MDS-G23

Guidance on Software as a Medical Device

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Foreword

IMDRF is a voluntary group of medical device regulators from around the world who have come together to accelerate international medical device regulatory harmonization and convergence.

SFDA has adopted the internationally converged principles related to Software as a Medical Device (SaMD) agreed upon by the IMDRF. The principles used in this document do not reflect SFDA regulatory requirements and are intended only to be considerations for SFDA, manufacturers and healthcare providers.

These principles are included in the following documents:

1. Software as a Medical Device (SaMD): Key Definitions
2. Software as a Medical Device: Possible Framework for Risk Categorization and Corresponding Considerations
3. Software as a Medical Device (SaMD): Application of Quality Management System
4. Software as a Medical Device (SaMD): Clinical Evaluation

IMDRF International Medical Device Regulators Forum

Final Document

Title: Software as a Medical Device (SaMD): Key Definitions

Authoring Group: IMDRF SaMD Working Group

Date: 9 December 2013

Despina Spanou, IMDRF Chair

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Preface

The document herein was produced by the International Medical Device Regulators Forum (IMDRF), a voluntary group of medical device regulators from around the world. The document has been subject to consultation throughout its development.

1.0 Introduction

Software is becoming increasingly important and pervasive in healthcare. Given the availability of a multitude of technology platforms (e.g., personal computers, smart phones, network servers, etc.), as well as increasing ease of access and distribution (e.g., internet, cloud), software created for medical purposes (software used to make clinical decisions) and non-medical purpose (e.g., administrative, financial) are being used in healthcare.

In general, existing regulations address public health risks of software when embedded in a traditional medical device. However, the current application of regulations and controls may not always translate or address the unique public health risks posed by Software as a Medical Device (SaMD) nor assure an appropriate balance between patient/consumer protection and promotion of public health by facilitating innovation.

This is the first of a collection of documents that will be developed by the International Medical Device Regulators Forum (IMDRF) to establish a common framework for regulators to incorporate converged controls into their regulatory approaches for SaMD..

This collection of IMDRF SaMD documents will provide regulators with the fundamental building blocks and a common understanding of the many kinds and importance of software for medical purposes in advancing public health. Generally medical purpose software[1] consists of:

(1) software in a medical device (sometimes referred to as “embedded” or “part of”);
(2) software as a medical device (SaMD).

This document IMDRF SaMD WG N10/Software as a Medical Device[2]: Key Definitions focuses on a common definition for when software is considered to be a medical device and a reminder of other key terms, some previously defined in Global Harmonization Task Force (GHTF) documents, with relevance to SaMD. The key definitions and terms developed in IMDRF SaMD WG N10 will be used to develop future documents that provide a common framework for identifying types of SaMD and associated risks and controls to minimize these risks.

Some regulators have taken individual approaches to assure safety, effectiveness, and performance of SaMD. Such approaches have common public health goals. The objective of this effort is to promote consistent expectations for SaMD and to provide an optimal level of patient safety while fostering innovation and ensuring patients and providers have continued access to advances in healthcare technology.

[1] Software used to make or maintain a device (testing, source code management, servicing, etc.) is not considered software with a medical purpose.

[2] This IMDRF document converges on the term SaMD to replace the term “standalone software” or “standalone medical device software”. However the concepts of standalone software are included in this converged definition of SaMD.

2.0 Scope

This document IMDRF SaMD WG N10/Software as a Medical Device: Key Definitions focuses on a common definition for when software is considered to be a medical device and a reminder of other key terms, some previously defined in Global Harmonization Task Force (GHTF) documents, with relevance to SaMD.

Software intended as an accessory to a medical device is not in the scope of this document, unless the software meets the definition of SaMD in this document.

This document focuses on the definition of the SaMD irrespective of software technology and/or platform (e.g., mobile app, cloud).

3.0 References

- GHTF/SG1/N55:2008 *Definition of the Terms Manufacturer, Authorised Representative, Distributor and Importer*
- GHTF/SG1/N70:2011 *Label and Instructions for Use for Medical Devices*
- GHTF/SG1/N71:2012 *Definition of Terms Medical Device and In Vitro Diagnostic Medical Device*
- ISO/IEC 14764:2006 *Software Engineering — Software Life Cycle Processes — Maintenance*

4.0 Definitions

This section is intentionally left blank as the definitions are contained within the body of this document.

5.0 Key Definitions

5.1 Software as a Medical Device

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[3]
- "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.

5.2 Medical purpose

The following two terms as defined in GHTF/SG1/N71:2012 (*italicized below*) identify medical purpose applicable to SaMD:

5.2.1 Medical Device

'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

- *diagnosis, prevention, monitoring, treatment or alleviation of disease,*
- *diagnosis, monitoring, treatment, alleviation of or compensation for an injury,*
- *investigation, replacement, modification, or support of the anatomy or of a physiological process,*
- *supporting or sustaining life,*
- *control of conception,*

[3] "Computing platforms" include hardware and software resources (e.g. operating system, processing hardware, storage, software libraries, displays, input devices, programming languages etc.).
"Operating systems" that SaMD require may be run on a server, a workstation, a mobile platform, or other general purpose hardware platform.

- *disinfection of medical devices,*
- *providing information by means of in vitro examination of specimens derived from the human body;*

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.

Note: *Products which may be considered to be medical devices in some jurisdictions but not in others include:*

- *disinfection substances,*
- *aids for persons with disabilities,*
- *devices incorporating animal and/or human tissues,*
- *devices for.in-vitro fertilization or assisted reproduction technologies.*

5.2.2 In Vitro Diagnostic (IVD) medical device

'In Vitro Diagnostic (IVD) medical device' means a medical device, whether used alone or in combination, intended by the manufacturer for the in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes.

Note 1: *IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological status.*

Note2: *In some jurisdictions, certain IVD medical devices may be covered by other regulations.*

5.2.3 Additional considerations for SaMD

SaMD may also:

- provide means and suggestions for mitigation of a disease;
- provide information for determining compatibility, detecting, diagnosing, monitoring or treating physiological conditions, states of health, illnesses or congenital deformities;
- be an aid to diagnosis, screening, monitoring, determination of predisposition; prognosis, prediction, determination of physiological status.

5.3 SaMD Changes

SaMD Changes refer to any modifications made throughout the lifecycle of the SaMD including the maintenance phase.

Software maintenance[4] can include adaptive (e.g. keeps pace with the changing environment), perfective (e.g. recoding to improve software performance), corrective (e.g. corrects discovered problems), or preventive (e.g. corrects latent faults in the software product before they become operational faults).

Examples of SaMD changes include, but are not limited to, defect fixes; aesthetic, performance or usability enhancements; and security patches.

5.4 SaMD Manufacturer

For SaMD manufacturer the definition in GHTF/SG1/N55:2009 applies:

"Manufacturer" means any natural or legal person[5] with responsibility for design and/or manufacture of a medical device with the intention of making the medical device available for use, under his name; whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by another person(s).

NOTES:

1. *This 'natural or legal person' has ultimate legal responsibility for ensuring compliance with all applicable regulatory requirements for the medical device in the countries or jurisdictions where it is intended to be made available or sold, unless this responsibility is specifically imposed on another person by the Regulatory Authority (RA) within that jurisdiction.*
2. *The manufacturer's responsibilities are described in other GHTF guidance documents. These responsibilities include meeting both pre-market requirements*

[4] ISO/IEC 14764:2006 Software Engineering — Software Life Cycle Processes — Maintenance

- adaptive maintenance: the modification of a software product, performed after delivery, to keep a software product usable in a changed or changing environment.
- perfective maintenance: the modification of a software product after delivery to detect and correct latent faults in the software product before they are manifested as failures
- corrective maintenance: the reactive modification of a software product performed after delivery to correct discovered problems
- preventive maintenance: the modification of a software product after delivery to detect and correct latent faults in the software product before they become operational faults

[5] The term "person" that appears here and in the other definitions of this document, includes legal entities such as a corporation, a partnership or an association.

and post-market requirements, such as adverse event reporting and notification of corrective actions.

3. *'Design and/or manufacture', as referred to in the above definition, may include specification development, production, fabrication, assembly, processing, packaging, repackaging, labelling, relabelling, sterilization, installation, or remanufacturing of a medical device; or putting a collection of devices, and possibly other products, together for a medical purpose.*
4. *Any person who assembles or adapts a medical device that has already been supplied by another person for an individual patient, in accordance with the instructions for use, is not the manufacturer, provided the assembly or adaptation does not change the intended use of the medical device.*
5. *Any person who changes the intended use of, or modifies, a medical device without acting on behalf of the original manufacturer and who makes it available for use under his own name, should be considered the manufacturer of the modified medical device.*
6. *An authorised representative, distributor or importer who only adds its own address and contact details to the medical device or the packaging, without covering or changing the existing labelling, is not considered a manufacturer.*
7. *To the extent that an accessory is subject to the regulatory requirements of a medical device*[6]*, the person responsible for the design and/or manufacture of that accessory is considered to be a manufacturer.*

5.5 Intended use / intended purpose

For SaMD intended use, the definition in GHTF/SG1/N70:2011 "Label and Instructions for Use for Medical Devices" applies:

The term "intended use / intended purpose" is the objective intent of the manufacturer regarding the use of a product, process or service as reflected in the specifications, instructions and information provided by the manufacturer.

5.5.1 Additional considerations for SaMD

Although not specifically included in the GHTF definition materials such as sales and marketing materials may be considered as "information provided by the manufacturer" and therefore reflect the objective intent of the manufacturer. Sales and marketing materials should be comprehensive and reflect the intended use of the SaMD.

[6] See GHTF/SG1/N29 *Information Document Concerning the Definition of the Term "Medical Device"*

IMDRF International Medical Device Regulators Forum

Final Document

Title: "Software as a Medical Device": Possible Framework for Risk Categorization and Corresponding Considerations

Authoring Group: IMDRF Software as a Medical Device (SaMD) Working Group

Date: 18 September 2014

Jeffrey Shuren, IMDRF Chair

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Preface

The document herein was produced by the International Medical Device Regulators Forum (IMDRF), a voluntary group of global medical device regulators from around the world. The document has been subject to consultation throughout its development.

1.0 Introduction

Software is playing an increasingly important and critical role in healthcare with many clinical and administrative purposes.

Software used in healthcare operates in a complex socio-technical environment—consisting of software, hardware, networks, and people—and frequently forms part of larger systems that must operate in a unified manner. This software frequently depends on other commercial off-the-shelf (COTS) software and on other systems and data repositories for source data.

A subset of software used in healthcare meets the definition of a medical device; globally, regulatory authorities regulate such software accordingly.

Existing regulations for medical device software are largely focused on medical device software that is embedded in dedicated hardware medical devices and are focused around physical harm, transmission of energy and/or substances to or from the body, the degree of invasiveness to the body, closeness to sensitive organs, duration of use, diseases, processes and public health risk, competence of user and effect on population due to communicable diseases, etc.

Today, medical device software is often able to attain its intended medical purpose independent of hardware medical devices. It is increasingly being deployed on general-purpose hardware and delivered, in diverse care settings, on a multitude of technology platforms (e.g., personal computers, smart phones, and in the cloud) that are easily accessible. It is also being increasingly interconnected to other systems and datasets (e.g., via networks and over the Internet).

The complexity of medical device software, together with the increasing connectedness of systems, results in emergent behaviors not usually seen in hardware medical devices.

This introduces new and unique challenges. For example:

- Medical device software might behave differently when deployed to different hardware platforms.
- Often an update made available by the manufacturer is left to the user of the medical device software to install.
- Due to its non-physical nature (key differentiation), medical device software may be duplicated in numerous copies and widely spread, often outside the control of the manufacturer.

Furthermore, there are lifecycle aspects of medical device software that pose additional challenges. For instance, software manufacturers often:

- Have rapid development cycles,
- Introduce frequent changes to their software, and
- Deliver updates by mass and rapid distribution.

This document is focused on a selected subset of medical device software. This software is called *Software as a Medical Device* (SaMD) and is defined in *IMDRF SaMD WG N10 / Software as a Medical Device: Key Definitions.*

Definition: Software as a Medical Device[1]

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.

The objective of this document is to introduce a foundational approach, harmonized vocabulary and general and specific considerations for manufacturers, regulators, and users alike to address the unique challenges associated with the use of SaMD.

The approach developed in this document is intended only to establish a common understanding for SaMD and can be used as reference. This document is not intended to replace or modify existing regulatory classification schemes or requirements. Further efforts are required prior to the use of this foundational approach for possible regulatory purposes.

2.0 Scope

Purpose of the document

The purpose of the document is to introduce a foundational approach, harmonized vocabulary and general and specific considerations, for manufacturers, regulators, and users alike to address the unique challenges associated with the use of SaMD by;

- Establishing common vocabulary and an approach for categorizing SaMD;
- Identifying specific information for describing SaMD in terms of the significance of the information provided by the SaMD to the healthcare decision, healthcare situation or condition, and core functionality;
- Providing criteria to categorize SaMD based on the combination of the significance of the information provided by the SaMD to the healthcare decision and the healthcare situation or condition associated with SaMD; and

[1] See Section 3.0 for full definition including notes.

- Identifying appropriate considerations, during the lifecycle process (requirements, design, development, testing, maintenance and use) of SaMD.

Field of application

- The categorization system in this document applies to SaMD defined in the related document, *IMDRF SaMD WG N10 / Software as a Medical Device: Key Definitions* and does not address other types of software.

- Software intended as an accessory to a medical device (i.e., software that does not in itself have a medical purpose) is not in the scope of this document.

- This document focuses on the SaMD irrespective of software technology and/or the platform (e.g., mobile app, cloud, server).

- This document does not address software that drives or controls a hardware medical device.

Relationship to other regulatory classification and standards[2]

- This document is not intended to replace or create new risk management practices rather it uses risk management principles (e.g., principles in international standards) to identify generic risks for SaMD.

- The categorization framework in this document is not a regulatory classification, nor implies a convergence of classifications rules. However, it does set a path towards common vocabulary and approach. Additional work is required to align existing classification rules with this framework.

- The categorization framework is not meant to replace or conflict with the content and/or development of technical or process standards related to software risk management activities.

[2] Additional details can be found in Appendix 0.

3.0 Definitions

3.1 Software as a Medical Device

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.*[3]
- *"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.*

3.2 Intended use / Intended Purpose

For SaMD intended use, the definition in GHTF/SG1/N70:2011 "Label and Instructions for Use for Medical Devices" applies:

The term "intended use / intended purpose" is the objective intent of the manufacturer regarding the use of a product, process or service as reflected in the specifications, instructions and information provided by the manufacturer.

3.3 Medical Purpose

The following two terms as defined in GHTF/SG1/N71:2012 "Definition of the Terms 'Medical Device' and 'In Vitro Diagnostic (IVD) Medical Device" (*italicized below*) identify medical purpose applicable to SaMD:

3.3.1 Medical Device

'Medical device' means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the

[3] "Computing platforms" include hardware and software resources (e.g. operating system, processing hardware, storage, software libraries, displays, input devices, programming languages etc.).
"Operating systems" that SaMD require may be run on a server, a workstation, a mobile platform, or other general purpose hardware platform.

manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

- *diagnosis, prevention, monitoring, treatment or alleviation of disease,*
- *diagnosis, monitoring, treatment, alleviation of or compensation for an injury,*
- *investigation, replacement, modification, or support of the anatomy or of a physiological process,*
- *supporting or sustaining life,*
- *control of conception,*
- *disinfection of medical devices,*
- *providing information by means of in vitro examination of specimens derived from the human body;*

and does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.

Note: *Products which may be considered to be medical devices in some jurisdictions but not in others include:*

- *disinfection substances,*
- *aids for persons with disabilities,*
- *devices incorporating animal and/or human tissues,*
- *devices for in vitro fertilization or assisted reproduction technologies.*

3.3.2 In Vitro Diagnostic (IVD) Medical Device

'In Vitro Diagnostic (IVD) medical device' means a medical device, whether used alone or in combination, intended by the manufacturer for the in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes.

Note 1: *IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological status.*

Note2: *In some jurisdictions, certain IVD medical devices may be covered by other regulations.*

3.3.3 Additional considerations for SaMD

SaMD may also:

- *Provide means and suggestions for mitigation of a disease.*
- *Provide information for determining compatibility, detecting, diagnosing, monitoring or treating physiological conditions, states of health, illnesses or congenital deformities.*
- *Aid to diagnosis, screening, monitoring, determination of predisposition; prognosis, prediction, determination of physiological status.*

3.4 SaMD Changes

SaMD changes refer to any modifications made throughout the lifecycle of the SaMD including the maintenance phase.

Software maintenance[4] can include adaptive (e.g. keeps pace with the changing environment), perfective (e.g. recoding to improve software performance), corrective (e.g., corrects discovered problems), or preventive (e.g., corrects latent faults in the software product before they become operational faults).

Examples of SaMD changes include, but are not limited to, defect fixes; aesthetic, performance or usability enhancements; and security patches.

4.0 SaMD Background and Aspects Influencing Patient Safety

There are many aspects in an ever-increasing complex clinical use environment that can raise or lower the potential to create hazardous situations to patients. Some examples of these aspects include:

- The type of disease or condition
- Fragility of the patient with respect to the disease or condition
- Progression of the disease or the stage of the disease/condition
- Usability of the application
- Designed towards a specific user type
- Level of dependence or reliance by the user upon the output information
- Ability of the user to detect an erroneous output information
- Transparency of the inputs, outputs and methods to the user
- Level of clinical evidence available and the confidence on the evidence
- The type of output information and the level of influence on the clinical intervention
- Complexity of the clinical model used to derive the output information
- Known specificity of the output information
- Maturity of clinical basis of the software and confidence in the output
- Benefit of the output information vs. baseline

[4]ISO/IEC 14764:2006 Software Engineering — Software Life Cycle Processes — Maintenance

- adaptive maintenance: the modification of a software product, performed after delivery, to keep a software product usable in a changed or changing environment
- perfective maintenance: the modification of a software product after delivery to detect and correct latent faults in the software product before they are manifested as failures
- corrective maintenance: the reactive modification of a software product performed after delivery to correct discovered problems
- preventive maintenance: the modification of a software product after delivery to detect and correct latent faults in the software product before they become operational faults

- Technological characteristics of the platform the software are intended to operate on
- Method of distribution of the software

Although many of these aspects may affect the importance of the output information from SaMD, only some of these aspects can be identified by the intended use of SaMD. Generally these aspects can be grouped into the following two major factors that provide adequate description of the intended use of SaMD:

A. Significance of the information provided by the SaMD to the healthcare decision, and
B. State of the healthcare situation or condition.

When these factors are included in the manufacturer's description of intended use, they can be used to categorize SaMD.

Section 6.0 provides a structured approach for a SaMD definition statement to describe the intended use. Section 7.0 provides a method for categorizing SaMD based on the major factors identified in the definition statement.

Other aspects that are not included in the two major factors (e.g., transparency of the inputs used, technological characteristics used by particular SaMD, etc.), although still important, do not influence the determination of the category of SaMD. These other aspects influence the identification of considerations that are unique to a specific approach/method used by the manufacturer of a particular category of SaMD. For example, the type of a platform, that is constantly changing, used in the implementation of SaMD may create considerations that are unique to that implementation. These considerations can also vary by the capabilities of the manufacturer or by the process rigor used to implement the SaMD. Appropriate considerations of these aspects by the manufacturers, users and other stakeholders can significantly minimize patient safety risks.

Section 8.0 provides general considerations and section 9.0 provides specific considerations that when taken into account can promote safety in the creation, implementation and use of SaMD.

5.0 Factors Important for SaMD Characterization

5.1 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.

5.1.1 To treat or to diagnose

Treating and diagnosing infers that the information provided by the SaMD will be used to take an immediate or near term action:

- To treat/prevent or mitigate by connecting to other medical devices, medicinal products, general purpose actuators or other means of providing therapy to a human body

- To diagnose/screen/detect a disease or condition (i.e., using sensors, data, or other information from other hardware or software devices, pertaining to a disease or condition).

5.1.2 To drive clinical management

Driving clinical management infers that the information provided by the SaMD will be used to aid in treatment, aid in diagnoses, to triage or identify early signs of a disease or condition will be used to guide next diagnostics or next treatment interventions:

- To aid in treatment by providing enhanced support to safe and effective use of medicinal products or a medical device.
- To aid in diagnosis by analyzing relevant information to help predict risk of a disease or condition or as an aid to making a definitive diagnosis.
- To triage or identify early signs of a disease or conditions.

5.1.3 To Inform clinical management

Informing clinical management infers that the information provided by the SaMD will not trigger an immediate or near term action:

- To inform of options for treating, diagnosing, preventing, or mitigating a disease or condition.
- To provide clinical information by aggregating relevant information (e.g., disease, condition, drugs, medical devices, population, etc.)

