: Healthcare systems services; Monitoring services for Chronic disease management; Monitoring services for aging; Post acute monitoring

Health and Wellness Solutions

- Improve Cognitive Function
- Promote Exercise & Weight Management
- Stress Management
- Mood and Resilience
- Disability Solutions
- Addressing Isolation
- Grief Counseling

Diagnostics and Therapeutic Solutions Areas:

Post-Traumatic Stress Disorder; Generalized Anxiety Disorder; Depression adjunct therapy; Mild Cognitive Impairment; Autism Spectrum Disorder; ADHD; Neuropsychological Diagnosis and Therapy; Behavioral Therapy

Post Care solution: Activities of Daily Living; Physical Medicine – OT/PT

Patient engagement: routine lab result; appointment reminders; treatment prompts prescription refills; adherence to treatment; Patient Education

Our team has identified technology areas of focus at the intersection of technology & healthcare

- Software as a Medical Device (SaMD)
- Artificial Intelligence/ Machine Learning
- Wearables
- Software in a Medical Device (SiMD)
- Wireless connectivity
- Interoperability
- Medical Device Cybersecurity
- Virtual Reality/ Augmented Reality
- Real-world Evidence and Advanced Clinical Studies
- Advanced Manufacturing
- Patient-Generated Health Data

The US FDA and the European Commission have issued several public documents to help navigate SaMD

US FDA	European Commission
Policy for Device Software Functions and Mobile Medical Applications	Is your software a medical device?
Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices	Guidance on classification of medical devices
Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act	Guidance on cybersecurity for medical devices
Use of Electronic Health Record Data in Clinical Investigations Guidance for Industry	Qualification and classification of software

Further Questions or Feedback

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CONSIDERATIONS AND POSSIBLE FRAMEWORK FOR SAMD RISK CATEGORIZATION

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Overview

- Purpose of a Framework
- A Harmonized Understanding of Device Intended Use
- Possible Framework for Risk Categorization
- Retaining a Nuanced Approach to Understanding Device Risk

There is value in a foundational approach, harmonized vocabulary, and mutually understood considerations for addressing unique challenges associated with SaMD

- Establishing common vocabulary
- Identifying specific information for describing SaMD
- Providing criteria to categorize SaMD
- Identifying appropriate considerations during the lifecycle process of SaMD

A common framework enables all stakeholders, including regulators, to promote safe innovation and protect patient safety.

https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf

Establishing a consistent means of describing a device can help to clarify intended use and offer a foundational understanding of device risk

- "Indications for Use"
  - A statement of intended use or intended purpose that clarifies the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended
- Device Use Description
  - The specifics of where, how, and by whom a device will be deployed
- Overview of Technical Features
  - Significant features of a device should have a clear purpose within the context of the overall design and intended use.

IMDRF categorized SaMD risk based on the healthcare situation and the information provided by a SaMD

State of Healthcare situation or condition	Significance of information provided by SaMD to healthcare decision		
	Treat or diagnose	Drive clinical management	Inform clinical management
Critical	IV	III	II
Serious	III	II	I
Non-serious	II	I	I

Significance of Information Provided by SaMD to Healthcare Decision

The intended use of the information provided by SaMD in clinical management has different significance on the action taken by the user

Treat or Diagnose	Drive Clinical Management	Inform Clinical Management
• Provides a clinical decision or action without requiring further interpretation by a healthcare provider • Or provides information that is necessary for a healthcare provider to make a clinical decision or action	• The information or function provided by the SaMD will prompt or contribute to a clinical decision or action • Concerned with identifying symptoms and identifiers of a disease or condition	• The information or function provided by the SaMD does not prompt an associated clinical decision or action

State of the Healthcare Situation or Condition

The state of the healthcare situation or condition for a SaMD function is determined by the highest risk factor(s)

Critical	Serious	Non-Serious
• Accurate and/or timely diagnosis or treatment action is vital to avoid death, long-term disability or other serious deterioration of health of an individual patient or to mitigating impact to public health	• Accurate diagnosis and treatment is important but not critical for interventions to mitigate long term irreversible consequences on an individual patient's health condition or public health	• An accurate diagnosis and treatment is important but not critical for interventions to mitigate long term irreversible consequences on an individual patient's health condition or public health

Categorizing the healthcare situation and the type information provided by a SaMD can be complex

Significance of information

- Identification of symptoms versus diagnosis of an underlying disease or condition
- Transparency of provided information or decision-making

Criticality of healthcare situation

- Disease and progression
- Intervention and time criticality
- Population and users

It can be helpful to conceptualize a spectrum of risk overlaying the discreet categories drawn by the proposed framework

State of the Healthcare Situation or Condition	Significance of the Information Provided by the 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

Risk categorization may change if a device is modified, has multiple functions, or if our clinical or technological understanding changes

- Categorization at the highest applicable risk category when:
  - A SaMD may be used across multiple healthcare situations or conditions
  - A SaMD may provide multiple functions or information of different significance

- Risk categorization may need to be revisited if:
  - A device is modified during its lifecycle
  - Understanding of a healthcare situation or condition changes
  - Understanding of the risk posed by certain technologies changes

A harmonized framework for understanding SaMD is a starting point, not an ending point

- SiMD – “Software in a Medical Device”
- Medical device accessory software
- Adaptive software
- Complex, interoperable systems
- Device security

Further Questions or Feedback

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OVERVIEW OF APPROACH TO TECHNICAL ASSESSMENT OF SOFTWARE AS A MEDICAL DEVICE (SAMD)