5.2 Healthcare Situation or Condition

5.2.1 Critical situation or condition

Situations or conditions where 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. SaMD is considered to be used in a critical situation or condition where:

- The type of disease or condition is:
  - Life-threatening state of health, including incurable states,
  - Requires major therapeutic interventions,
  - Sometimes time critical, depending on the progression of the disease or condition that could affect the user's ability to reflect on the output information.
- Intended target population is fragile with respect to the disease or condition (e.g., pediatrics, high risk population, etc.)
- Intended for specialized trained users.

5.2.2 Serious situation or condition

Situations or conditions where accurate diagnosis or treatment is of vital importance to avoid unnecessary interventions (e.g., biopsy) or timely interventions are important to mitigate long term irreversible consequences on an individual patient's health condition or public health. SaMD is considered to be used in a serious situation or condition when:

- The type of disease or condition is:
  - Moderate in progression, often curable,
  - Does not require major therapeutic interventions,
  - Intervention is normally not expected to be time critical in order to avoid death, long-term disability or other serious deterioration of health, whereby providing the user an ability to detect erroneous recommendations.
- Intended target population is NOT fragile with respect to the disease or condition.
- Intended for either specialized trained users or lay users.

  Note: SaMD intended to be used by lay users in a "serious situation or condition" as described here, without the support from specialized professionals, should be considered as SaMD used in a "critical situation or condition".

5.2.3 Non-Serious situation or condition

Situations or conditions where 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. SaMD is considered to be used in a non-serious situation or condition when:

- The type of disease or condition is:
  - Slow with predictable progression of disease state (may include minor chronic illnesses or states),
  - May not be curable; can be managed effectively,
  - Requires only minor therapeutic interventions, and
  - Interventions are normally noninvasive in nature, providing the user the ability to detect erroneous recommendations.
- Intended target population is individuals who may not always be patients.
- Intended for use by either specialized trained users or lay users.

6.0 SaMD Definition Statement

The intended use of SaMD is normally reflected in various sources such as the manufacturer's specifications, instructions, and other information provided by the manufacturer.

The purpose of the SaMD definition statement and the components identified below are to provide an organized factual framework. Statement "A" and "B" are to help the SaMD developer determine the SaMD category in the categorizing framework, while statement "C" is to help the manufacturer manage changes to SaMD that may result in change of the category and to address considerations specific to SaMD.

The SaMD definition statement should include a clear and strong statement about intended use, including the following:

A. The "**significance of the information provided by the SaMD to the healthcare decision**" which identifies the intended medical purpose of the SaMD. The statement

should explain how the SaMD meets one or more of the purposes described in the definition of a medical device[5], e.g. supplying information for diagnosis, prevention, monitoring, treatment etc. **This statement should be structured in the following terms as defined in section 5.1.**

- Treat or diagnose
- Drive clinical management
- Inform clinical management

B. The "**state of the healthcare situation or condition**" that the SaMD is intended for. **This statement should be structured in the following terms as defined in section 5.2.**

- Critical situation or condition
- Serious situation or condition
- Non-serious situation or condition

C. **Description of the SaMD's core functionality**[6] which identifies the critical features/functions of the SaMD that are essential to the intended significance of the information provided by the SaMD to the healthcare decision in the intended healthcare situation or condition. This description should include only the critical features. (See applicability of this in section 8.0, 9.0).

7.0 SaMD Categorization

This section provides an approach to categorize SaMD based on the factors identified in the SaMD definition statement.

7.1 Categorization Principles

The following are necessary principles important in the categorization approach of SaMD.

- The categorization relies on an accurate and complete SaMD definition statement.
- The determination of the categories is the combination of the significance of the information provided by the SaMD to the healthcare decision and the healthcare situation or condition.
- The four categories (I, II, III, IV) are based on the levels of impact on the patient or public health where accurate information provided by the SaMD to treat or diagnose, drive or inform clinical management is vital to avoid death, long-term disability or other serious deterioration of health, mitigating public health.
- The categories are in relative significance to each other. Category IV has the highest level of impact, Category I the lowest.

[5] IMDRF key definitions Final document "medical purposes" also repeated here in Section 3.3.
[6] These could include specific functionality that is critical to maintain performance and safety profile, attributes identified by risk management process undertaken by the manufacturer of SaMD.

- When a manufacturer's SaMD definition statement states that the SaMD can be used across multiple healthcare situations or conditions it is categorized at the highest category according to the information included in the SaMD definition statement.
- When a manufacturer makes changes to SaMD[7], during the lifecycle that results in the change of the definition statement, the categorization of SaMD should be reevaluated appropriately. The SaMD is categorized according to the information included in the changed (new) SaMD definition statement.
- SaMD will have its own category according to its SaMD definition statement even when a SaMD is interfaced with other SaMD, other hardware medical devices, or used as a module in a larger system.

7.2 SaMD Categories

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

7.3 Criteria for Determining SaMD Category

Criteria for Category IV –

i. SaMD that provides information to treat or diagnose a disease or conditions in a critical situation or condition is a Category IV and is considered to be of very high impact.

Criteria for Category III –

i. SaMD that provides information to treat or diagnose a disease or conditions in a serious situation or condition is a Category III and is considered to be of high impact.

ii. SaMD that provides information to drive clinical management of a disease or conditions in a critical situation or condition is a Category III and is considered to be of high impact.

Criteria for Category II –

i. SaMD that provides information to treat or diagnose a disease or conditions in a non-serious situation or condition is a Category II and is considered to be of medium impact.

[7] "SaMD changes" are defined in section 3.4

ii. SaMD that provides information to drive clinical management of a disease or conditions in a serious situation or condition is a Category II and is considered to be of medium impact.

iii. SaMD that provides information to inform clinical management for a disease or conditions in a critical situation or condition is a Category II and is considered to be of medium impact.

Criteria for Category I –

i. SaMD that provides information to drive clinical management of a disease or conditions in a non-serious situation or condition is a Category I and is considered to be of low impact.

ii. SaMD that provides information to inform clinical management for a disease or conditions in a serious situation or condition is a Category I and is considered to be of low impact.

iii. SaMD that provides information to inform clinical management for a disease or conditions in a non-serious situation or condition is a Category I and is considered to be of low impact.

7.4 Examples of SaMD:

The examples below are intended to help illustrate the application of the framework and resulting categories.

Category IV:

- SaMD that performs diagnostic image analysis for making treatment decisions in patients with acute stroke, i.e., where fast and accurate differentiation between ischemic and hemorrhagic stroke is crucial to choose early initialization of brain-saving intravenous thrombolytic therapy or interventional revascularization.

  This example uses criteria IV.i from Section 7.3 in that the information provided by the above SaMD is used to treat a fragile patient in a critical condition that is life threatening, may require major therapeutic intervention, and is time sensitive.

- SaMD that calculates the fractal dimension of a lesion and surrounding skin and builds a structural map that reveals the different growth patterns to provide diagnosis or identify if the lesion is malignant or benign.

  This example uses criteria IV.i from Section 7.3 in that the information provided by the above SaMD is used to diagnose a disease that may be life threatening, may require major therapeutic intervention, and may be time sensitive.

- SaMD that performs analysis of cerebrospinal fluid spectroscopy data to diagnose tuberculosis meningitis or viral meningitis in children.

  This example uses criteria IV.i from Section 7.3 in that the information provided by the above SaMD is used to diagnose a disease in a fragile population with possible broader public health impact that may be life threatening, may require major therapeutic intervention, and may be time sensitive.

- SaMD that combines data from immunoassays to screen for mutable pathogens/pandemic outbreak that can be highly communicable through direct contact or other means.

  This example uses criteria IV.i from Section 7.3 in that the information provided by the above SaMD is used to screen for a disease or condition with public health impact that may be life threatening, may require therapeutic intervention and may be time critical.

Category III:

- SaMD that uses the microphone of a smart device to detect interrupted breathing during sleep and sounds a tone to rouse the sleeper.

  This example uses criteria III.i from Section 7.3 in that the information provided by the above SaMD is used to treat a condition where intervention is normally not expected to be time critical in order to avoid death, long term disability or other serious deterioration of health.

- SaMD that is intended to provide sound therapy to treat, mitigate or reduce effects of tinnitus for which minor therapeutic intervention is useful.

  This example uses criteria III.i from Section 7.3 in that the information provided by the above SaMD is used to treat a condition that may be moderate in progression, may not require therapeutic intervention and whose treatment is normally not expected to be time critical.

- SaMD that is intended as a radiation treatment planning system as an aid in treatment by using information from a patient and provides specific parameters that are tailored for a particular tumor and patient for treatment using a radiation medical device.

  This example uses criteria III.ii from Section 7.3 in that the information provided by the above SaMD is used as an aid in treatment by providing enhanced support to the safe and effective use of a medical device to a patient in a critical condition that may be life threatening and requires major therapeutic intervention.

- SaMD that uses data from individuals for predicting risk score in high-risk population for developing preventive intervention strategies for colorectal cancer.

  This example uses criteria III.ii from Section 7.3 in that the information provided by the above SaMD is used to detect early signs of a disease to treat a condition that may be

life-threatening disease impacting high-risk populations, may require therapeutic intervention and may be time critical.

- SaMD that is used to provide information by taking pictures, monitoring the growth or other data to supplement other information that a healthcare provider uses to diagnose if a skin lesion is malignant or benign.

  This example uses criteria III.ii from Section 7.3 in that the information provided by the above SaMD is used as an aid to diagnosing a condition that may be life-threatening, may require therapeutic intervention and may be time critical by aggregating relevant information to detect early signs of a disease.

Category II:

- SaMD that analyzes heart rate data intended for a clinician as an aid in diagnosis of arrhythmia.

  This example uses criteria from II.ii Section 7.3 in that the information provided by the above SaMD is used to aid in the diagnosis of a disease of a condition that may be moderate in progression, may not require therapeutic intervention and whose treatment is normally not expected to be time critical.

- SaMD that interpolates data to provide 3D reconstruction of a patient's computer tomography scan image, to aid in the placement of catheters by visualization of the interior of the bronchial tree; in lung tissue; and placement of markers into soft lung tissue to guide radiosurgery and thoracic surgery.

  This example uses criteria II.ii from Section 7.3 in that the information provided by the above SaMD is used to aid in the next treatment intervention of a patient where the intervention is not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

- SaMD that uses data from individuals for predicting risk score for developing stroke or heart disease for creating prevention or interventional strategies.

  This example uses criteria II.iii from Section 7.3 in that the information provided by the above SaMD is used to detect early signs of a disease to treat a condition that is not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

- SaMD that integrates and analyzes multiple tests utilizing standardized rules to provide recommendations for diagnosis in certain clinical indications, e.g., kidney function, cardiac risk, iron and anemia assessment.

  This example uses criteria II.ii from Section 7.3 in that the information provided by the above SaMD is used to detect early signs of a disease to treat a condition that is not

normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

Note: This example includes both serious and potentially non-serious conditions but per the categorization principle in Section 7.1 when a manufacturer's SaMD definition statement states that the SaMD can be used across multiple healthcare situations or condition it will be categorized at the highest category according to the SaMD definition statement.

- SaMD that helps diabetic patients by calculating bolus insulin dose based on carbohydrate intake, pre-meal blood glucose, and anticipated physical activity reported to adjust carbohydrate ratio and basal insulin.

  This example uses criteria II.ii from Section 7.3 in that the information provided by the above SaMD is used to aid in treatment of a condition not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

Category I:

- SaMD that sends ECG rate, walking speed, heart rate, elapsed distance, and location for an exercise-based cardiac rehabilitation patient to a server for monitoring by a qualified professional.

  This example uses criteria I.ii from Section 7.3 in that the information provided by the above SaMD is an aggregation of data to provide clinical information that will not trigger an immediate or near term action for the treatment of a patient condition that is not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

- SaMD that collects data from peak-flow meter and symptom diaries to provide information to anticipate an occurrence of an asthma episode**.**

  This example uses criteria I.ii from Section 7.3 in that the information provided by the above SaMD is an aggregation of data to provide best option to mitigate a condition that is not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

- SaMD that analyzes images, movement of the eye or other information to guide next diagnostic action of astigmatism.

  This example uses criteria I.i from Section 7.3 in that the information provided by the above SaMD is an aggregation of data to provide clinical information that will not trigger an immediate or near term action for the treatment of a patient condition that

even if not curable can be managed effectively and whose interventions are normally noninvasive in nature.

- SaMD that uses data from individuals for predicting risk score (functionality) in healthy populations for developing the risk (medical purpose) of migraine (non-serious condition.

  This example uses criteria I.i from Section 7.3 in that the the information provided by the above SaMD is an aggregation of data to provide clinical information that will not trigger an immediate or near term action for the treatment of a patient condition that even if not curable can be managed effectively and whose interventions are normally noninvasive in nature.

- SaMD that collects output from a ventilator about a patient's carbon dioxide level and transmits the information to a central patient data repository for further consideration.

  This example uses criteria I.ii from Section 7.3 in that the the information provided by the above SaMD is an aggregation of data to provide clinical information that will not trigger an immediate or near term action for the treatment of a patient condition that is not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

- SaMD that stores historical blood pressure information for a health care provider's later review.

  This example uses criteria I.ii from Section 7.3 in that the information provided by the above SaMD is an aggregation of data to provide clinical information that will not trigger an immediate or near term action for the treatment of a patient condition that is not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

- SaMD intended for image analysis of body fluid preparations or digital slides to perform cell counts and morphology reviews.

  This example uses criteria I.ii from Section 7.3 in that the information provided by the above SaMD is an aggregation of data to provide clinical information that will not trigger an immediate or near term action for the treatment of a patient condition that is not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

- SaMD intended for use by elderly patients with multiple chronic conditions that receives data from wearable health sensors, transmits data to the monitoring server, and identifies higher-level information such as tachycardia and signs of respiratory infections based on established medical knowledge and communicates this information to caregivers.

  This example uses criteria I.ii from Section 7.3 in that the information provided by the above SaMD is an aggregation of data to provide clinical information that will not trigger an immediate or near term action for the treatment of a patient condition that is

not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

- SaMD that uses hearing sensitivity, speech in noise, and answers to a questionnaire about common listening situations to self-assess for hearing loss.

  This example uses criteria from I.ii Section 7.3 in that the information provided by the above SaMD is an aggregation of data to provide clinical information that will not trigger an immediate or near term action for the treatment of a patient condition that is not normally expected to be time critical in order to avoid death, long-term disability, or other serious deterioration of health.

8.0 General Considerations for SaMD

SaMD often forms part of a clinical workflow sequence in order to improve diagnosis, treatment and patient management. However, issues with the design and/or implementation of SaMD into a workflow can lead to users making incorrect choices / decisions and can cause delays in decisions being made - this may lead to adverse consequences for patients.

Developing SaMD that are safe entails identifying risks and establishing measures that give confidence that the risks are acceptable. It is generally accepted that testing of software is not sufficient to determine that it is safe in operation. As a consequence, it is recognized that confidence should be built into software in order to assure its safety.

IEC 62304 is a standard for life-cycle development of medical device software. The standard specifies a risk-based decision model, defines some testing requirements, and highlights three major principles that promote safety relevant to SaMD:

- Risk management;
- Quality management; and
- Methodical and systematic systems engineering according to best industry practices.

The combination of these concepts allows SaMD manufacturers to follow a clearly structured and consistently repeatable decision-making process to promote safety for SaMD.

Further information on these major principles is provided below followed by discussion on some specific considerations in the areas of:

- Socio-technical environment
- Technology and system environments
- Information security with respect to safety

8.1 Design and development

Manufacturers should select and implement an adequate process for the planning, design, development, deployment, and documenting of robust and dependable software commensurate

with risk—as informed by its intended purpose, reasonable foreseeable use, and the understood and defined socio-technical environment of use.

	*Safety needs to be addressed early in the design and development process.*

Development of software in a quality-assured manner should consider the appropriate selection and implementation of system design and development methods that:

- Include a methodical and systematic development process using models, methods, architecture, and design-modelling techniques appropriate for the development language(s) and the device's intended purpose,
- Cover the various software lifecycle stages through the application of software development standards, e.g., IEC 62304, and use of software engineering guidebooks, e.g., SWEBoK guide, SEBoK guide, and
- Systematically and methodically document the design and development process (using tools as appropriate.)

8.1.1 Post Market Surveillance

Software risks can never be totally eliminated so SaMD manufacturers should continually monitor customer issues to maintain the safety level. A monitoring process should include ways to capture customer feedback, e.g., through inquiries, complaints, market studies, focus groups, servicing, etc. The inherent nature of software including SaMD allows for efficient methods to understand and capture user experiences. It is recommended that SaMD manufacturers utilize these feedback techniques to understand failure modes and perform analysis to address safety situations. It is also recommended that SaMD manufacturers extend their monitoring to automatically detect errors of the software or system, i.e., discover and recover from an error before a failure can occur.

General considerations associated with the monitoring of SaMD include:

1. Due to its non-physical nature, a SaMD may be duplicated and numerous copies and widely spread, often outside the control of the manufacturer.

2. Often an update made available by the manufacturer is left to the user of the SaMD to install. Manufacturers should make sure that appropriate mitigations address any risks that arise from the existence of different versions of the SaMD on the market.

3. Incident investigations should consider any specific case or combination of use cases that may have contributed to the failure and as appropriate manufacturers should consider accident reconstruction principles, e.g., data logging, black box recorder, etc.[8]

8.2 Changes

Manufacturers of SaMD are expected to have an appropriate level of control to manage changes. Due to the non-physical nature of software, a software change management process needs specific considerations to achieve the intended result regarding traceability and documentation.

These specific considerations include:

- Socio-technical environment considerations
- Technology and system environment considerations
- Information security with respect to safety considerations

	*SaMD changes may have a significant unforeseeable effect on the healthcare situation or condition and socio-technical environment of use if not managed systematically, not only with respect to a design change in itself, but also to the impact of the changed software after it is installed and implemented.*

With any product lifecycle, change is inevitable. Failures occur and may be due to errors, ambiguities, oversights or misinterpretation of the specification that the software is intended to satisfy, carelessness or incompetence in writing code, inadequate testing, incorrect or unexpected usage of the software or other unforeseen problems. An SaMD may also fail with changes to the running environment. Changes to SaMD or its operating environment can affect its safety, quality and performance.

SaMD changes refer to any modifications made throughout the lifecycle of the SaMD including the maintenance phase. The nature of software maintenance changes can include adaptive (e.g. keeps pace with the changing environment), perfective (e.g. recoding to improve software performance), corrective (e.g. corrects discovered problems), or preventive changes (e.g. corrects latent faults in the software product before they become operational faults). These changes should be clearly identified and defined with a method of tracing the change to the specific affected software.

In order to effectively manage the changes and their impact, manufacturers must perform a risk assessment to determine if the change(s) affect the SaMD categorization and the core functionality of the SaMD as outlined in the definition statement.

8 Leveson, N. 2012. *Engineering a Safer World: Systems Thinking Applied to Safety*. Cambridge, MA, USA: MIT Press.

Changes should undergo appropriate verification and validation before being released by the manufacturer for use.

Examples of software changes (some may be considered significant and others not):

- Modification to an algorithm affecting the diagnosis or therapy delivered;
- A software change that affects the way data is read or interpreted by the user, such that the treatment or diagnosis of the patient may be altered when compared to the previous version of the software;
- Addition of a new feature to the software that may change the diagnosis or therapy delivered to the patient;
- A software change that incorporates a change to the operating system or change to the configuration on which the SaMD runs;
- A software change that affects clinical workflow.

9.0 Specific Considerations for SaMD

9.1 Socio-technical environment considerations

The term socio-technical environment concerns the SaMD's setting of use - often comprising hardware, networks, software, and people. More formally, it may be characterized into spatial (e.g., location), activity (e.g., workflow), social (e.g., responsibility), technological (e.g., devices, systems, data sources, and connections), and physical (e.g., ambient conditions) components[9].

SaMD supplies information and/or a structure for information.

	*The proper and safe functioning of SaMD is highly dependent on a sufficient and common understanding of the socio-technical environment that includes the manufacturer and the user.*

Manufacturers should be aware of the socio-technical environment where inadequate considerations could lead to incorrect, inaccurate, and/or delayed diagnoses and treatments;

[9] (Adapted from IEC 62366)

and/or additional cognitive workload (which may, over time, make clinicians more susceptible to making mistakes)[10].

Similarly, users should also be aware of the socio-technical environment as presumed and designed for (limitations of the SaMD's capabilities) and by the manufacturer, as not being aware may lead to overreliance or other inaccurate use of the SaMD.

For example:

- If the user does not have sufficient skills and expertise for correct operation of the SaMD, possible inaccurate output data may not be questioned. The same may happen if the user becomes habituated and over-reliant on SaMD over time.
- The introduction of SaMD sometimes changes clinical workflows in unanticipated ways; these changes may be detrimental to patient safety.
- The user may seek alternate pathways to achieve a particular functionality, otherwise called a *workaround*. When workarounds circumvent built-in safety features of a product, patient safety may be compromised.

Considerations for the manufacturer when identifying effects/implications and appropriate measures to safety and performance of SaMD throughout the product's design, development, and installation:

- Transparency of information on limitations with algorithms, clinical model, quality of data used to build the models, assumptions made, etc. can help users question the validity of output of the SaMD and avoid making incorrect or poor decisions;

- Integrating SaMD within real-world clinical workflows (including sufficient involvement of users from all relevant disciplines) requires attention to *in situ* use and tasks to ensure appropriate use of safety features;

- SaMD (and other systems connected to the SaMD) may be configured by the user in different ways than intended or foreseen by the manufacturer;

- Though not specific to SaMD, design of the user interface including: whether designs are overly complex (e.g., multiple, complicated screens), the appropriateness of designs for the target platform (e.g., smart phone screen versus desktop monitor), the dynamic nature of data (e.g., showing information at appropriate times and for an appropriate duration);

[10] Leveson, N. 2012. *Engineering a Safer World: Systems Thinking Applied to Safety*. Cambridge, MA, USA: MIT Press.

- Though not specific to SaMD, identification of appropriate means to display information such that it is understood by the intended user (e.g., usability including regionalization parameters, language translation, and selection/display of units);
- Communicating relevant information to the user (based on the activities conducted above) for the purpose of:
    - Enabling the user to decide whether or not the user can use the device in the organization in terms of available hardware, competence, network, required quality for data input. And, if he/she decides to do this, information necessary to do those measures in order to use it: inform users, establish different routines, obtain necessary hardware.
    - Enabling correct installation and configuration of SaMD for appropriate integration with clinical workflows.

9.2 Technology and system environment considerations

Technology and system environment refers to the ecosystem where the SaMD resides, including installed systems, interconnections, and hardware platform(s). Instructions on how to verify the appropriateness of installation of and update to SaMD as well as any changes made to the system environment (e.g., hardware and software) should be provided to the user. Reliance on hardware over which the manufacturer does not have control (operating systems not designed for a medical purpose, general-purpose hardware, networks and servers, Internet, links) should be considered and addressed by the manufacturer during design and development of SaMD (for instance, by designing robust and resilient SaMD designs).

	*SaMDs are always dependant on a hardware platform and often a connected environment. SaMD can be affected by cross-link interconnections – both physical connections and interoperability, i.e., the seamless communication between devices, technology and people.*

Disruption in the ecosystem (e.g., resulting from service disruptions, systems maintenance or upgrades, platform failures) can result in loss of information, delayed, corrupted, or mixed patient information, or inaccurate information which may lead to incorrect or inaccurate diagnoses and/or treatments.
For example: an incorrect diagnosis is made after the connection to a clinical dataset was lost because the patient diagnosis data is not available.

Considerations for the manufacturer when identifying effects/implications to safety and performance of SaMD:

- Connections to other systems (e.g., reliability of the connection, resilience, quality of service, access, security, load capacity of connections to other systems and connection methods, system integration)

- Presenting information to the users and system integrators about the system requirements and resultant performance of the SaMD (e.g., the effect that changes to firewall rules might have on the operation of the system)
- Hardware platform(s)—such as smart phones, PC, servers—(e.g., reliability, dependencies, and interconnections with others hardware and software);
- Operating system(s) platform—such as Windows, GNU/Linux—compatibility; and
- Modifications and changes to the SaMD integration (e.g., platform updates) may have effects on SaMD that the manufacturer did not anticipate/foresee.

9.3 Information security with respect to safety considerations

Information security may be defined as the preservation of confidentiality, integrity and availability of information[11].

	*Incorrect management or transmission of information by an SaMD can lead to incorrect or delayed diagnosis or treatment.*

SaMD may be affected by particular factors relating to information security that may affect the integrity, availability, or accessibility of information output from the SaMD needed for correct diagnosis or treatment:

- SaMD are typically used by a variety of users with different access needs, e.g., restricted access or varying information security requirements
- Platforms where a SaMD is installed typically runs many other software applications.
- SaMD are typically connected to the Internet, networks, databases, or servers with varying information security requirements.

Considerations for the manufacturer when identifying implications for safety and performance of SaMD:

- The SaMD information security and privacy control requirements may need to be balanced with the need for timely information availability.

[11] (From ISO/IEC 27000:2009 - Information technology — Security techniques — Information security management systems — Overview and vocabulary)

- Information security requires the identification and implementation of safe (and formalized) ways to store, convert and/or transmit data.
- The design should use appropriate control measures to address data integrity when common information is accessed by multiple applications and users.
- Manufacturers should make it feasible for users to safely implement information security updates.
- The protection of sensitive information requires support for sufficient access control and appropriate restriction to system settings and assets for important data.
- The design should address possible adverse system interactions with the inclusion of appropriate resilience and robustness measures.
- Instructions for users related to information security should include how to safely:
    - Install SaMD in appropriate operating environments (e.g., OS, integration of other software);
    - Manage authentication mechanisms; and
    - Update security software/spyware, operating environments, and other systems and applications, etc.

10.0 Appendix

10.1 Clarifying SaMD Definition

This Appendix provides a representative list of features and functionalities that either meet or don't meet the definition of SaMD. This list is not exhaustive; it is only intended to provide clarity and assistance in identifying when a feature or functionality is considered to be SaMD.

Examples of software that are SaMD:

- Software with a medical purpose that operates on a general purpose computing platform, i.e., a computing platform that does not have a medical purpose, is considered SaMD. For example, software that is intended for diagnosis of a condition using the tri-axial accelerometer that operates on the embedded processor on a consumer digital camera is considered a SaMD.
- Software that is connected to a hardware medical device but is not needed by that hardware medical device to achieve its intended medical purpose is SaMD and not an accessory to the hardware medical device. For example, software that allows a commercially available smartphone to view images for diagnostic purposes obtained from a magnetic resonance imaging (MRI) medical device is SaMD and not an accessory to MRI medical device.

- The SaMD definition notes states that "SaMD is capable of running on general purpose (non-medical purpose) computing platforms." SaMD running on these general purpose computing platform could be located in a hardware medical device, For example, software that performs image post-processing for the purpose of aiding in the detection of breast cancer (CAD - computer-aided detection software) running on a general purpose computing platform located in the image-acquisition hardware medical device is SaMD.

- The SaMD definition notes states that "SaMD may be interfaced with other medical devices, including hardware medical devices and other SaMD software, as well as general purpose software." Software that provides parameters that become the input for a different hardware medical device or other SaMD is SaMD. For example, treatment planning software that supplies information used in a linear accelerator is SaMD.

Examples of software that are not SaMD:

- The SaMD definition states "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". Examples of software that are considered "part of" include software used to "drive or control" the motors and the pumping of medication in an infusion pump; or software used in closed loop control in an implantable pacemaker or other types of hardware medical devices. These types of software, sometimes referred to as "embedded software", "firmware", or "micro-code" are, not SaMD".

- Software required by a hardware medical device to perform the hardware's medical device intended use is not SaMD even if/when sold separately from the hardware medical device.

- Software that relies on data from a medical device, but does not have a medical purpose, e.g., software that encrypts data for transmission from a medical device is not SaMD.

- Software that enables clinical communication and workflow including patient registration, scheduling visits, voice calling, video calling is not SaMD.

- Software that monitors performance or proper functioning of a device for the purpose of servicing the device, e.g., software that monitors X-Ray tube performance to anticipate the need for replacement; or software that integrates and analyzes laboratory quality control data to identify increased random errors or trends in calibration on IVDs is not SaMD.

- Software that provides parameters that become the input for SaMD is not SaMD if it does not have a medical purpose. For example, a database including search and query functions by itself or when used by SaMD is not SaMD.

10.2 Analysis of SaMD framework with existing classifications

This Annex is intended to clarify the following:

A – Categorization of SaMD relative to medical device classification

There are different classification schemes for different purposes.

Typically classification is based on a set of parameters/questions that assigns the object of interest into groups that suit a certain purpose.

Classifications may have the purpose to determine, for example

- Appropriate levels of regulatory oversight such as requirements for
    - Levels of third party intervention
    - Levels of conformity controls
    - Levels of quality system
- Appropriate levels of technical measures, for example
    - Technical protective means, e.g., for
        - Laser protection 1,2 or 3
        - electrical isolation, protective earth or double insulated
        - ingress of liquids, IP XX

Classification of medical devices is commonly focused on regulatory controls based on risk classes.

Categorization for SaMD, as in the case of laser protection, is only identifying different categories of SaMD by level of impact. Categorization in this document by itself does not imply regulatory controls needed to manage risks. It is only intended to provide guidance for appropriate considerations for SaMD**.**

B - Relationship between this document and GHTF documents.

It is important to note the following to understand the relationship between the categorization framework in this document and the classification principles for medical devices and in vitro diagnostic medical devices:

- GHTF classification principles, unlike this document, were intended to build classification rules for regulatory control purposes. As explained earlier, this document identifies different categories of SaMD by level of impact and does not address corresponding regulatory risk classes identified in GHTF documents.
- The high-level principles used for identifying SaMD categories build substantially on the principles (rationale) underlying the classification rules established in the GHTF classification principles documents. Key factors like individual risks, public health risks, user skills, and importance of the information provided are common to both frameworks.

11.0 References

IMDRF SaMD WG N10 / Software as a Medical Device: Key Definitions

GHTF/SG1/N70:2011 “Label and Instructions for Use for Medical Devices”

GHTF/SG1/N71:2012 “Definition of the Terms ‘Medical Device’ and ‘In Vitro Diagnostic (IVD) Medical Device”

IEC 62304:2006 - Medical device software -- Software life cycle processes

ISO/IEC 14764:2006 Software Engineering — Software Life Cycle Processes — Maintenance

Guide to the Software Engineering Body of Knowledge - SWEBOK (2004), pp. 1-202 by Alain Abran, Pierre Bourque, Robert Dupuis, James W. Moore, Leonard L. Tripp edited by Alain Abran, Pierre Bourque, Robert Dupuis, James W. Moore, Leonard L. Tripp

[SEBoK] Guide to the Systems Engineering Body of Knowledge (http://www.sebokwiki.org/)

ISO/IEC 27000:2009 - Information technology — Security techniques — Information security management systems

IEC 62366:2007 Medical devices — Application of usability engineering to medical devices

Leveson, N. ‘Engineering a Safer World: Systems Thinking Applied to Safety, MIT, USA (2011)

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Table of Contents

Preface

The document herein was produced by the International Medical Device Regulators Forum (IMDRF), a voluntary group of medical device regulators from around the world. The document has been subject to consultation throughout its development.

1.0 Introduction

The International Medical Device Regulators Forum (IMDRF) seeks to establish a common and converged understanding for software intended for medical purposes and specifically for a subset of such software that is intended to function as a medical device. The IMDRF Software as a Medical Device Working Group (WG) defines this subset of software as Software as a Medical Device (SaMD) in the *IMDRF/SaMD WG/N10* document *Software as a Medical Device (SaMD): Key Definitions*; this document is the foundation for developing a common vocabulary; it defines SaMD for both manufacturers and regulators.

The SaMD WG has also provided a framework to categorize types of SaMD based on impact to patient and public health in the *IMDRF/SaMD WG/N12* document *Software as A Medical Device: Possible Framework for Risk Categorization and Corresponding Considerations.* This framework establishes a common approach for categorizing SaMD, using criteria based on the combination of the significance of the information provided by the SaMD to the healthcare decision and on the healthcare situation or condition where the SaMD is used.

The IMDRF/SaMD WG/N12 document also highlights the use of quality management as a general consideration towards the safety, effectiveness, and performance of SaMD and as key to ensuring the predictability and quality of SaMD.

Quality Management System (QMS) principles, for many industrial sectors, can be found in the ISO 9000 family of standards. In addition, there are also a wide variety of current industry software development lifecycle methodologies, guidance documents, and standards that address best practices of the many aspects of software engineering quality practices. These principles are the foundation for good practices to maintain and control the quality of products in organizations of any size, ranging from a one-person enterprise to a multi-national corporation.

In the medical device sector it is generally accepted that following QMS requirements is one of the controls used to minimize and manage unintentional outcomes related to patient safety. QMS requirements for medical devices are defined by regulatory agencies in their regulations and in the international standard ISO 13485—*Medical Devices—Quality Management Systems—Requirements for Regulatory Purposes*.

In the software industry, good software quality and engineering practices are used to control the quality of software products. These practices may readily align with the general principles of medical device QMS requirements when the patient safety perspective is included.

This document highlights elements of good software quality and engineering practices and reinforces medical device quality principles that should be appropriately incorporated for an effective SaMD QMS.

This is a companion document to *IMDRF/SaMD WG/N10* and *N12* documents, further enabling convergence in vocabulary, approach, and a common thinking for regulators and industry.

2.0 Scope

The objective of the document is to provide guidance on the application of existing standardized and generally accepted QMS practices to SaMD. Furthermore, the purpose of this document is to:

- Inform the reader of SaMD specific practices. It assumes the reader is following generally accepted software lifecycle processes[1] and may not be familiar with medical device QMS;
- Provide guidance for the application of QMS for the governance of organizations responsible for delivering SaMD products and managing the SaMD lifecycle support processes (product planning; risk management; document and record control; configuration management and control; measurement, analysis, and improvement of processes and products; and managing outsourced processes, activities and products) and SaMD realization and use processes (requirements management, design, development, verification and validation, deployment, maintenance, and decommissioning);
- Highlight SaMD realization and use processes from the perspective of patient safety and clinical environment considerations as well as technology and systems environment considerations that should be addressed to ensure the safety, effectiveness, and performance of SaMD;
- Help manufacturers and regulators attain a common understanding and vocabulary for the application of medical device quality management system requirements to SaMD; and
- Complement the IMDRF SaMD framework for risk categorization and corresponding considerations found in *IMDRF/SaMD WG/N12*.

This document is intended for the following audience:

- Groups and/or individuals who are or want to become developers of SaMD;
- Software development organizations (large or small) that apply good software quality and engineering practices and that may not necessarily be familiar with medical device QMS requirements; and
- Organizations (divisions/departments) working within established medical device quality systems that intend to communicate the linkage between medical device quality system practice and software development practices.

Document organization and content:

- Terminology used is intended to be familiar to the software industry and illustrates how typical software-engineering activities (e.g., determining requirements) translate to equivalent activities in a medical device quality management system (e.g., identifying

[1] These lifecycle processes are intended to include commonly referred lifecycle processes such as software development lifecycle processes (SDLC), software product lifecycle processes (SPLC) and Software System lifecycle processes (SSLC).

design inputs) used in the management, design, development, implementation, monitoring, and support of SaMD;

- Sections are organized based on processes and activities commonly found in software engineering lifecycle approaches as well as on leadership and management processes of the organization as a whole;
- SaMD lifecycle support processes (Section 7) and realization and use processes (Section 8) include considerations that are necessary to address patient safety and clinical environment as well as the technology and systems environment for SaMD;
- Examples using two fictitious companies—Magna (a large organization) and Parva (a small start-up)—are provided throughout in order to highlight some of the key points being made; and
- References ISO13485:2003, a QMS standard currently published within the medical device industry.

Field of application:

- The guidance for the application of QMS provided in this document applies to SaMD as defined in *IMDRF/SaMD WG/N10* and does not address other types of software; and
- This document focuses on SaMD irrespective of technology and/or platform (mobile app, cloud, server, etc.).

This document is not intended to:

- Provide guidance on how to undertake good software quality and engineering practices or how to implement QMSs; and
- Rewrite, repeat, or contradict QMS principles that are articulated in medical device regulations or standards.

Relationship to regulatory requirements and to technical standards:

- The document does not replace or create new QMS standards, software quality and engineering practices, or regulations; rather, it highlights certain common practices and terminology used by successful software organizations;
- This document is not intended to replace or conflict with medical device legislation, regulations, or procedures required in individual regulatory jurisdictions;
- This document is not a tutorial on risk management practices for software; rather, it highlights risk management principles throughout the software lifecycle processes and activities that are critical to the safety, effectiveness, and performance of SaMD; and
- The activities highlighted in this document are not meant to replace or conflict with the content and/or development of technical or process standards related to software risk-management activities or software-development practices but may provide input to these processes and activities.

3.0 References

- IMDRF/SaMD WG/N10 - Software as a Medical Device (SaMD): Key Definitions.
- IMDRF/SaMD WG N12 - Software as a Medical Device: Possible Framework for Risk Categorization and Corresponding Considerations.
- ISO 13485:2003 – Quality management system – Requirements for regulatory purposes.

4.0 Definitions

This document does not introduce any new definitions but rather relies on the following:

- Definition of SaMD as identified in *IMDRF/SaMD WG/N10*.
- Terms typically used in standards and regulations as they relate to QMS for medical devices.
- Terms and vocabulary used in software quality and engineering practices.

5.0 SaMD Quality Management Principles

Medical device QMS principles allow for scaling of activities depending on the type of medical device; risk of the product to patients; size of the organization; technology or automation used to manufacture; and other factors that are determined by the manufacturer to control quality and maintain the safe and effective performance of the medical device.

The manufacturing of SaMD, which is a software-only product, is primarily based on the development lifecycle activities often supported by the use of automated software development tools (build automation, use of source code management tools, etc.). These automated activities may in some cases replace discrete or deliberate activities (e.g., transfer of design to production) typically found in the manufacturing of hardware products. However, the principles in a QMS that provide structure and support to the lifecycle processes and activities are still applicable and important to control the quality of SaMD.

An effective QMS for SaMD should include the following principles:

- An organizational structure that provides leadership, accountability, and governance with adequate resources to assure the safety, effectiveness, and performance of SaMD (outer circle in *Figure 1*);
- A set of SaMD lifecycle support processes that are scalable for the size of the organization and are applied consistently across all realization and use processes (middle circle in *Figure 1*); and
- A set of realization and use processes that are scalable for the type of SaMD[2] and the size of the organization; and that takes into account important elements required for assuring the safety, effectiveness, and performance of SaMD (innermost circle in *Figure 1*).

[2] As identified by IMDRF SaMD WG N12 document

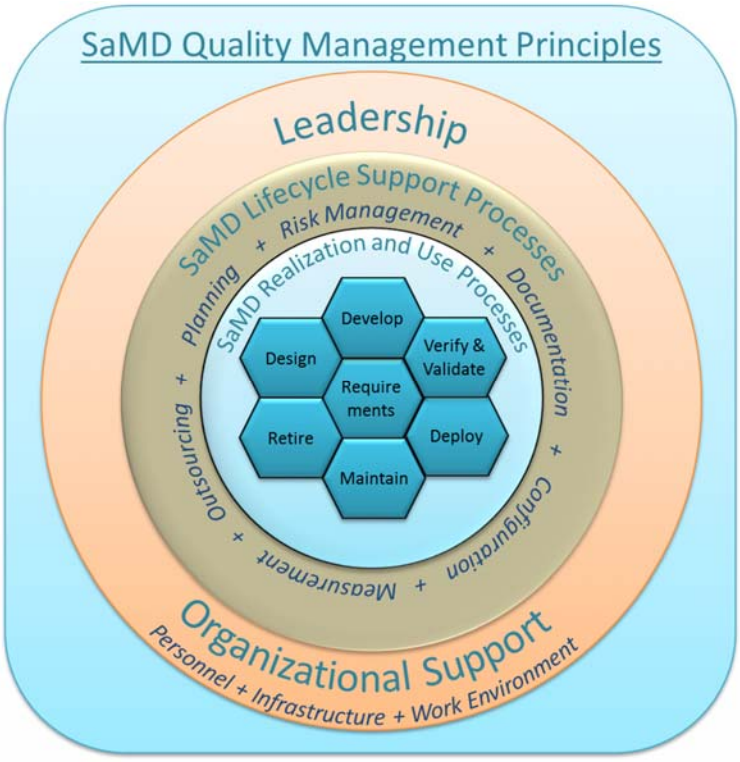


Figure 1: SaMD Quality Management Principles: *Leadership and Organization Support, Processes, and Activities*

The three principles outlined above should not be considered independently as a separate series of processes in an organization. Instead, an effective QMS establishes a distinct relationship (see *Figure 2* below) between the three principles as follows:

- The governing structure of Leadership and Organization Support should provide the foundation for SaMD lifecycle support processes; and
- The SaMD lifecycle support processes should apply across the SaMD realization and use processes.

Figure 2: Relationship between Quality Management Principles

The concepts presented in this section relate to clauses 4 *and* 5 *in ISO 13485:2003.*

6.0 SaMD Leadership and Organizational Support

6.1 Leadership and accountability in the organization

Management of the organization provides the leadership and governance of all activities related to the lifecycle processes of SaMD including defining the strategic direction, responsibility, authority, and communication to assure the safe and effective performance of the SaMD.