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Overview

- An Introduction to Case Study: “SaMD x”
- Reaching Technical Review
- Risk-Based Approach to Documentation
- Overview of SaMD Documentation to Support Technical Review
- Additional Considerations and Special Cases

"SaMD x" is a Software Application intended to provide neurocognitive tests to aid in the assessment and management of mild traumatic brain injury (TBI)

SaMD x:

- Can be run on a desktop computer or certain tablets
- Measures certain aspects of neurocognitive function, such as reaction time and memory
- Records the patient's symptoms of concussion
- Is only intended as an adjunctive tool to evaluate cognitive function
- Is for use by healthcare professionals

The regulatory requirements that apply to “SaMD x” may differ depending on the product’s risk and intended use

- Apply regulatory oversight to software functions that are medical devices and whose functionality could pose a risk to a patient's safety

  - Certain software functions were excluded from the definition of a medical device in the United States
  - Certain software functions are understood to be low risk, and the US FDA has chosen to exercise enforcement discretion
  - Certain SaMDs are understood to be low risk, and are exempt from pre-market notification requirements in the United States

Regulatory requirements that apply to “SaMD x” are focused on the software; the platform it runs on may not be a regulated medical device

- Consider “functionality of the software” rather than “platform”
    - SaMDs may be run on computing platforms that are not regulated medical devices

We take a risk-based approach when reviewing devices; this affects the level of documentation that may be needed for “SaMD x.”

Differences in technical documentation recommendations are predicated on effective implementation and maintenance of a Quality Management System

Information should demonstrate:

- Requirements
- Risk assessment
- Design reviews
- Change management
- Testing (plans and results)

We look for demonstration that medical device software is safe and effective for patients

Describe device design	Document design implementation	Demonstrate device testing	Show hazards identification and risk management	Provide traceability
• Overview of significant features, analyses, inputs, and outputs • Architecture design charts including modules, layers, interfaces, and their relationships	• Requirements specification • Design specification • Development and Maintenance Practices	• Unit, integration, and system level test protocols • Expected and observed results	• Management plan • Risk assessment • Management report	• Revision level history • Traceability between risk management, design, and testing documentation

- It can be helpful to align provided documentation with existing standards, such as ISO 14971 and IEC 62304
- Technical documentation can serve as a snapshot providing evidence that the software is, and will be maintained, safe over the life of the product

We look for demonstration that “SaMD x” has been designed and developed with good practices

- **Device description and architecture:** The manufacturer clearly captures how “SaMD x’s” functional modules interact with each other, how users are intended to access and interact with the device, and specific design requirements

  - The diagrams and details provided are useful to both regulators and the software development team, reducing ad hoc development practices and providing transparency

We look for demonstration of robust risk management throughout the design and development cycle of “SaMD x”

- **Risk management file:** “SaMD x” has a risk management plan that clearly connects software requirements and testing to risk mitigations
  - “SaMD x’s” risk evaluation includes an assessment of acceptability – some remaining risks are identified as acceptable because the intended user is a healthcare provider
  - When the manufacturer considers expanding “SaMD x’s” use by laypersons, there are clear requirements, risk mitigations, and tests to revisit

We look for demonstration that the infrastructure to maintain “SaMD x” has been established

- **Testing plans, results, and traceability:** Tests run, the requirements to which they trace, and their results, are well documented
  - “SaMD x” failed several requirement verification test cases; these are documented with record of bug fixes and retesting
  - After a minor version update during development, the subset of test cases that needed retest were easily identifiable
  - When a new feature is added, new and repeat test cases are clearly documented

We look for demonstration that “SaMD x” is validated for its intended use, considering user needs and intended use environment

Software validation can be considered:

> *Confirmation by examination and provision of objective evidence that software specifications conform to user needs and intended uses, and that the particular requirements implemented through software can be consistently fulfilled.*[1]

Based on the risk posed by the device, consider the “level of confidence” that may be needed

1. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-principles-software-validation

Validation testing helps to establish that "SaMD x" meets its intended use

"SaMD x" is intended to be used by healthcare providers in a clinic or hospital.

Validation testing might demonstrate that:

- "SaMD x" can be adequately used by any healthcare provider included in the intended user population
- Implemented test and questionnaire modules, and combinations thereof, are adequately sensitive to the cognitive effects of mild TBI for the intended patient population
- "SaMD x" can send/receive data per the established user requirements
- "SaMD x" can perform adequately in a clinic setting on the range of indicated compatible platforms

Certain software may have unique considerations that may need to be addressed to adequately demonstrate safety and effectiveness

Use of novel or complex technologies, such as machine learning	• What if “SaMD x” included a continuously learning machine learning algorithm to refine or expand its outputs?
Incorporation of off-the-shelf software	• What if “SaMD x” includes a test module that wasn’t developed by “SaMD x’s” manufacturer?
Cybersecurity risk	• What if “SaMD x” is provided on a tablet without internet access versus provided as an app downloaded onto users’ personal devices?
Device interoperability	• What if “SaMD x” is intended to gather data from other medical devices?

The US FDA has issued several public documents to help navigate these recommendations

"Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices"

"Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning-Based Software as a Medical Device"

"General Principles of Software Validation"

"Good Machine Learning Practice for Medical Device Development: Guiding Principles"

"Content of Premarket Submissions for Management of Cybersecurity in Medical Devices"

"Off-The-Shelf Software Use in Medical Devices"

Further Questions or Feedback

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