The organization's leadership is also responsible for implementing the QMS, which can include developing a quality policy, quality objectives, and project-specific plans that are customer focused.

The governance structure should provide support for creating and establishing appropriate processes that are important for maintaining the quality objectives and policies[3].

In addition, the governance should include activities for systematically verifying the effectiveness of the established quality management system, such as undertaking QMS internal audits. Management review of the results of the QMS audits is a tool to ensure that the established QMS is suitable, adequate, and effective and that any necessary adjustments may be made as a result.

Example: Both Magna and Parva management have responsibilities to ensure that a QMS has been established and that the necessary patient safety considerations have been built in to the QMS and managed when entering the SaMD market. In the case of Magna, the company has an organizational structure that resulted in its Chief Medical Officer being identified as being responsible for these aspects. In the case of Parva, the company has nominated its Software Development Manager to be responsible for including necessary patient safety aspects.

The concepts presented in this section relate to clauses 5 *and* 8.2.2 *in ISO 13485:2003.*

6.2 Resource and Infrastructure Management

The purpose of resource management is to provide the appropriate level of resources (including people, tools, environment, etc.), as needed for ensuring the effectiveness of the SaMD lifecycle processes and activities in meeting regulatory and customer requirements.

The concepts presented in this section relate to clause 6 *in ISO 13485:2003.*

[3] These processes should be tailored specifically towards the needs of the organizations and the level of documented processes, objectives, and policies should be adjusted appropriately for the type, size, and distributed nature of the organization.

6.2.1 People

It is important to ensure that people who are assigned to SaMD projects should be competent in performing their jobs. For SaMD, such a team should have competencies in technology and software engineering including an understanding of the clinical aspects of the use of the software.

Example: Both companies realize the importance of ensuring that there are competent employees to perform their assigned duties. In the case of Magna, there is a broader base of skills amongst the staff with the SaMD skills gap being addressed through an extension of already existing in-house training and education programs. For Parva, the skills gap was bridged by looking to other sources such as temporary recruits and external training programs.

The concepts presented in this section relate to clauses 6.1 *and* 6.2 *in ISO 13485:2003.*

6.2.2 Infrastructure and Work Environment

Infrastructure such as equipment, information, communication networks, tools, and the physical facility, etc., should be made available throughout SaMD lifecycle processes. Such infrastructure is used to support the development, production, and maintenance of SaMD and consequently needs to be provided and maintained.

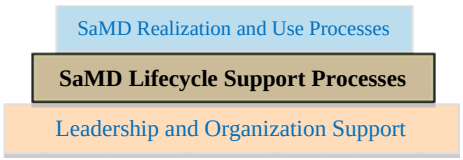
For SaMD, this may entail identifying and providing the software development and test environment that supports the SaMD realization and use processes. This may include providing a test environment that simulates the intended environment of use and tools that support managing various software configurations during the lifecycle processes, e.g., version management for source code during development.

As work environments become increasingly virtual, the reliability and dependability of the collective infrastructure environment is an important consideration (e.g., dependence on 3rd party networks and equipment).

Example: Both companies need specific environments for ensuring code and data integrity across these different infrastructure environments. In the case of Magna, existing computer networks and secure building access is leveraged directly for SaMD development. In the case of Parva, the development environment is hosted by a qualified service provider, ensuring the code and data integrity is part of the service agreement between them and the provider.

The concepts presented in this section relate to clauses 6.3 *and* 6.4 *in ISO 13485:2003.*

7.0 SaMD Lifecycle Support Processes



An organization's QMS should be built and managed around processes that support the lifecycle activities of SaMD.

This section addresses important processes that are applicable across the SaMD lifecycle, regardless of the intended use of the SaMD (i.e., significance of the information provided by the SaMD to the healthcare decision and the state of the healthcare situation or condition).

There are many available methods to conduct SaMD lifecycle processes. These processes are typically scaled to address the complexity and size of the SaMD product and project (e.g., during new product introduction or for an upgrade) that needs to be created.

The elements discussed in this section are common processes and activities that should be considered throughout the SaMD lifecycle regardless of specific software product development approach or method used by the organization.

Appropriate implementation of clearly structured and consistently repeatable decision-making processes by SaMD organizations can provide confidence that efforts to minimize patient safety risk and promote patient safety have been considered.

7.1 Product Planning

The objective of planning is to provide a roadmap to be followed during the product development lifecycle. This comes from the quality principle that better results can be achieved by following a methodical and rigorous plan for managing projects such as a plan-do-check-act approach.

Product planning includes the definition of phases, activities, responsibilities, and resources needed for developing the SaMD. It is important to understand that planning is not static—it needs to be updated when new information is gathered or milestones are reached.

IMDRF/SaMD WG/N12 identifies that for SaMD, a thorough understanding of the socio-technical[4] environment (clinical perspective), and the technology and system environment (software perspective) is important in planning, as inadequate considerations could lead to incorrect, inaccurate, and/or delayed diagnoses and treatments.[5]

The implementation of SaMD lifecycle processes should adequately be informed and tailored for the type of SaMD as identified in *IMDRF/SaMD WG/N12*.

[4] Socio-technical systems are systems that include technical systems but also operational processes and people who use and interact with the technical system. Socio-technical systems are governed by organizational policies and rules.
[5] *IMDRF SaMD WG N12*: Section 9.1—*Socio-technical environment considerations* and Section 9.2—*Technology and system environment considerations*.

Example: Both companies carry out product planning to decide which operating systems best suited their SaMD application. The larger Magna company has chosen to build its application to work on the top five mobile phone operating systems as the company has the resources to develop on multiple platforms. While the smaller Parva has chosen to develop for the platform that is currently the market leader due to the company's constraints of resources. For both Parva and Magna, this planning phase can allow each company to take deliberate approaches to the assignment of resources.

The concepts presented in this section relate to clauses 5.4, 7.1, *and* 7.3.1 *in ISO 13485:2003.*

7.2 Risk Management: A Patient Safety Focused Process

IMDRF/SaMD WG/N12 provides a possible framework to categorize types of SaMD based on impact to patient and public health. Using the foundational categorization in *IMDRF/SaMD WG/N12*, the safety, effectiveness, and performance of SaMD can be enhanced by appropriate risk management. This risk management process should be integrated across the entire lifecycle of SaMD.

Organizations that engage in general software development continuously monitor and manage schedules and budget risks of a software project. Similarly, a SaMD organization should also monitor and manage risks to patients and users across all lifecycle processes.

For SaMD, product risk should be informed by the intended purpose; the normal use and reasonably foreseeable misuse; and the understood and defined socio-technical environment of use of the SaMD. Some general considerations associated with SaMD patient safety risk include the ease with which a SaMD may be updated, duplicated, and distributed due to its non-physical nature, and where these updates, made available by the SaMD organization, may be installed by others.

Risk management in the context of this document, outlines a risk-based approach to patient safety.[6] Specifically, related to QMS, some points that should be considered include:

- Identification of hazards;
- Estimation and evaluation of associated risks;
- Actions to control risks; and
- Methods to monitor effectiveness of the actions implemented to control risks.

[6] ISO 14971:2007 is one commonly used standard that can be used to guide an appropriate medical device risk management process.

For example, it is helpful to chart sources of hazards along multiple dimensions, such as:

User-Based

Is the SaMD product appropriate for all intended users? For instance, are there hazards posed by visual acuity for an elderly user, or for patients with peripheral neuropathy? Is the device being used in a clinical or home environment?

Application-Based

Should a SaMD application be available on any device, or should it be restricted to certain devices in such a way that it could help to mitigate user risk?

Device-Based

Is a device with a smaller screen, such as a smartphone, adequate for the intended application? Can a smaller screen display a large set of information without losing the information or making it cumbersome to the users in a way that could affect patient safety?

Environment-Based

Is continuity of use (and therefore, safety) of the SaMD product compromised when there are environmental disruptions (e.g., interruptions in use, background noise, loss of network connectivity)?

Security-Based

Is analysis being performed that includes evaluating the security threats to SaMD product software code during manufacturing, maintenance and in-service use? Does this analysis also include, for example, intrusion detection, penetration testing, vulnerability scanning, and data integrity testing to minimize system and patient risks?

Software risk management requires a balanced evaluation of both safety and security. Security risks may affect the confidentiality, integrity, and availability of data handled by the SaMD. When considering mitigations to protect device security, the manufacturer should ensure that security risk controls do not take precedence over safety considerations.

Example: Both Magna and Parva know the importance of carrying out systematic risk management activities throughout their SaMD lifecycles. Magna has a dedicated department whose members ensure that the risk of the product is within acceptable limits, including considerations of patient harm. Parva has chosen to train its SaMD developers in risk-management activities and, with this knowledge, they collectively ensure that the risk of the product is within acceptable limits, including considerations of patient harm. Both of the above approaches ensure that the necessary risk management activities are carried out.

The concepts presented in this section relate to clause 7.1 *in ISO 13485:2003.*

7.3 Document and Record Control

Records are used to provide evidence of results achieved or activities performed as a part of the QMS or SaMD lifecycle processes as well as justifications for any QMS or SaMD lifecycle processes not performed. Records can be in paper or electronic form.

For SaMD lifecycle processes, document control and records management makes it easier for the users of those documents and records, both within and outside (outsourced contractors, customers, etc.) the organization, to share and collaborate in the many activities related to the SaMD lifecycle processes. Document control and records management also serves to help communicate and preserve the rationale for why certain decisions were made, such as those related to patient safety or risk management.

Records generated to demonstrate QMS conformity should be appropriately identified, stored, protected, and retained for an established period of time. The following activities are examples of ways to manage and maintain appropriate documentation in the QMS system:

- Reviewing and approving documents before use;
- Ensuring current versions of applicable documents are available at points of use to help prevent the use of obsolete documents;
- Retaining obsolete documentation for an established period;
- Controlling documents against unauthorized or unintended changes; and
- Maintaining and updating documents across all SaMD lifecycle processes.

Example: In the cases of Magna and Parva, it is important to manage and control documentation throughout the SaMD lifecycle processes. Documentation does not mean bureaucracy; rather, it is the foundation to drive traceability, repeatability, scalability, and reliability in SaMD projects. Magna uses established documentation processes and techniques that include the use of a commercially available requirements management tool throughout the SaMD lifecycle processes. Parva has re-purposed its source-code control software to enable the company to manage its documentation in a controlled way.

The concepts presented in this section relate to clause 4.2 *in ISO 13485:2003.*

7.4 Configuration Management and Control

Control of configurable items, including source code, releases, documents, software tools, etc., is important in order to maintain the integrity and traceability of the configuration throughout the SaMD lifecycle.

A systematic documentation of the SaMD and its supporting design and development, including a robust and documented configuration and change management process, is necessary to identify its constituent parts, to provide a history of changes made to it, and to enable recovery/recreation of past versions of the software, i.e., traceability of the SaMD.

For SaMD, configuration is also an important consideration to enable the correct installation and integration of the SaMD into the clinical environment. This information enables users to decide, for example, whether or not the SaMD can be used with available hardware and networks,

whether it is necessary to establish different routines and training, or whether it is necessary to obtain new or reconfigure existing hardware.

In the management of SaMD configuration, software tools are generally used to manage source code, releases, documents, deployment, maintenance, etc. In SaMD, the notion of configuration management and its complexity is amplified by the heterogeneity of the environment in which the SaMD will operate; using the right tools and techniques is important.

Example: For Magna and Parva the importance of configuration management is well understood. In both cases the companies' patients can access the SaMD products through multiple devices (e.g., smartphone, PC, and tablet) each of which require specific configurations and optimization of user experiences. The need for multi-device access enforces the importance of a robust and documented configuration management process to ensure the integrity and traceability of the various configurations across product lines.

The concepts presented in this section relate to clauses 4.2.3*,* 4.2.4*,* 7.3.7*,* 7.5.1*, and* 7.5.3 *in ISO 13485:2003.*

7.5 Measurement, Analysis, and Improvement of Processes and Products

Measurement of quality characteristics of software products and processes is used to manage and improve product realization and use. An effective measurement of key factors, often associated with issues related to risk, can help identify the capabilities needed to deliver safe and effective SaMD. Opportunities to monitor, measure, and analyze for improvement exist before, during, and after SaMD lifecycle processes, activities and tasks, and are completed with the intent to objectively demonstrate the quality of the SaMD. Post market surveillance including monitoring, measurement and analysis of quality data can include logging and tracking of complaints, clearing technical issues, determining problem causes and actions to address, identify, collect, analyze, and report on critical quality characteristics of products developed. For SaMD, monitoring to demonstrate through objective measurement that processes are being followed does not itself guarantee good software, just as monitoring software quality alone does not guarantee that the objectives for a process are being achieved. Aspects important for the measurement, analysis, and improvement of SaMD processes and products include:

- Evaluation of the SaMD and its lifecycle processes should be based on defined responsibilities and predetermined activities including using leading and lagging safety indicators and collecting and analyzing appropriate quality data. The analysis of this data, such as analysis of customer complaints, problem reports, bug reports, nonconformity to product requirements, service reports, and trends of processes and products should be used to evaluate the quality of the SaMD and the quality of the SaMD lifecycle processes and where/if improvement of these processes can be made. For SaMD, customer complaints may be the major source of the quality data that the organization should analyze.

- Corrections and corrective actions may be required when a process is not correctly followed or the SaMD does not meet its specified requirements (i.e., when a nonconforming process or product exists).
- Nonconforming SaMD should be contained to prevent unintended use or delivery. The detected nonconformity should be analyzed and actions taken to eliminate the detected nonconformity (i.e., correction); and to identify and eliminate the cause(s) of the detected nonconformity (i.e., corrective action) to prevent recurrence of the detected nonconformity in the future. In some cases a potential nonconformity may be identified, and actions such as safeguards and process changes can be taken, to prevent nonconformities from occurring (i.e., preventive action).
- Actions taken to address the cause of SaMD nonconformities, as well as actions taken to eliminate potential SaMD nonconformities, should be verified/validated before SaMD release and should be evaluated for effectiveness.
- Lessons learned from the analysis of past projects, including the results from internal or external audits of the SaMD lifecycle processes, can be used to improve the safety, effectiveness, and performance of SaMD. The manufacturer should also have processes in place for the collection of active and passive post market surveillance information in order to make appropriate decisions relating to future releases.
- After the product is in the market, it is important to maintain vigilance for vulnerability to intentional and unintentional security threats as part of post market surveillance.

Example: Customer feedback is an important part of monitoring the performance to improve the product over time. Both Magna and Parva are in the process of developing a new and improved version of their SaMD. Magna has a dedicated department that works independently but in conjunction with sales, marketing, and product development to formally survey its large customer base to gain insights into product performance. In the case of Parva, the company invites some of its early adopters and customers into an office to conduct a round-table discussion to get to the same kind of feedback. Both companies also use embedded analytical tools to gain insights into customer behavior with respect to their use of their respective products. They also routinely review and evaluate customer complaints to identify trends and potential areas for improvement. Based on the review of various sources of data, both Magna and Parva redesigned their SaMD to address common issues identified by customer feedback, complaints, and any new/updated clinical evidence.

The concepts presented in this section relate to clauses 7.2.3, 7.3.7, 7.5.1.1, 8.1, 8.2, 8.3, 8.4, *and* 8.5 *in ISO 13485:2003.*

7.6 Managing Outsourced Processes, Activities, and Products

An effective QMS system takes into account and ensures quality of SaMD when processes, activities, or products are outsourced (i.e., are not completely conducted / made in-house). An organization may choose to outsource different parts of its SaMD process, activities, or product based on its in-house strengths and competencies. Similarly, an organization may procure a commercial-off-the-shelf (COTS) product or another SaMD for integration into its SaMD. In both of these instances, understanding, maintaining control, and managing the effect

of such outsourced processes, activities, or products is important and necessary to deliver safe and effective SaMD.

A SaMD organization may, for example, outsource customer service as a process, or outsource the development activity for a particular module of the SaMD. As with any outsourcing strategy, the following are considerations that are commonly achieved through the use of contractual terms in order to provide confidence in the services and products delivered to manage or mitigate patient safety risk of SaMD:

- Understand the capabilities and competencies of potential outsourcing suppliers;
- Clearly communicate the roles and responsibilities of the outsourcing supplier;
- Extensively define the quality requirements for the outsourced process, activity, or product;
- Clearly establish upfront the criteria for and review of deliverables, frequency of intermediate inspections, and relevant audits of the supplier; and
- Select and qualify the appropriate outsourcing supplier to deliver safe and effective SaMD.

When a SaMD organization plans to procure a COTS product, such as a third-party database for integration in its SaMD, or procure another SaMD to be integrated as a module, the following are examples that may enhance the understanding of the effect of these decisions and help manage the resultant effect on the SaMD:

- Understanding the capabilities and limitations of the COTS product can inform the management of the risks, design choices, and extent of verification and validation needed for the SaMD; and
- Understanding the processes/methods/frequency that the COTS manufacturer employs to update, enhance, or make corrections to its products should be used to inform the selection of the COTS product and the potential effect on the SaMD manufacturer's QMS processes and activities.

Example: Magna and Parva have historically used open-source code or other COTS code as part of product development. In the development of SaMD, it is critical for both Magna and Parva to properly verify and validate the integration of open source code or COTS code. When appropriate, it is also critical to formally evaluate, document, and periodically audit suppliers to ensure compliance with QMS requirements. Both companies are also responsible for monitoring and managing the potential for defects in the COTS, as these defects can contribute to the overall risks of the SaMD and may introduce threats to the larger system within which the SaMD resides. Regardless of the type of code that is used and who is supplying the code, Magna and Parva are ultimately responsible for the safety and performance of the SaMD.

The concepts presented in this section relate to clauses 7.4, 7.4.1, 7.4.2, 7.4.3, *and* 8.5.1 *in ISO 13485:2003.*

8.0 SaMD Realization and Use Processes

This section identifies key lifecycle processes [7] that should be identified in the methodologies used in an organization that manufactures SaMD.

The following are important perspectives that should be considered for each of the activities in this section.

- SaMD lifecycle support processes in Section 0 (product planning; risk management: a patient safety focused approach; document and record control; configuration management and control; measurement, analysis and improvement of processes and product; managing outsourced processes and products) should be applied throughout the SaMD realization and use processes.
- This section highlights those activities commonly found in software engineering lifecycle approaches (process, activities, tasks, etc.) that are important for an effective SaMD QMS.
- The activities presented in this section should be included irrespective of methodology used. The presentation of the material does not imply executing the activities in a serial fashion or as discrete phases in the SaMD project; rather, these activities should be looked upon as elements to be addressed as part of any development methodology employed.

The concepts presented in this section relate to clause 7 in ISO 13485:2003.

8.1 Requirements Management

Developing appropriate requirements helps to ensure that SaMD will satisfy the needs across the socio-technical environment including those of users and patients. These clinical needs should be clearly articulated and the requirements captured in line with the intended use of SaMD as characterized by the "state of the healthcare situation or condition" and the "significance of information provided by SaMD to the healthcare decision" and the resulting impact to patient and public health as identified in IMDRF SaMD WG N12.

This is a customer-driven process that requires clear, and often repeated, customer interaction to understand the user needs. These user needs are then translated into requirements. Well-documented requirements can then inform the testing activities later in the design cycle. There are other sources of requirements that can include regulatory or non-customer specified performance requirements.

[7] IEC 62304:2006 is one commonly used software development lifecycle standard that can be used to develop a medical device software lifecycle process.

Patient Safety and Clinical Environment Considerations

- SaMD is used in various clinical and home use environments and, consequently, in addition to functional requirements, there are requirements that include considerations of patient/user safety. Some requirements originate from the risk-management process that evaluates risks to patients and users, and which may identify mitigations that become part of the requirements.
- Further considerations need to be given to the integrity of data used in the SaMD which may result in specific requirements to ensure that data is secure and to mitigate against the loss or corruption of sensitive data.[8]
- Requirements for SaMD often need to include additional and specific requirements for performing upgrades that consider potential effects on peripheral components of the system as well as appropriate notification and coordination with customers.[9]

Technology and Systems Environment Considerations

- SaMD runs on an underlying platform and operating system, often from a third party, the functionality of which should be considered as part of the requirements, as the platforms and operating systems can be potential sources of harm.
- Requirements may also need to define non-functional aspects of a system such as service or performance related requirements for the hardware platforms that may host the SaMD or means of connecting/networking to the wider environment.
- Requirements should be captured in concert with stakeholders (patients, clinicians, end users, etc.) in the process of use of the SaMD.

Note: Requirements may change as the developer better understands how the SaMD functions in the clinical environment and how a customer uses it. Consequently, it is important to apply usability engineering principles to the formative development and testing of the software to ensure that the requirements were appropriately translated into design inputs.

Example: The definition and maintenance of requirements are important in ensuring that the product meets its intended use. For Magna and Parva, requirements serve the purpose of clearly defining what is to be developed in their respective SaMD products. In the case of Magna, a cross-functional product team leverages existing document templates to capture requirements and an existing document-review process to approve the requirements for use. In the case of Parva, screen shots, sketches, and rapid prototypes are used to refine and capture the product requirements for the SaMD features. In both cases, the requirements are captured in a way that ensures that user, patient, and regulatory requirements are satisfied/met.

The concepts presented in this section relate to clauses 7.2.1, 7.2.2, 7.2.3, 4.2, *and* 7.1d *in ISO 13485:2003.*

[8] *IMDRF SaMD WG N12*: Section 9.3—*Information security with respect to safety considerations*

[9] *IMDRF SaMD WG N12*: Section 8.2—*Changes*

8.2 Design

The purpose of the design activity is to define the architecture, components, and interfaces of the software system based on user requirements, and any other performance requirements, in line with the intended use of the SaMD and the various clinical and home use environments it is intended to operate in.

The requirements are analyzed in order to produce a description of the software's internal structure that will serve as the basis for its implementation. When complete, the SaMD design activity should describe the software architecture, i.e., how the software is decomposed and organized into its components, including considerations for safety critical elements, the interfaces between those components (and any external elements), and a sufficiently detailed description of each component.

One of the key aspects of the design process is to arrive at a clear and concise design solution that is an effective, well described (e.g., captured in software requirements specifications) logical architecture that best meets the user needs and that enables other lifecycle processes and activities such as development, verification, validation, safe deployment, and maintenance of the SaMD.

Building quality into SaMD requires that safety and security should be evaluated within each phase of the product lifecycle and at key milestones. Security threats and their potential effect on patient safety should be considered as possible actors on the system in all SaMD lifecycle activities.
The goal is to engineer a system that: a) maintains patient safety and the confidentiality, availability, and integrity of critical functions and data; b) is resilient against intentional and unintentional threats; and c) is fault-tolerant and recoverable to a safe state in the presence of an attack.

Patient Safety and Clinical Environment Considerations

- Where a SaMD will be used—in the home, at the hospital bedside, in a physician's office or clinic—the users (e.g., patients, clinicians, and others who may interact or use the SaMD) should be considered in the design activities.
- Clinical hazards already identified should be an input in the design phase.

Technology and Systems Environment Considerations

- Architectural design may be driven by the safety critical nature of SaMD and by the risk-mitigation solutions. Risk mitigation solutions may include segregation of specific functions into particular modules that are isolated from other areas/modules of the software.
- SaMD design should have appropriate controls in place to ensure robustness in the event of unanticipated upgrades of the underlying platform.
- SaMD design should include consideration and the taking of appropriate measures when integrating or using software components or infrastructure with limited or uncontrollable knowledge of capabilities and limitations, such as legacy software, undocumented application programing interfaces (API), and wireless network infrastructure.

Such measures should identify the risks that could be introduced to the SaMD product and the extent of implications to the design of the SaMD.

- External resources, sensors, and services used by high-risk aspects of the application should be abstracted such that automated testing can be performed based on consistently simulated values and that operational health considerations can be enforced as a separated concern through mitigated access and mutually understood error conditions.

Example: Magna has a structure within its software department that enables it to distribute the design of different software modules amongst different teams. These teams work in parallel to each other with the interface considerations of the modules being discussed as a specific activity at pre-defined points in the design phase. Parva use uses one multi-disciplined team to develop the design. The company develops its design in an iterative way and considers the internal interfaces as each design effort is complete. Both companies complete their design activity in a controlled and effective manner.

The concepts presented in this section relate to clauses 7.3, 7.3.2, 7.3.3, 7.3.4, 7.3.7 *and* 7.3.1b *in ISO 13485:2003.*

8.3 Development

The development activity transforms the requirements, architecture, design (including interface definition), recognized coding practices (secure), and architecture patterns into software items and the integration of those software items into a SaMD.

The result is a software item/system/product that satisfies specified requirements, architecture, and design. Good development practice incorporates appropriate review activities, (e.g. code review, peer review, creator self-review) and follows a defined implementation strategy (e.g., build new, acquire new, re-use of existing elements). Design changes resulting from the review activity or development activity should be adequately captured and communicated to ensure that other development and QMS activities remain current.

Use of appropriately qualified automated tools and supporting infrastructure is important for managing configuration and having traceability to other lifecycle activities.

Patient Safety and Clinical Environment Considerations

- The implementation of clinical algorithms adopted should be transparent to the user in order to avoid misuse or unintended use.
- The implementation of proper access controls and audit trail mechanisms should be balanced with the usability of SaMD as intended.

Technology and Systems Environment Considerations

- Development activity should leverage the inherent nature of SaMD that allows for efficient methods to understand the user's environment and prevent and manage failures.
- Attention to detail is critical in areas of underlying implementation of the algorithm—a simple data overwrite can potentially lead to an adverse event. Some examples of these

critical areas include: memory usage and allocation, dependency on communication, speed of operation, and prioritization of tasks.

- Many SaMD deal with data entry, and the methods through which data is validated and the effect on the downstream data consumer is an important SaMD consideration.
- As SaMD runs on an underlying platform, rigorous and strict adherence to development guidance as set forth by the platform developer should be followed to ensure backward compatibility.

Example: For both Magna and Parva, coding is central to the delivery of the companies' SaMD product. Magna conducts peer code reviews for SaMD by scheduling periodic peer-review sessions with multiple coders who are not directly involved with the code under review. In the case of Parva, the company does not have a large coding team, and has only one developer who is an expert in his or her chosen operating system. The company uses a technique of "design for code readability", thereby allowing the code review activity to be conducted with a member of the team who is not an expert. Both achieve what is required by good software code review guidelines including the need for independence in the review activity.

The concepts presented in this section relate to clauses 7.3, 7.3.2, 7.3.3, 7.3.4, 7.3.7 *and* 7.3.1b *in ISO 13485:2003.*

8.4 Verification and Validation

The verification and validation (V&V) activities should be targeted towards the criticality and impact to patient safety of the SaMD, as discussed in *IMDRF/SaMD WG/N12*.

Typically, verification (providing assurance that the design and development activity at each development stage conforms to the requirements) and validation (providing reasonable confidence that the software meets its intended use/user needs and operational requirements) activities ensure that all elements from the SaMD design and development—including any changes made during maintenance/upgrades—have been implemented correctly and that objective evidence of this implementation is recorded.

A defined set of V&V activities should focus on the interface of the SaMD to the operating system, outsourced components, and other dependencies related to the computing platform.

Patient Safety and Clinical Environment Considerations

- These V&V activities should include scenarios that cover the clinical user/use environment (usability, instructions for use, etc.). This can be accomplished, in part, through structured human factors testing using a subset of patients/clinicians.
- These activities should confirm that software safety elements work properly (i.e., patient safety / clinical use risk elements, etc.). These activities are also commonly included as part of user acceptance testing (UAT).
- Confirmation of acceptable failure behavior in the clinical environment should be established. This may include confirmation of the ability of the software to continue to operate in the specified degraded modes (e.g., fail-safe, fail-secure, or fail-soft).

- Consideration of a variety of user groups to ensure software can be used by persons of different demographics.

Technology and Systems Environment Considerations

- The extent of test coverage should be driven by the risk profile of the device determined by the intended use and SaMD definition statement[10].
- Interoperability of components and compatibility to other platforms/devices/interfaces, etc. with which SaMD works should be considered.
- Adequate coverage and traceability to the known hazard-related functions of SaMD should be provided.
- The coverage of boundary conditions and exceptions (robustness, stress testing, data security, integrity, and continuity of SaMD availability) should be included.
- Companies should employ rigorous impact analysis of changes made to SaMD (i.e., regression testing) to ensure updates do not compromise the safety, effectiveness, and performance of SaMD.

Example: In both Magna and Parva, testing coverage and regression testing are important. Magna has a number of test engineers that execute the test plans and regression testing while monitoring coverage. Parva invested in a test automation tool that allows continuous test/build cycle which monitors coverage and regression testing on each checked-in build. Where automation is not possible an independent software developer runs the manual test suite prior to each release. Both companies achieve the appropriate level of test coverage with the necessary levels of independence.

The concepts presented in this section relate to clauses 7.3.5, 7.3.6 *and* 7.4.3 *in ISO 13485:2003.*

8.5 Deployment

Deployment activities include aspects of delivery, installation, setup, and configuration that support a controlled and effective distribution of SaMD to the customer, including any planned risk mitigation for hazards identified throughout the SaMD lifecycle support processes and SaMD realization and use processes.

Some aspects of deployment activities may need to be performed every time a SaMD is distributed to the user (e.g., distributing an upgrade or fix as a result of maintenance activity). In some cases, especially when SaMD is a large system or is part of a large system, the deployment activities may depend on an extensive collaborative effort with the user (which can include training the users) for an effective use of SaMD or the system.

Patient Safety and Clinical Environment Considerations

- Deploying SaMD into a clinical environment can require considerations of peripheral components if it is intended to be part of a clinical IT network, such as establishing

[10] *IMDRF SaMD WG N12*: Section 6—*SaMD Definition Statement.*

platform and OS requirements as well as responsibility agreements. The deployment activity should be clearly defined for the customer as the cooperation of hospital IT, integration engineers, clinical engineers, hospital risk managers and others who often may not be part of a typical deployment of other products may often be required.

- Deployment needs to consider the end user and use environment(s) of SaMD. This would be particularly true if used in the home. The deployment activity needs to be tailored to the user's abilities and background. Appropriate human factors engineering practices can aid in understanding this aspect and would affect the user requirements capture activity.
- Where possible, user documentation and user training materials should identify any limitations with SaMD. These may include limitations of the algorithm, provenance of data used, assumptions made, etc., that should be considered during deployment.
- There should be communication of relevant information to enable correct installation and configuration of the SaMD for appropriate integration with clinical workflows. This can include instructions on how to verify the appropriateness of the installation and update to SaMD as well as any changes made to the system environment.

Technology and Systems Environment Considerations

- Deployment should also include the collection of the settings and the environment of each installation for configuration management. This information should be maintained throughout the life of SaMD at each installation.
- Deployment of SaMD when installed on specific platforms should be according to the intended use that was verified and validated.
- Processes should be in place to ensure the appropriate and correct version is delivered to the user.
- The choice of deployment method should consider the integrity of the SaMD to ensure that the software can be delivered in a secure and reliable manner.
- Deployment methods and procedures should ensure repeatability of SaMD delivery, installation, setup, configuration, intended operation, and maintenance.
- Methods that confirm that the software is delivered consistently and comprehensively and that it is used in a defined environment are also important. Non-technical measures may have to be implemented as part of the software product package for deployment.
- When deploying an update to SaMD, updating user manual(s), anomaly lists, or providing training may be necessary.

Note: Non-technical measures can include warning/confirmation dialogs, warning displays, usage notes, and user training requirements.

Example: For Both Magna and Parva, when a SaMD is deployed on 'the cloud' or a mobile platform, it is critical to ensure integrity of the deployment activity with an extended network of stakeholders. For instance, a SaMD application that is designed for use on a smart phone should be supported with proper processes and documentation that include parties such as app stores

and private app clouds, as well as third-party hosting service providers, etc. Unlike the deployment of general consumer software, for example, these extended deployment stakeholders should be qualified and integrated per the QMS requirements for outsourcing and third-party supplier management.

The concepts presented in this section relate to clauses 7.2.3, 7.5, 7.5.1.2.1, 7.5.1.2.2, 7.5.1.2.3[11] *and* 7.5.5 *in ISO 13485:2003.*

8.6 Maintenance

Maintenance includes activities and tasks to modify a previously deployed SaMD. Maintenance activities can be adaptive, perfective, preventive, and corrective activities originating from software lifecycle processes and activities including in-service monitoring, customer feedback, in-house testing or other information, or changes to user requirements or changes in the socio-technical environment.

When a previously deployed SaMD requires maintenance, all appropriate SaMD lifecycle support processes, and SaMD realization and use processes should be considered. Maintenance activities should preserve the integrity of the SaMD without introducing new safety, effectiveness, performance, and security hazards.

To effectively manage the maintenance activities and any resulting changes and their effect on SaMD, a risk assessment should be performed to determine if the change(s) affect SaMD categorization and the core functionality of SaMD as outlined in the SaMD definition statement.[12]

Patient Safety and Clinical Environment Considerations

- Within the context of SaMD it is important to understand how systems, software, context of use, usability, data, and documentation might be affected by changes, particularly with regards to safety, effectiveness, and performance.
- The SaMD manufacturer should take into account implications and introduction of patient safety risk as a result of changes to architecture and code.
- As highlighted in other SaMD lifecycle processes and SaMD lifecycle activities, people, technology, infrastructure, and new hazards resulting from implementation and use activities should be considered.
- It is important to understand the effect of the change on patient safety and the need for addressing the change in a timely manner when appropriate.

[11] For software products, capabilities like performance, security and safety heavily depend on the computing environment and platforms put in place. The use context and the processes used with the software product will generally influence the above capabilities. Though at the time of deployment or runtime the SaMD organization may have little or no technical control over such factors, the SaMD organization's hazards or mitigations analysis should consider the socio-technical aspects of the intended use and the intended/foreseeable use context of the SaMD

[12] *IMDRF SaMD WG N12* - Section 8.2 Changes

Technology and Systems Environment Considerations

- There should be processes that manage risk arising from changes to system, environment, and data.
- SaMD manufacturers should make it feasible for users to safely implement information security updates.
- Instructions for users related to information security should include how to safely update security software/spyware, operating environment, and other systems and applications, etc.

Example: Magna has a process that controls change of its SaMD through a change-control board. This is a multi-disciplined team that meets at regular intervals to review the change requests and recommend (or reject) them for incorporation in the next version of software. Parva has assigned its project manager to act as a customer representative; as part of this role, she reviews the feedback items received and adds any relevant issue to the backlog of the next release. Both companies prioritize the change requests to ensure that any significant issues are dealt with in a timely manner.

The concepts presented in this section relate to clauses 7.2.3, 7.5, 7.5.1.2.3, 7.5.4, 7.6 *and* 8.2.1 *in ISO 13485:2003.*

8.7 Decommissioning (Retirement or End-of-Life Activity)

The purpose of decommissioning activities is to terminate maintenance, support, and distribution of SaMD in a controlled and a managed fashion. Although not specifically mentioned in ISO 13485 as a clause, the standard does require planning of product realization in the design which would include decommissioning.

Decommissioning activities are important to minimize the impact to patient and public health safety as a result of retiring the SaMD. These activities may include aspects of configuration management that apply to the document; source code or the delivered SaMD; and communicating a plan to the user for gracefully terminating maintenance and support of SaMD.

This process indicates an end to active support, and may entail deactivation and/or removal of SaMD and its supporting data. The decommissioning of SaMD data is of special importance. While the product and/or access may be terminated, there may be country specific requirements for managing the data.

Patient Safety and Clinical Environment Considerations

- Provide clarity to users which services (e.g., bug fixes, updates, patches, technical support, etc.) will be available once end-of-life (EOL) is signed-off.
- Appropriately safeguard patient data and any other confidential data. This may include removal, migrating patients to a new SaMD or another product, safe archival of user information, etc.

Technology and Systems Environment Considerations

- Inform customers of important EOL milestones, with sufficient lead-time for users to find, evaluate, and qualify possible alternatives.
- Archive a user's environment in an agreed-upon state, which may include steps to protect the security and integrity of information and/or systems.

Example: For both Magna and Parva, it is necessary to have procedures that ensure effective decommissioning, documentation, and data archival for SaMD products. Both have a process that asks for a decommissioning plan to be created. This plan takes consideration of the following points to arrive at an effective solution for decommissioning a SaMD:

- *What minimum retention time periods are defined by each territory in which the devices are marketed;*
- *Will any data be migrated onto new/replacement devices/software systems and, if so, will any data conversion be needed and how will this be validated;*
- *Will the SaMD be withdrawn or will it be only a withdrawal of support for the device;*
- *How sensitive legacy data (patient information, etc.) will be securely stored; and*
- *How the users of the device that is to be decommissioned will be informed and supported.*

In this way both companies can make the appropriate decisions to effectively and gracefully plan the decommissioning of their devices.

The concepts presented in this section relate to clauses 4.2, 7, *and* 7.5.1.1 *in ISO 13485:2003.*

Appendix A: Mapping Medical Device Regulations to IMDRF/SaMD WG/N23

The following table provides a mapping of applicable clauses, articles, and subsections of the regulations for a QMS for SaMD for the jurisdictions represented in the current IMDRF SaMD WG members. It is important to note that not all jurisdictions may require demonstration of compliance to a QMS for all types of medical devices. Regulatory requirements may also permit exclusions or provide alternative arrangements to be addressed in a QMS. It is the responsibility of the organization to ensure conformity with appropriate jurisdictional regulatory requirements. The objective of this table is to share how QMS requirements map to the elements presented in the IMDRF/SaMD WG/N23 when compliance to a QMS is required in the specified jurisdictions.

Applicability to Health Canada regulations:

- The Medical Devices Regulations require class II, III and IV medical devices to be manufactured (class II) or designed and manufactured (class III & IV) under CAN/CSA ISO 13485:2003.

Applicability to Europe Union regulations:

- EU legislation foresees the QMS to be assessed by third parties only for certain classes of products.
- EN ISO 13485:2012 Annexes ZA, ZB, ZC specify in detail which parts of the relevant Annexes to Directive 90/385 (Active Implantable Medical Devices (AIMD) Directives 93/42 (Medical Device Directive (MDD) and 98/79 (In Vitro Diagnostic Directive (IVDD) align to clauses of ISO 13485:2012.
- Note: MEDDEV Guidance 2.1/6 Guidelines On The Qualification And Classification Of Stand Alone Software Used In Healthcare Within The Regulatory Framework Of Medical Devices", while not binding, constitutes a significant additional reference.

Applicability to Australian regulations:

- The *Therapeutic Goods (Medical Devices) Regulations* 2002 require manufacturers to demonstrate compliance with appropriate conformity assessment procedures as specified in Division 3.2, three of which require implementation of a QMS.
- The *Conformity assessment standards order (standard for quality management systems and quality assurance techniques) 2008* enables the use of ISO13485 to demonstrate compliance with applicable clauses of those procedures. Mapping is as per the following table key: [Code]—Procedure name (legislative reference):
    - [P5]—Product Quality Assurance procedures (Schedule 3, Part 5, Clause 5.4)
    - [P4]—Production Quality Assurance procedures (Schedule 3, Part 4, Clause 4.4)
    - [P1]—Full Quality Assurance procedures (Schedule 3, Clause Part 1, 1.4)
    - [All]—required for all (Product, Production, and Full Quality Assurance) conformity assessment procedures
- The # symbol is used to indicate clauses of ISO 13485 considered to additionally be applicable to software medical devices under Australian legislation.

N23	Topic	ISO 13485:2003	Australia	Brazil RDC 16/2013	China MD GMP ([2014]64)	Japan MHLW QMS Ordinance	US 21 CFR
5.0--SAMD QUALITY MANAGEMENT PRINCIPLES	Quality management strategy	4	All	2.1	3,24	5	820.5
	Management responsibility	5			5-7,78		
6.0--SAMD LEADERSHIP AND ORGANIZATIONAL SUPPORT							
6.1--LEADERSHIP AND ACCOUNTABILITY IN THE ORGANIZATION	Management responsibility	5	All				
	Management commitment	5.1		2.2.5, 2.2.6	6	10	820.20b
	Customer focus	5.2				11	
	Quality policy	5.3		2.2.1	6	12	820.20a
	Quality planning	5.4			6	13, 14	820.20d
	Responsibility and authority	5.5		2.2.3	5	15	820.20b1
	Management representative	5.5.2		2.2.5	7	16	820.20b3
	Internal communication	5.5.3		2.2.1		17	
	Management review	5.6		2.2.6	78	18, 19, 20	820.20c
	Internal audit	8.2.2					
6.2--RESOURCE AND INFRASTRUCTURE MANAGEMENT	Resource Management	6	All				
6.2.1--PEOPLE	Provision of resources	6.1	All	2.3	6	21	820.20b2
	Skill management	6.2		2.3	8-10	22, 23	820.25
6.2.2--INFRASTRUCTURE AND WORK ENVIRONMENT	Infrastructure	6.3	All	5.1	12-23	24	820.70f,g
	Work environment	6.4		5.1	11	25	820.70c
7.0--MANAGING SaMD LIFECYCLE SUPPORT PROCESSES							
7.1--PRODUCT PLANNING	Quality planning	5.4	All		6	13	820.20d
	Planning of product realization	7.1	All	4.1	28,29	26	820.30a, 70a
	Design planning	7.3.1	P1	4.1	28,29	30	820.30a,b

N23	Topic	ISO 13485:2003	Australia	Brazil RDC 16/2013	China MD GMP ([2014]64)	Japan MHLW QMS Ordinance	US 21 CFR
7.2--RISK MANAGEMENT: A PATIENT SAFETY FOCUSED PROCESS	Planning of product realization	7.1	All	2.4	4,38	26-5, 26-6	820.30g
7.3--DOCUMENT CONTROL AND RECORDS	Quality system record		All	3.1.6	24		820.186
	Documentation requirements - General	4.2.1			24	6	820.20e
	Quality manual	4.2.2		2.2.1	24	7	820.20e
	Document control	4.2.3		3.1	25,26	8	820.4
	Control of records	4.2.4		3.1.6.2	27	9	820.18
	Device master record			4.2	50	6-2	820.181
7.4--CONFIGURATION MANAGEMENT AND CONTROL	Document control	4.2.3	All	3.1	25,26	8	820.4
	Control of records	4.2.4	All	3.1.6.2	27	9	820.18
	Control of design and development changes	7.3.7	P1	4.1.10	37	36	820.30i
	Production and service provision - General requirements	7.5.1.1	All	5.1	45,46	40	820.70a,g, I,h
	Identification	7.5.3.1	All	6.4	51	47	820.6
	Traceability	7.5.3.2	All	6.4	53	48	820.65
	Status identification	7.5.3.3	All		52	50	820.86
7.5--MEASUREMENT, ANALYSIS AND IMPROVEMENT OF PROCESSES, ACTIVITIES AND PRODUCT	Measurement, analysis, and improvement	8	All				
	Conformity assurance	8.1		2.2.5.1, 2.2.6	78	54	820.8
	Feedback	8.2.1			66	55	
				7.2	71		820.198
				7.2.1.4, 7.2.1.5	75,76		822
	Internal audits	8.2.2		7.3	77	56	820.22
	Process monitoring	8.2.3		7.3, 2.2.6		57	820.70a
	Product monitoring	8.2.4		7.3, 2.2.6	59,60	58	820.8
	Nonconforming product	8.3		6.5	67-70	60	820.9
	Data analysis	8.4		2.2.6, 9	73	61	820.25
	Improvement	8.5					
	Improvement - General	8.5.1		2.2.1	71,76	62	

N23	Topic	ISO 13485:2003	Australia	Brazil RDC 16/2013	China MD GMP ([2014]64)	Japan MHLW QMS Ordinance	US 21 CFR
	Improvement - General	8.5.1		7.2	72,75	62	803
	Corrective action	8.5.2		7.1	74	63	820.1
	Preventive action	8.5.3		7.1	74	64	820.1
	Customer communication	7.2.3		7.2	66,71	29	
	Control of design and development changes	7.3.7	P1	4.1.10			820.70b
	Production and service provision - General requirements	7.5.1.1	All	4.1.11	62		820.184
7.6--MANAGING OUTSOURCED PROCESSES, ACTIVITIES AND PRODUCTS	Purchasing process	7.4	All	2.5	39,40	37	820.5
	Vendor evaluation	7.4.1		2.5.2	41,42	37	820.50a
	Purchasing information	7.4.2		2.5.1	43	38	820.50b
	Verification of purchased product	7.4.3		2.5.4	44		820.8
	Improvement - General	8.5.1		2.2.1	71,76	62	
	Improvement - General	8.5.1		7.2	72 ,75	62	803
8.0--SAMD REALIZATION AND USE PROCESSES							
8.1--REQUIREMENTS MANAGEMENT	Customer requirements capture	7.2.1	All	4.1.3		27	
	Contract review	7.2.2		4.1.6		28	
	Customer communication	7.2.3		7.2	66,71	29	
	Quality system record			3.1.6	24		820.186
	Documentation requirements - General	4.2.1			24	6	820.20e
	Quality manual	4.2.2		2.2.1	24	7	820.20e
	Document control	4.2.3		3.1	25,26	8	820.4
	Control of records	4.2.4		3.1.6.2	27	9	820.18
	Documentation requirements - General	4.2.1		4.2	50	6-2	820.181
	Requirements records	7.1d			24		
8.2--DESIGN + 8.3--DEVELOPMENT	Design and development	7.3	P1				
	Design inputs	7.3.2		4.1.3	30	31	820.30c
	Design and development outputs	7.3.3		4.1.5	31	32	820.30d
	Design and development outputs	7.3.3		4.1.11			820.30j
	Design review	7.3.4		4.1.6	33	33	820.30e
	Design transfer	7.3.1b		4.1.7	32	30-3-2	820.30h
	Control of design and development changes	7.3.7			37	36	

N23	Topic	ISO 13485:2003	Australia	Brazil RDC 16/2013	China MD GMP ([2014]64)	Japan MHLW QMS Ordinance	US 21 CFR
8.4--VERIFICATION AND VALIDATION	Design verification	7.3.5	P1	4.1.4	34	34	820.30f
	Design validation	7.3.6	P1	4.1.8	35,36	35	820.30g
	Verification of purchased product	7.4.3	All	2.5.6	44	39	820.80b
8.5—DEPLOYMENT	Customer communication	7.2.3	All	7.2	66,71	29	
	Production and service provision						
	Contamination control	7.5.1.2.1		6.2.1	48	41	820.70e
	Installation	7.5.1.2.2		8.1	65	42	820.17
	Distribution	7.5.5		6.3	62		820.16
	Servicing	7.5.1.2.3		8.2	64	43	820.2
8.6--MAINTENANCE	Customer communication	7.2.3	All	7.2	66,71	29	
	Production and service provision						
	Servicing	7.5.1.2.3		8.2	64	43	820.2
	Customer property (confidential health information)	7.5.4				51	
	Monitoring & measuring devices	7.6		5.4	56-58	53	820.72
	Feedback	8.2.1			66	55	
8.7--DECOMMISSIONING	Control of records	4.2.4	All	3.1.6	24		820.186
	Documentation requirements - General	4.2.1			24	6	820.20e
	Quality manual	4.2.2		2.2.1	24	7	820.20e
	Document control	4.2.3		3.1	25,26	8	820.4
	Control of records	4.2.4		3.1.6.2	27	9	820.18
	Production and service provision - General requirements	7.5.1.1		4.2	50	6-2	820.181
	Product realization	7					

The following clauses are not specifically addressed in this document:

N23	Topic	ISO 13485:2003 [13, 14]	Australia [15]	Brazil RDC 16/2013	China MD GMP ([2014]64)	Japan MHLW QMS Ordinance	US 21 CFR
These clauses are not specifically addressed by N23	Control of production and service provisions	7.5.1.2	All[#]		47	41	
	Process validation	7.5.2	P1[#], P4[#]		49	45	820.75
	Traceability documentation	7.5.3.2.1	All[#]			48	
	Requirements for active implantable	7.5.3.2.2				49	
	Status identification	7.5.3.3	All[#]			50	
	Device packaging	7.5.5	All[#]		55	52	820.13
	Handling	7.5.5	All[#]		55		820.14
	Storage	7.5.5	All[#]		55		820.15
	Monitoring and measurement	8.2.4.1	All[#]			58	
	Monitoring and measurement of active implantable	8.2.4.2				59	
	Sterilization records	7.5.1.3				44	820.184
	Production personnel						820.70d
	Production and service provision - General requirements	7.5.1.1	P1[#], P4[#]				820.12
	Issue and implementation of advisory notices		All[#]				806
	Medical device tracking						821
	Device classification						860
	Label design						801

IMDRF International Medical Device Regulators Forum

Final Document

Title: Software as a Medical Device (SaMD): Clinical Evaluation

Authoring Group: Software as a Medical Device Working Group

Date: 21 September 2017

J. Patrick Stewart, IMDRF Chair

Table of Contents

Preface

The document herein was produced by the International Medical Device Regulators Forum (IMDRF), a voluntary group of medical device regulators from around the world. The document has been subject to consultation throughout its development.

1.0 Executive Summary

This document is the fourth issued by the International Medical Device Regulatory Forum (IMDRF) that provides a path for global regulators to converge on terminology, a risk-based framework, an understanding of quality management system principles, and in this document, an approach to making Software as a Medical Device (SaMD) clinically meaningful to users[1]. This document focuses on the activities needed to clinically evaluate SaMD -- and relies on the reader to gain knowledge from the previous documents as a pre-requisite to this document.

This document, and previous documents, provides harmonized principles for individual jurisdictions to adopt based on their own regulatory framework. They are not regulations.

This document describes a converged approach for planning the process for clinical evaluation of a SaMD (software with a medical purpose as defined in *SaMD N10*[1][2]), as illustrated in Figure 1, to establish that:

- There is a valid clinical association between the output of a SaMD and the targeted clinical condition (to include pathological process or state); and
- That the SaMD provides the expected technical and clinical data.

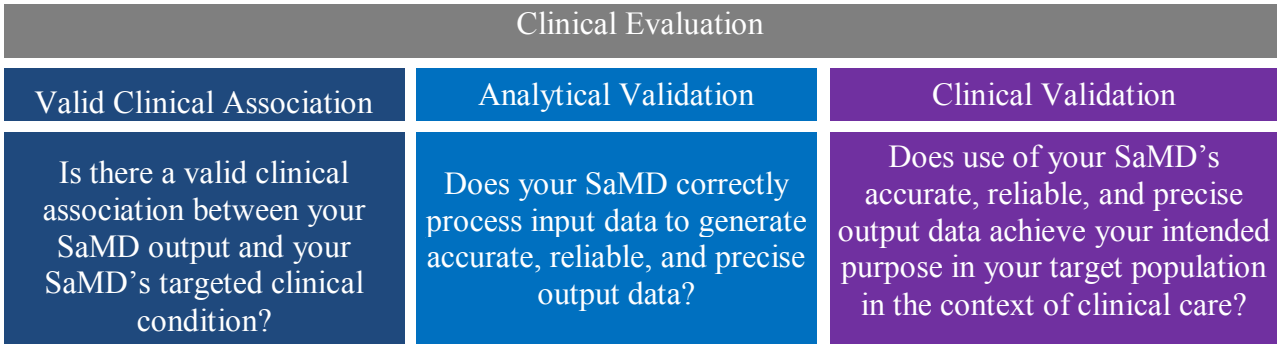


Figure 1 - Clinical Evaluation Process

The knowledge gained from previous documents is critical to the understanding of information in this document. This document builds on previously introduced vocabulary, risk-based considerations, and SaMD lifecycle processes and activities to help emphasize the clinical considerations essential to the success and adoption of SaMD as illustrated in Figure 2.

[1] Users include patients, healthcare providers, specialized professionals, lay users, consumers.
[2] Internet addresses (URLs) can be found in the References section.

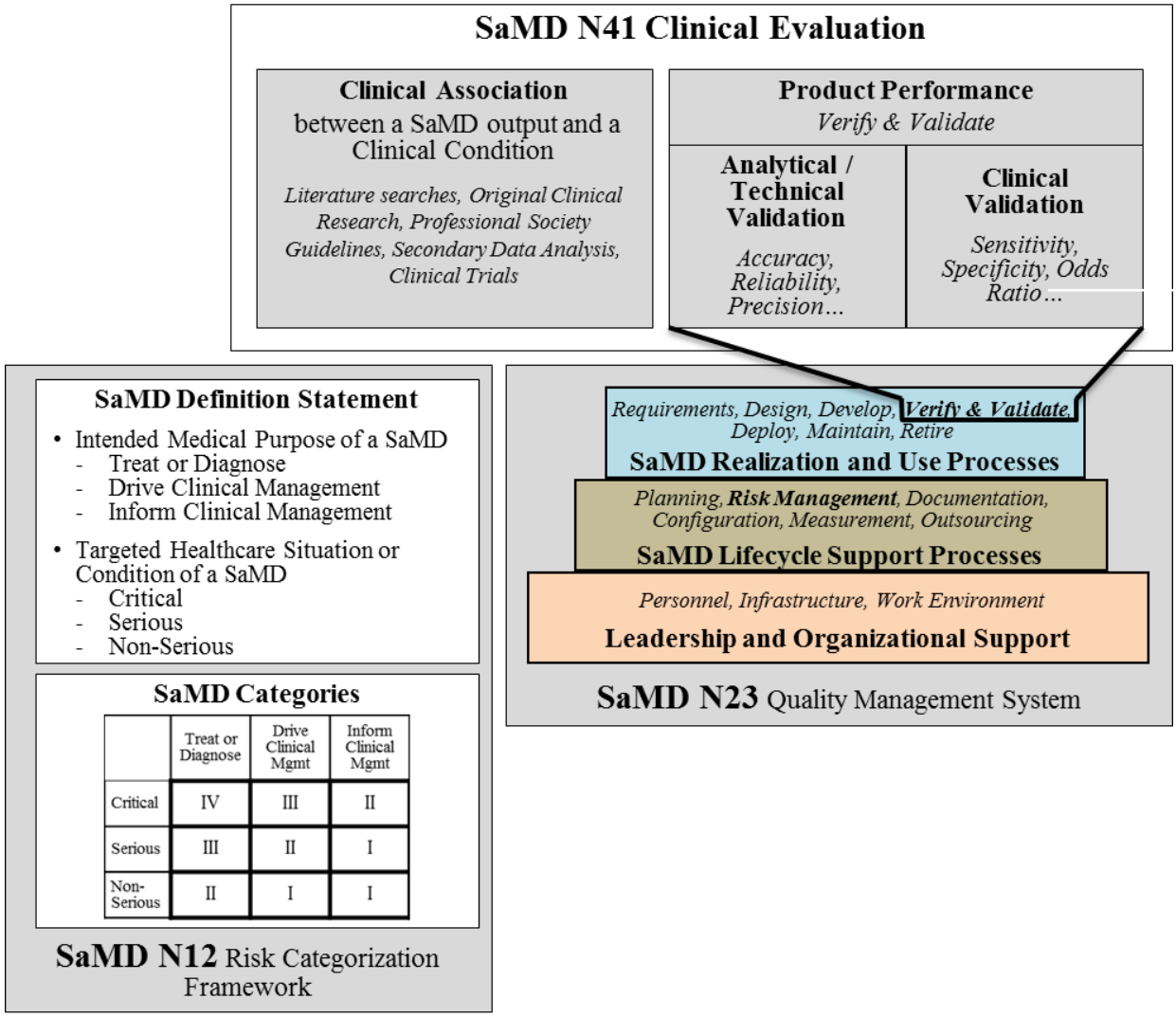


Figure 2- SaMD Landscape

2.0 Background

The IMDRF has acknowledged that software is an increasingly critical area of healthcare product development and has developed a series of documents concerning the definition, the categorization, and the application of quality systems principles of SaMD.

In 2013, IMDRF's SaMD Working Group released SaMD N10[1] *Software as a Medical Device (SaMD): Key Definitions* to create a standard terminology for SaMD. The following year, IMDRF adopted SaMD N12[2] *Software as a Medical Device: Possible Framework for Risk Categorization and Corresponding Considerations* which proposes a method for categorizing SaMD based on the seriousness of the condition the SaMD is intended to address. In 2015, the SaMD Working Group published SaMD N23[3] *Software as a Medical Device (SaMD): Application of Quality Management System*, outlining how manufacturers should follow Quality Management System (QMS) Principles for medical devices as well as good software engineering practices.

Knowledge of the previous three IMDRF SaMD documents is a prerequisite for readers of this document.

This document, and previous documents, provides harmonized principles for individual jurisdictions to adopt based on their own regulatory framework. They are not regulations.

The goal, strategy, principles and concepts, and implementation pathway for a harmonized SaMD framework are illustrated below in Figure 3.

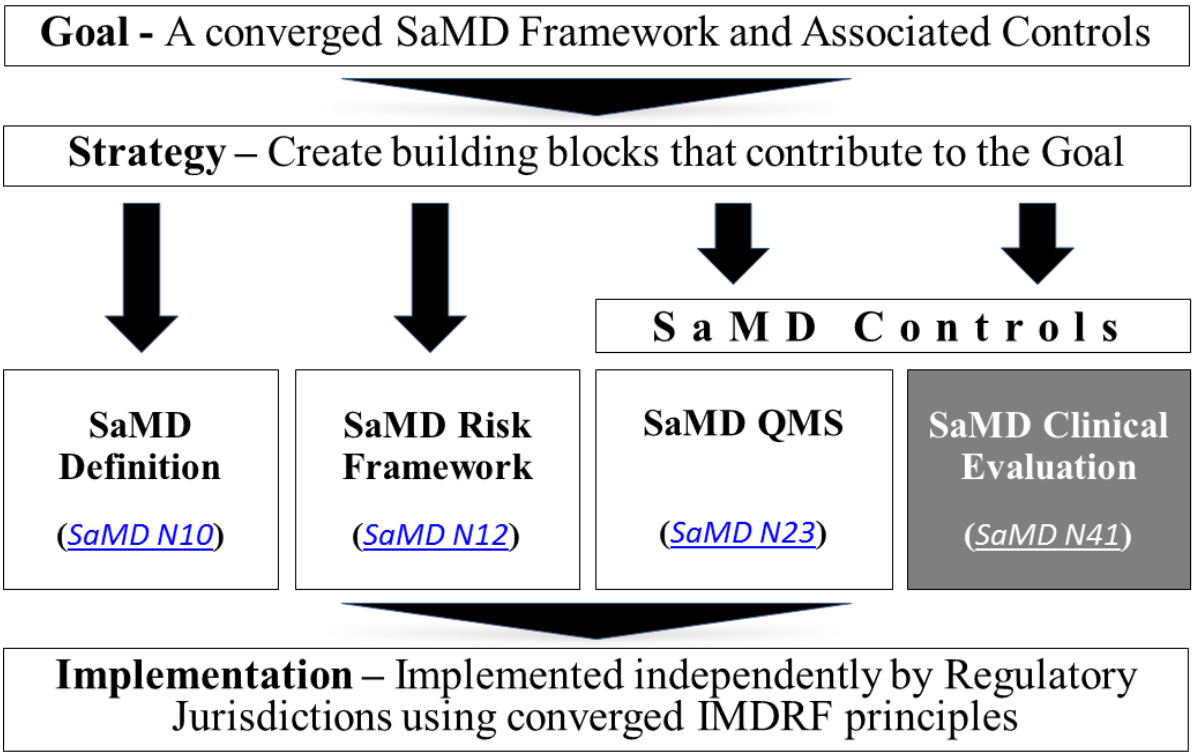


Figure 3 - SaMD Regulatory Pathway

3.0 Introduction

The International Medical Device Regulators Forum (IMDRF) seeks to establish a common and converged understanding of clinical evaluation and principles for demonstrating the safety, effectiveness and performance of SaMD.

As illustrated in Figure 4, this document represents a global harmonization effort to articulate this process.

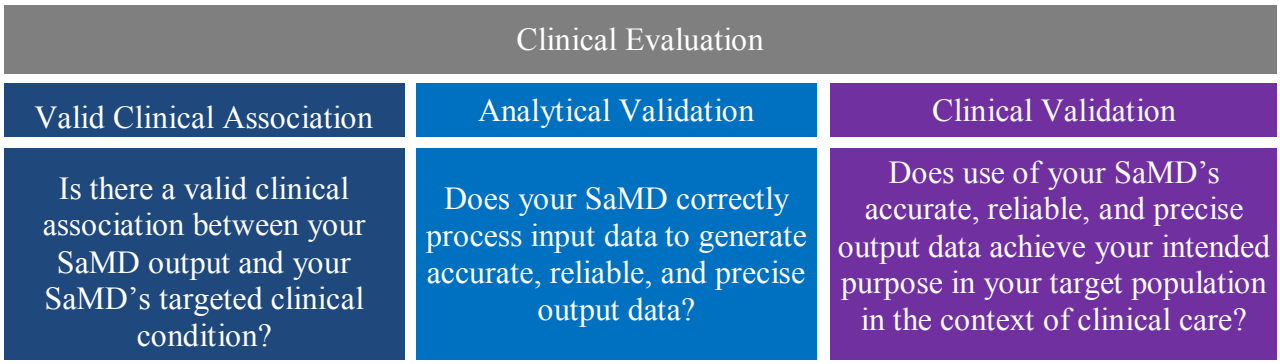


Figure 4- Clinical Evaluation Process

The document further explains that:

- Clinical evaluation should be an iterative and continuous process as part of the quality management system for medical devices *(See SaMD N23[3] for more information)*;
- Certain SaMD may require independent review of the results of the clinical evaluation, akin to peer review or design review, to ensure that the SaMD is clinically meaningful to users. The level of evaluation and independent review should be commensurate with the risk posed by the specific SaMD (*See SaMD N12[2] for more information*); and
- Software is unique in its level of connectivity, which may allow the continuous monitoring of the safety, effectiveness, and performance of SaMD. This document encourages manufacturers to use this feature to understand and modify software based on real-world performance. (*See 9.0 Pathway for Continuous Learning Leveraging Real World Performance Data for more information*).

Healthcare decisions increasingly rely on information provided by the output of SaMD where these decisions can impact clinical outcomes and patient care. As such, global regulators expect that performance metrics for a SaMD have a scientific level of rigor that is commensurate with the risk and impact of the SaMD to demonstrate assurance of safety, effectiveness, and performance.

4.0 Scope

This document focuses on the activities needed to clinically evaluate SaMD -- and relies on the reader to gain knowledge from the previous documents as a pre-requisite to this document. Specifically, this document:

- Expects readers to have knowledge of the vocabulary, approach, and common thinking of previous IMDRF SaMD documents;
- Expects readers to understand that the concepts are limited to SaMD, as defined in *SaMD N10*[1], which focuses on software with a medical purpose; and
- Refers to – and paraphrases as needed -- previous Global Harmonization Task Force (GHTF[3]) and IMDRF documents that provide a common understanding and application of terminology, concepts and principles for a clinical evaluation that demonstrates the performance metrics of a SaMD.

This document does NOT exhaustively address all regulatory requirements relevant to SaMD, which may vary by jurisdiction (e.g., informed consent, pre-market regulatory review). In addition, this document does not repeat the following concepts from previous SaMD documents:

- The definition of a SaMD (*SaMD N10*[1]);
- Examples of SaMD (*SaMD N12*[2]);
- Where a SaMD fits in the risk categorization and the descriptions of the risk categories (*SaMD N12*[2]); and
- Which Quality Management principles are appropriate for SaMD (*SaMD N23*[3]).

[3] GHTF was a voluntary group of representatives from national medical device regulatory authorities and industry representatives. GHTF was disbanded in 2012 and its mission has been taken over by the IMDRF.

5.0 Definitions

5.1 Clinical Evaluation of a SaMD

For purposes of this document "Clinical evaluation of a SaMD" is defined as a set of ongoing activities conducted in the assessment and analysis of a SaMD's clinical safety, effectiveness and performance as intended by the manufacturer in the SaMD's definition statement.

This definition is consistent with prior SaMD documents and is adapted from *GHTF SG5 N2R8:2007*[8].

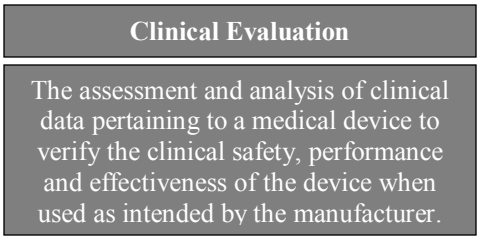


Figure 5- Clinical Evaluation

Clinical Evaluation *see GHTF SG5 N2R8:2007*[8]

5.2 Valid Clinical Association of a SaMD

For purposes of this document, valid clinical association, also known as scientific validity, is used to refer to the extent to which the SaMD's output (concept, conclusion, measurements) is clinically accepted or well-founded (based on an established scientific framework or body of evidence[4]), and corresponds accurately in the real world to the healthcare situation and condition identified in the SaMD definition statement.

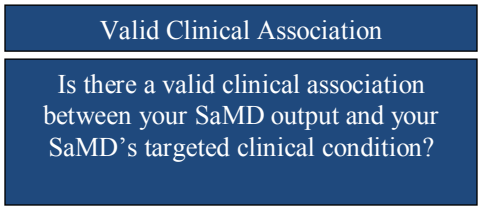


Figure 6- Valid Clinical Association

A valid clinical association is an indicator of the level of clinical acceptance and how much meaning and confidence can be assigned to the clinical significance of the SaMD's output in the intended healthcare situation and the clinical condition/physiological state. [5]

SaMD Definition Statement *see Section 6.0 in SaMD N12*[2]
SaMD Clinical Considerations *see Section 9.1 in SaMD N12*[2]

5.3 Analytical / Technical Validation of a SaMD

Analytical validation measures the ability of a SaMD to accurately, reliably and precisely generate the intended technical output from the input data. Said differently, analytical validation:

- Confirms and provides objective evidence that

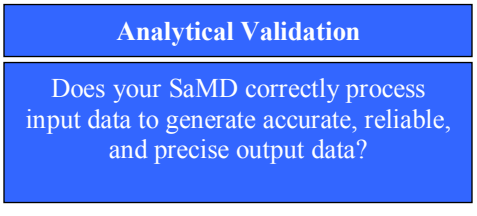


Figure 7-Analytical Validation

[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3261486/
[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2993536/

the software was correctly constructed – namely, correctly and reliably processes input data and generates output data with the appropriate level of accuracy, and repeatability and reproducibility (i.e., precision); and

- Demonstrates that (a) the software meets its specifications and (b) the software specifications conform to user needs and intended uses.

The analytical validation is generally evaluated and determined by the manufacturer during the verification and validation phase of the software development lifecycle using a QMS.

Analytical validation is necessary for any SaMD.

SaMD Verification and Validation *see Section 8.4 in SaMD N23*[3]

5.4 Clinical Validation of a SaMD

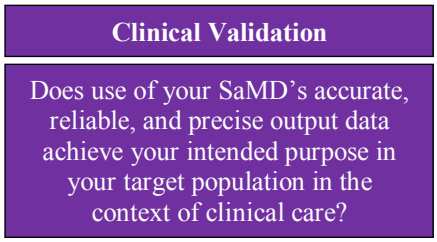


Figure 8-Clinical Validation

Clinical validation measures the ability of a SaMD to yield a clinically meaningful output associated to the target use of SaMD output in the target health care situation or condition identified in the SaMD definition statement. Clinically meaningful means the positive impact of a SaMD on the health of an individual or population, to be specified as meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to the function of the SaMD (e.g., diagnosis, treatment, prediction of risk, prediction of treatment response), or a positive impact on individual or public health.

Clinical validity is evaluated and determined by the manufacturer during the development of a SaMD before it is distributed for use (pre-market) and after distribution while the SaMD is in use (post-market).

Clinical validation of a SaMD can also be viewed as the relationship between the verification and validation results of the SaMD algorithm and the clinical conditions of interest. Clinical validation is a necessary component of clinical evaluation for all SaMD and can be demonstrated by either:

- Referencing existing data from studies conducted for the same intended use;
- Referencing existing data from studies conducted for a different intended use, where extrapolation of such data can be justified; or
- Generating new clinical data for a specific intended use.

Clinical validation is necessary for any SaMD.

SaMD Verification and Validation *see Section 8.4 in SaMD N23*[3]

6.0 General Principles and Context of SaMD Clinical Evaluation Process

A SaMD can best be described as software that utilizes an algorithm (logic, set of rules, or model) that operates on data input (digitized content) to produce an output that is intended for medical purposes as defined by the SaMD manufacturer (Figure 9). The risks and benefits posed by SaMD outputs are largely related to the risk of inaccurate or incorrect output of the SaMD, which may impact the clinical management of a patient.

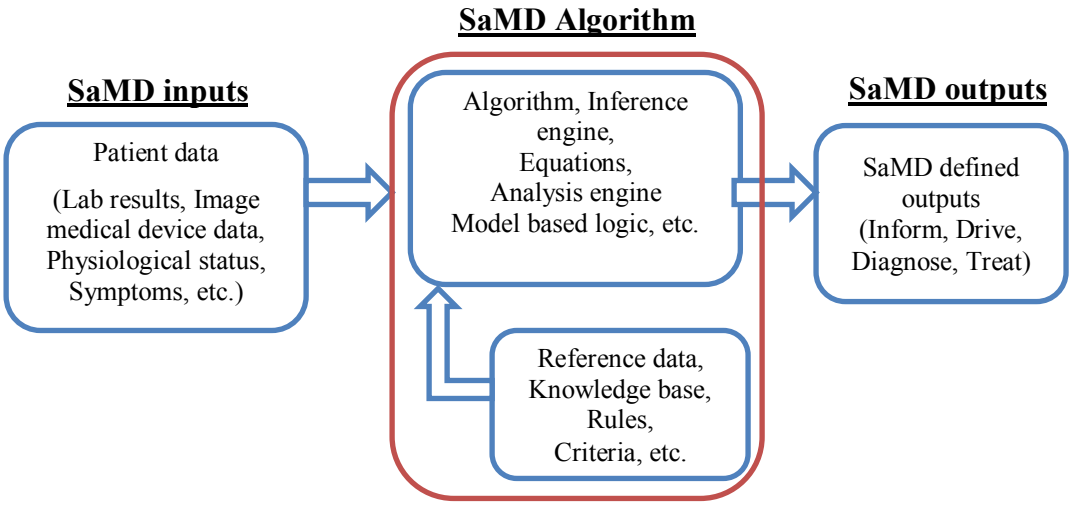


Figure 9 - SaMD Basic Programming Model

6.1 SaMD Definition Statement and SaMD Category

The SaMD definition statement, as defined in *SaMD N12*[2], is used by the SaMD manufacturer to identify the intended medical purpose of the SaMD (treat, diagnose, drive clinical management, inform clinical management), to state the healthcare situation or condition that the SaMD is intended for (critical, serious, non-serious), and to describe the core functionality of the SaMD.

The SaMD manufacturer will use the factors identified in the SaMD definition statement to determine the category of a SaMD in the SaMD categorization framework as illustrated in Figure 10.

State of Healthcare Situation or Condition	Significance of 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

Figure 10 - SaMD N12[2] Framework

SaMD Definition Statement *see Section 6.0 in SaMD N12*[2]
SaMD Risk Categorization Framework *see Section 7.0 in SaMD N12*[2]

6.2 Clinical Evaluation Processes

A SaMD manufacturer is expected to implement on-going lifecycle processes to thoroughly evaluate the product's performance in its intended market. As part of normal new product introduction processes, prior to product launch (pre-market) the manufacturer generates evidence of the product's accuracy, specificity, sensitivity, reliability, limitations, and scope of use in the intended use environment with the intended user, and generates a SaMD definition statement. Once the product is on the market (post-market), as part of normal lifecycle management processes, the manufacturer continues to collect real world performance data (e.g., complaints, safety data), to further understand the customer's needs to ensure the product is meeting those needs, and to monitor the product's continued safety, effectiveness and performance in real-world use. This real world performance data allows the manufacturer to identify and correct any problems, support future expansions in functionality, meet anticipated user demands, or improve the effectiveness of the device.

Product lifecycle activities, which include clinical evaluation activities as illustrated in Figure 11, should follow appropriate planning processes as part of an organization's lifecycle activities and processes, as described in SaMD N23[3].

Risk assessment done as part of the SaMD's lifecycle activities and processes should also be considered when conducting clinical evaluation.

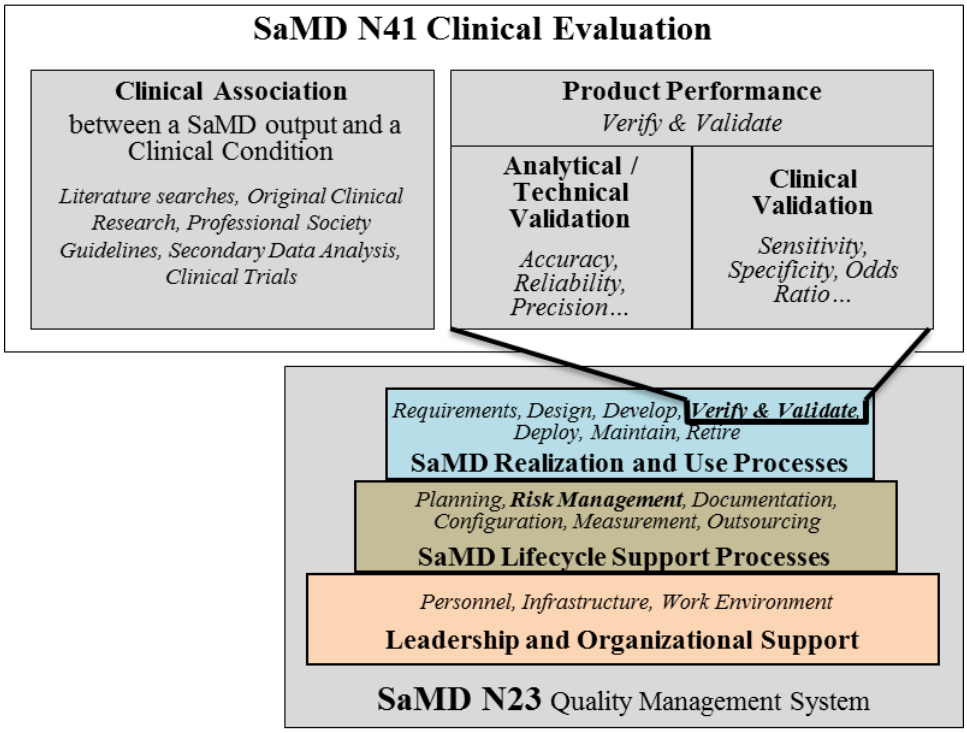


Figure 11 - SaMD Clinical Evaluation Landscape

Pre-market *see GHTF Study Group 1 documents*[4]
Post-market *see GHTF Study Group 2 documents*[5]
SaMD Considerations for Risk Management *see Section 7.2 in SaMD N23*[3]
SaMD User Needs Intended Use *see Section 8.3 of SaMD N23*[3]
SaMD Clinical Evidence *see Section 8.4 in SaMD N23*[3]

7.0 SaMD Clinical Evaluation Process Flow Chart

Clinical evaluation is a systematic and planned process to continuously generate, collect, analyze, and assess the clinical data[6] pertaining to a SaMD in order to generate clinical evidence verifying the clinical association and the performance metrics of a SaMD when used as intended by the manufacturer. The quality and breadth of the clinical evaluation is determined by the role of the SaMD for the target clinical condition, and assures that the output of the SaMD is clinically valid and can be used reliably and predictably.

This section uses simple steps to help SaMD manufacturers through the approach to generating evidence for the clinical evaluation of a SaMD and provides links to techniques, definitions and sources that are available to help a SaMD manufacturer generate appropriate evidence.

Note: The examples used are not intended to be comprehensive. All data sources and statistical methods should be tailored to the specific SaMD and its intended use.

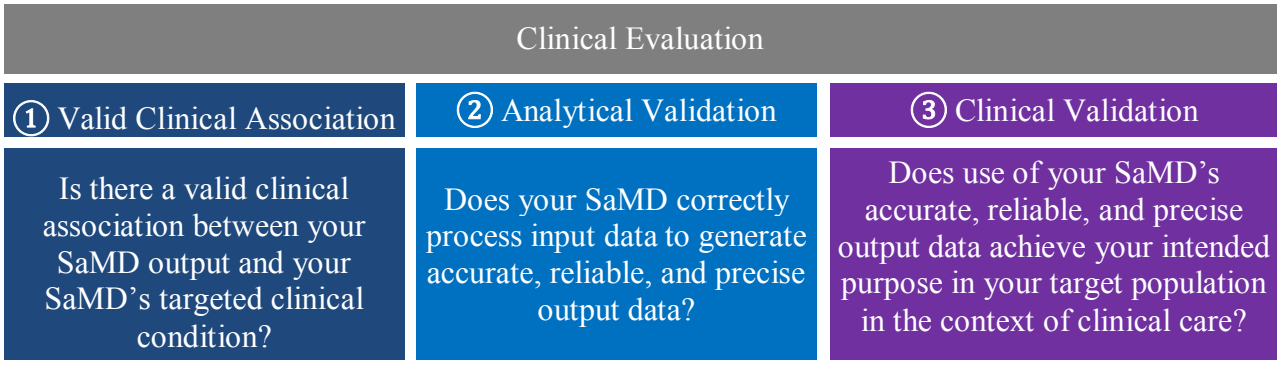


Figure 12 - Clinical Evaluation

① Valid Clinical Association:

Is there a valid clinical association between your SaMD output, based on the inputs and algorithms selected, and your SaMD's targeted clinical condition?

Step 1: Verify that the association between the SaMD output and the targeted clinical condition is supported by evidence.

Examples of existing evidence
- Literature searches
- Original clinical research
- Professional society guidelines

Examples of generating new evidence
- Secondary data analysis
- Perform clinical trials

Note: All SaMD should demonstrate a valid clinical association.

Question: How do I "generate evidence"?

You can verify by using existing evidence or you can verify by generating new evidence.

[6] Clinical data is defined as safety and/or performance information that are generated from the clinical use of a medical device. *Source:* GHTF SG5 N1R8:2007[7]

② Analytical Validation:

Does your SaMD meet technical requirements?

Step 1: Generate evidence that shows that the output of your SaMD is technically what you expected.

Note: All SaMD should demonstrate analytical validation.

Verification – confirmation through provision of objective evidence that specified requirements have been fulfilled. Source: *GHTF SG3 N18:2010*[6] Section 2.7

Validation – confirmation through provision of objective evidence that the requirements for a specific intended use or application have been fulfilled. Source: *GHTF SG3 N18:2010*[6] Section 2.8

Question: How do I "generate evidence"?

You can generate evidence during verification and validation activities as part of your quality management system or as part of your good software engineering practices, or by generating new evidence through use of curated databases or use of previously collected patient data.

③ Clinical Validation:

Does your SaMD generate clinically relevant outputs?

Step 1: Generate evidence that shows your:

- SaMD has been tested in your target population and for your intended use; and that
- Users can achieve clinically meaningful outcomes through predictable and reliable use.

Note: All SaMD should demonstrate clinical validation.

Examples of measures of clinical validation

- Sensitivity
- Specificity
- Positive predictive value (PPV)
- Negative predictive value (NPV)
- Number needed to treat (NNT)
- Number needed to harm (NNH)
- Likelihood ratio negative (LR-)
- Likelihood ratio positive (LR+)
- Odds ratio (OR)
- Clinical usability / User Interface
- Confidence interval

Question: How do I "generate evidence"?

You can generate evidence to validate clinical significance during verification and validation activities as part of your quality management system or as part of your good software engineering practices, referencing existing data sources from studies conducted for the same intended use. Where available data references studies conducted for a different intended use, extrapolation or generation of new clinical data may be required.

7.1 Considerations for Generating and Assessing Evidence

Being able to generate evidence to demonstrate the valid clinical association, analytical validation and clinical validation of a SaMD is essential to establishing the SaMD's value for users. The degree of evidence generation needed for a given SaMD will depend on parameters including but not necessarily limited to the:

- Maturity of evidence underlying the clinical association; and
- Confidence in the evidence, as applied to a specific SaMD.

The purpose of the assessment of the evidence is to select information based on its merits and limitations to demonstrate that the clinical evaluation evidence is high-quality, relevant, and supportive of the SaMD intended use.

For example, an assessment of clinical association would classify a SaMD as having either a:

a) **Well-established clinical association**: These SaMD have outputs with well-documented association as identified in sources such as clinical guidelines, clinical studies in peer reviewed journals, consensus for the use of the SaMD, international reference materials or other similar well-established comparators in terms of previously marketed devices / SaMD; or a
b) **Novel clinical association**: These SaMD may involve new inputs, algorithms or outputs, new intended target population, or new intended use. An example may include the combination of non-standard inputs such as mood or pollen count, with standard inputs such as gait, blood pressure or other physiological and environmental signals using novel algorithms to detect early onset of a deterioration of health or diagnosis of a disease.

What if I can't generate evidence to demonstrate ①, ②, or ③?

- Perform ongoing data analysis
- Modify your intended use to one that can be supported by available evidence
- Modify the target clinical association
- Make changes to the software

8.0 Importance of Independent Review of a SaMD's Clinical Evaluation

SaMD categories are based on the levels of impact on the patient or public health where accurate information provided by the SaMD is important to treat or diagnose, drive clinical management or inform clinical management. For additional information on SaMD categorization, please see Section 7.0 in *SaMD N12*[2]. As part of the risk-based approach, and subject to individual jurisdiction's laws, independent review of clinical evidence of certain low-risk SaMD may be less important and the manufacturer may 'self-declare' the appropriateness of the evidence. Again, subject to individual jurisdiction's laws, independent review of clinical evidence of more high-risk SaMD is more important in providing users the confidence in the SaMD's performance metrics, including but not limited to, identification of design errors or limitation, broadening technical competence, testing the appropriateness of assumptions, and management of bias.

The recommendation for independent review highlights where the evidence generated from the clinical evaluation of the SaMD should be reviewed by someone who has not been significantly involved in the development of the SaMD, and who does not have anything to gain from the SaMD, and who can objectively assess the SaMD's intended purpose and the conformity with the overall clinical evaluation evidence. The level of clinical evaluation and importance of independent review should be commensurate with the risk posed by the SaMD. This document recommends where independent review is more or less important.

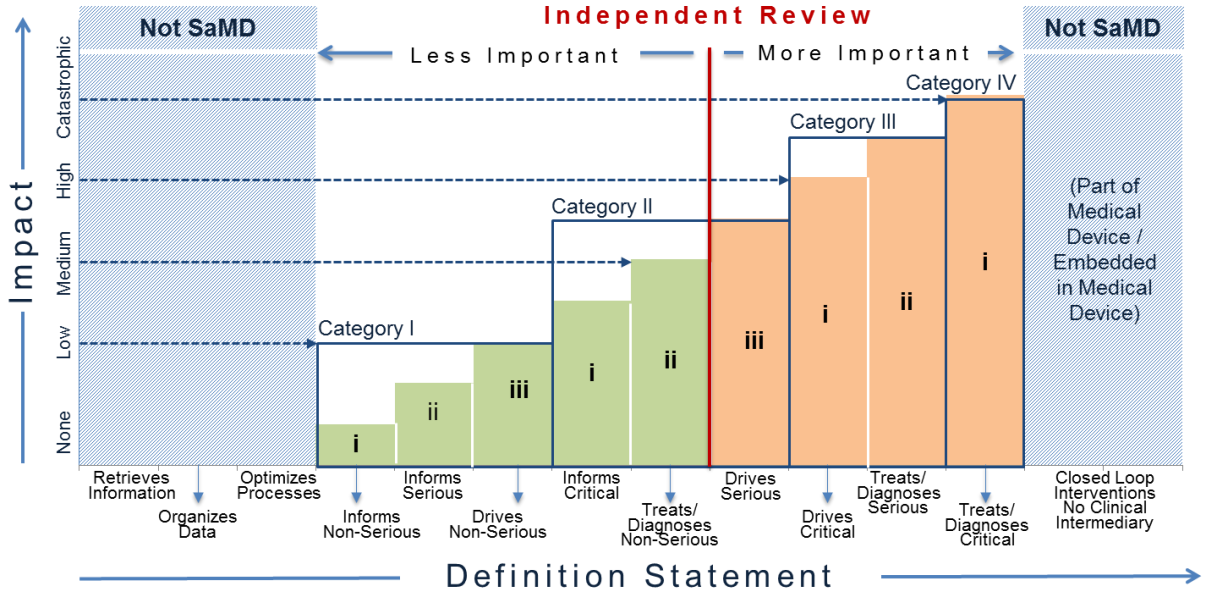


Figure 13 - Risk Based Approach to Importance of Independent Review

Figure 13 illustrates where independent review is more or less important. In the figure, the red, vertical dividing line differentiates where independent review is less important and where independent review is more important for different SaMD categories. Independent review is more important for SaMD that 'Treats/Diagnoses Serious and Critical' health care situations and

conditions and SaMD that 'Drives Critical' health care situations and conditions. Independent review in this document does not necessarily imply regulatory review but instead demonstrates the concept where independence in review of the results is important.

For purposes of this document 'less important' independent review is analogous to the concept of design review performed in the QMS system. Less important independent reviews can be conducted by individuals within the company or by utilizing outside experts.

For purposes of this document 'more important' independent review may be conducted by outside experts such as formal consultation with regulators, third parties on behalf of regulators, or the editorial board of a peer-reviewed journal, but may also be conducted by "non-conflicted" internal expert reviewers without significant involvement in the development of the SaMD.

9.0 Pathway for Continuous Learning Leveraging Real World Performance Data

SaMD may leverage connectivity between devices, and people to continuously monitor the safety, effectiveness and performance of the SaMD.

A SaMD manufacturer may have a hypothesis about future functionality and intended use of a SaMD that may be informed by continuously collecting and analyzing data on use of the SaMD in a post-market setting. Monitoring real world performance data can help the SaMD functionality and intended use evolve after initial introduction into the market. Such data may include post-market information such as safety data, results from performance studies, on-going clinical evidence generation for medical devices, new research publications / results that support or strengthen the clinical association of the SaMD output to a clinical condition, or direct end-user feedback, that can help the SaMD manufacturer understand the real world performance of the SaMD. This may lead to a change to the SaMD definition statement if supported by the clinical evidence generated through clinical evaluation leveraging real world performance data from the continuous monitoring as illustrated in Figure 14.

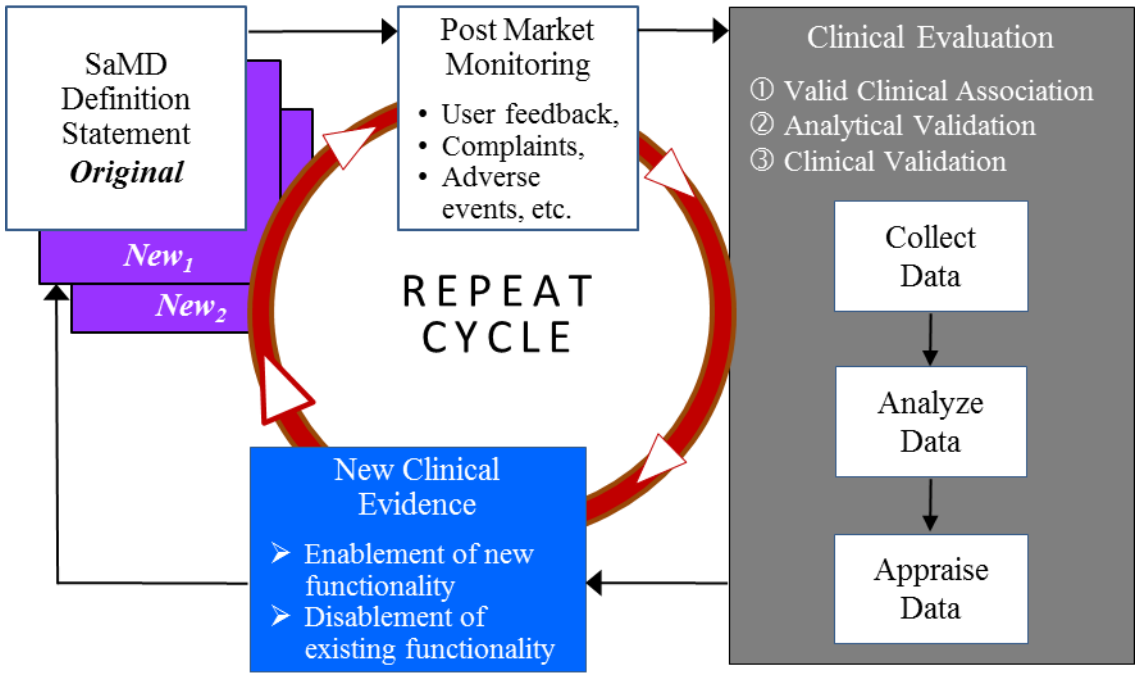


Figure 14 - Pathway for Continuous Learning - Use of Real World SaMD Performance Data in Ongoing SaMD Clinical Evaluation

Learning may impact the original category of a SaMD in the following ways:

- Real world performance data may provide evidence that the analytical or clinical validity of a SaMD is superior to the performance measures initially evaluated by the SaMD manufacturer, or

- Real world performance data may provide evidence that analytical or clinical validity of a SaMD is inferior to the performance measures initially evaluated by the SaMD manufacturer.

As additional clinical evidence is gathered to confirm the hypothesis and create and support new intended use, the SaMD manufacturer will update the clinical evaluation and generate a new definition statement. Then the cycle repeats.

This document encourages SaMD manufacturers to leverage SaMD's capability to capture real-world performance data to understand user interactions with the SaMD, and conduct ongoing monitoring of analytical and technical performance to support future intended uses.

9.1 Considerations for Continuous Learning Leveraging Real World Performance Data

- SaMD should facilitate post-market information gathering to allow for disablement of existing or enablement of new functionality within the SaMD.
- It is not necessary for the collection of real world performance data by the SaMD manufacturer to rely on the active involvement of the end user. The SaMD manufacturer should aim to impose the least burdensome approach possible in its data collection and leverage the capability of SaMD to collect clinical evidence.
- With ongoing clinical evaluation the risk categorisation may potentially change, necessitating a change in the SaMD definition statement.

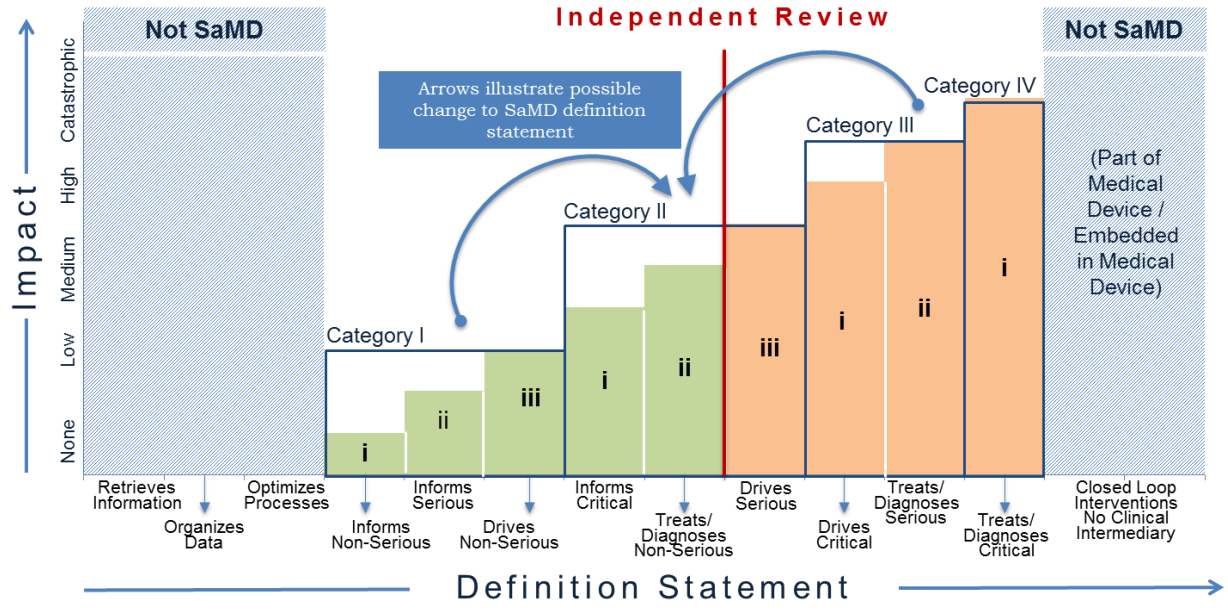


Figure 15 - Change to SaMD category from continuous learning

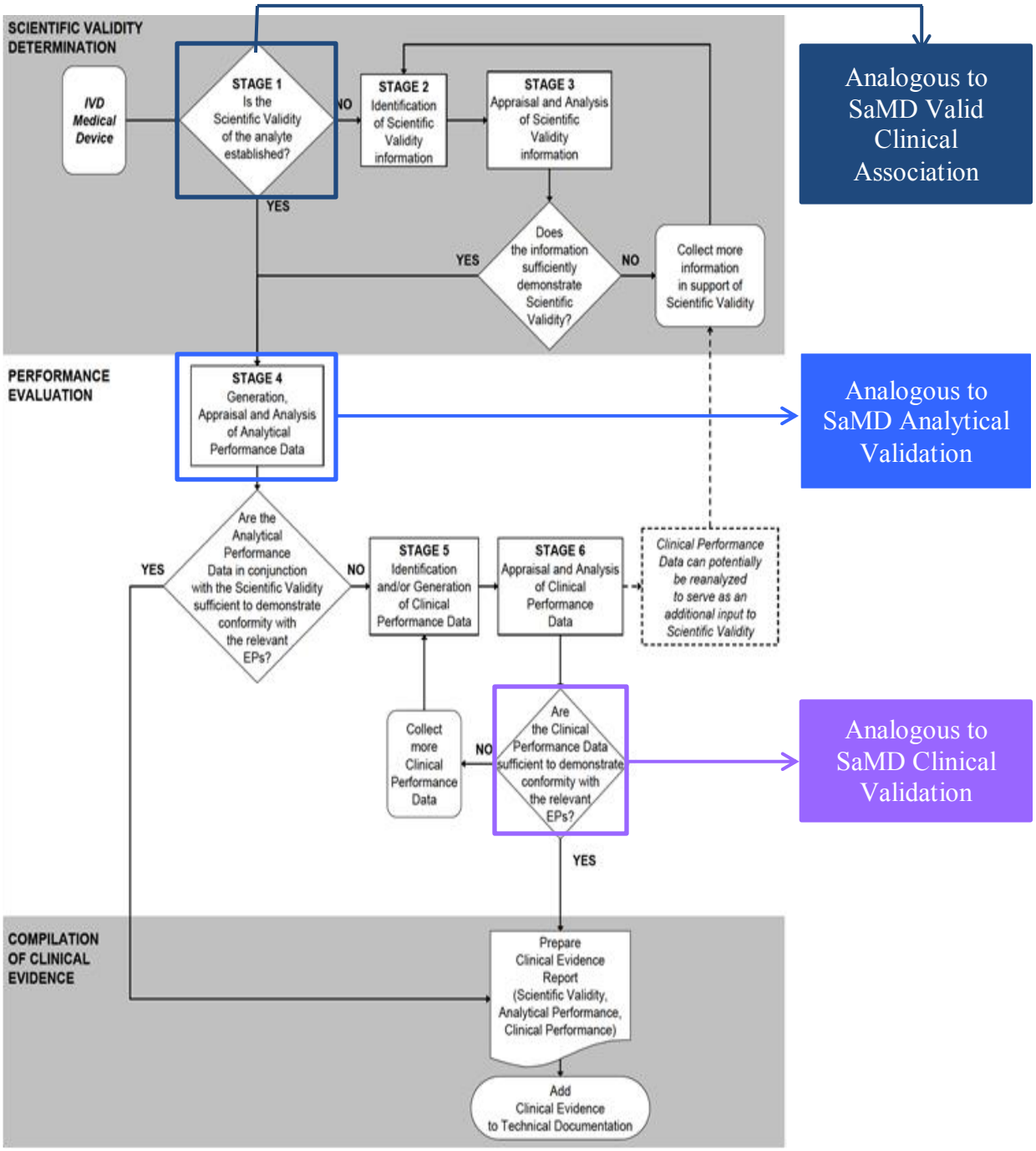
- Real world performance data including post-market information may not be sufficient to generate complete clinical evidence necessary for a change to the SaMD definition statement; as such the SaMD manufacturer should appropriately take into account other clinical evaluation steps required to support the change in SaMD definition statement.

- During the continuous learning across the life cycle, SaMD manufacturers should consider the recommendations in the previous section on independent review when new information changes the category of the SaMD as illustrated in Figure 15.
- The "continuous learning" referred to here is not "machine learning software" (i.e., where software device keeps learning automatically after it has been released into the market); rather it refers to collecting post-market information.
- Manufacturers should appropriately review the post-market information collected to determine if there are any changes to the safety, effectiveness or performance, or possible impact on benefits and risks of the SaMD that would indicate a need for a design change or a labeling change regarding contraindications, warnings, precautions or instructions for use. The labeling should identify limitations of the SaMD relevant to its clinical performance and interpretation of its output in a way that is understood by end users. The assessment of post-market information may also lead to a change of intended use (e.g., expansion, modification, or restriction).

NOTE: A change to the SaMD definition statement may be subject to regulatory requirements in the individual jurisdiction and a SaMD manufacturer should consult with the regulatory authorities in their jurisdiction.

SaMD Software Changes *see Section 7.5 in SaMD N23*[3]
SaMD Continuous Improvement *see Section 7.5 in SaMD N23*[3]
Medical Devices Post Market *see GHTF SG3 N79R11:2009*[15]
Medical Devices Observation Studies *see Section 6.1 in GHTF SG5 N8:2012*[16]

Appendix – Comparison of SaMD Clinical Evaluation Process to Process for Generating Clinical Evidence for IVD Medical Devices in *GHTF/SG5/N7:2012*[13]



References

IMDRF Documents:

1. SaMD N10: *Software as a Medical Device (SaMD): Key Definitions -- http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-131209-samd-key-definitions-140901.pdf*

2. SaMD N12: *Software as a Medical Device (SaMD): Possible Framework for Risk Categorization and Corresponding Considerations -- http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf*

3. SaMD N23: *Software as a Medical Device (SaMD): Application of Quality Management System -- http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-151002-samd-qms.pdf*

GHTF Documents:

4. GHTF Pre-market: *GHTF Study Group 1 documents -- http://www.imdrf.org/documents/doc-ghtf-sg1.asp*

5. GHTF Post-market: *GHTF Study Group 2 documents--http://www.imdrf.org/documents/doc-ghtf-sg2.asp*

6. GHTF SG3 N18:2010: *Quality management system –Medical Devices – Guidance on corrective action and preventive action and related QMS processes -- http://www.imdrf.org/docs/ghtf/final/sg3/technical-docs/ghtf-sg3-n18-2010-qms-guidance-on-corrective-preventative-action-101104.pdf*

7. GHTF SG5 N1R8:2007: *Clinical Evidence – Key Definitions and Concepts-- http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n1r8-clinical-evaluation-key-definitions-070501.pdf*

8. GHTF SG5 N2R8:2007: *Clinical Evaluation -- http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n2r8-2007-clinical-evaluation-070501.pdf*

9. GHTF SG5 N3:2010: *Clinical Investigations -- http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n3-clinical-investigations-100212.pdf*

10. GHTF SG5 N4: *Post-Market Clinical Follow-up Studies -- http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n4-post-market-clinical-studies-100218.pdf*

11. GHTF SG5 N6:2012: *Clinical Evidence for IVD medical devices – Key Definitions and Concepts -- http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n6-2012-clinical-evidence-ivd-medical-devices-121102.pdf*

12. GHTF SG1 N68:2012: *Essential Principles of Safety and Performance of Medical Devices -- http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n68-2012-safety-performance-medical-devices-121102.pdf*

13. GHTF SG5 N7:2012: *Clinical Evidence for IVD medical devices - Scientific Validity Determination and Performance Evaluation-- http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n7-2012-scientific-validity-determination-evaluation-121102.pdf*

14. GHTF SG1 N70:2011: *Label and Instructions for Use for Medical Devices-- http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n70-2011-label-instruction-use-medical-devices-110916.pdf*

15. GHTF SG2 N79R11:2009: *Medical Devices: Post Market Surveillance: National Competent Authority Report Exchange Criteria and Report Form -- http://www.imdrf.org/docs/ghtf/final/sg2/technical-docs/ghtf-sg2-n79r11-medical-devices-post-market-surveillance-090217.pdf*

16. GHTF SG5 N8:2012: *Clinical Evidence for IVD Medical Devices - Clinical Performance Studies for In Vitro Diagnostic Medical Devices -- http://www.imdrf.org/docs/ghtf/final/sg5/technical-docs/ghtf-sg5-n8-2012-clinical-performance-studies-ivd-medical-devices-121102.pdf*

International Standards:

17. ISO 14155:2011: *Clinical investigation of medical devices for human subjects -- Good clinical practice -- http://www.iso.org/iso/home/store/catalogue_ics/catalogue_detail_ics.htm?csnumber=45557*

18. ISO 14971:2007: *Application of risk management to medical devices -- http://www.iso.org/iso/en/CatalogueDetailPage.CatalogueDetail?CSNUMBER=31550&ICS1=11&ICS2=40&ICS3=1*

19. ISO 62304/A1: 2015: *Medical device software – Software life-cycle processes -- https://www.iso.org/standard/64686.html*

20. IEC 62366-1:2015: *Medical Devices – Part 1: Application of usability engineering to medical devices -- https://www.iso.org/standard/63179.html*

21. *IEC 80002-1:2009*: *Medical device software -- Part 1: Guidance on the application of ISO 14971 to medical device software -- http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=54146*

22. *ISO 82304-1:2016: Health software – Part 1: General requirements for product safety -- https://www.iso.org/standard/59543.html*

Glossary

Algorithm -- a finite set of instructions (or rules) that defines a sequence of operations for solving a particular computational problem for all problem instances for a problem set.

Analytical Validation -- measures the ability of a SaMD to accurately and reliably generate the intended technical output, from the input data.

Basic Programming -- problem-solving process used to create a computer program.

Claim -- the objective intent of the manufacturer regarding the use of a product, process or service as reflected in the specifications, instructions and information provided by the manufacturer.
(*Also see Intended Use / Purpose)*
Additional resources: see Section 4.0 in *GHTF SG1 N68:2012*[12]

Clinical Association -- refers to the extent to which the SaMD's output (concept, conclusion, measurements) is clinically accepted or well founded (existence of an established scientific framework or body of evidence) that corresponds accurately in the real world to the healthcare situation and condition identified in the SaMD definition statement.
(Also see Scientific Validity)

Clinical Considerations -- aspects that can raise or lower the potential to create hazardous situations to patients.
Additional resources: see Sections 4.0 and 9.1 in *SaMD N12*[2]

Clinical Data -- defined as safety and/or performance information that is generated from the clinical use of a medical device.
Additional resources: see *GHTF SG5 N1R8:2007*[7]

Clinical Evaluation -- the assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety, performance and effectiveness of the device when used as intended by the manufacturer.
Additional resources: see *GHTF N2R8:2007*[8]

Clinical Evidence -- an important component of the technical documentation of a medical device, which along with other design verification and validation documentation, device description, labelling, risk analysis and manufacturing information, is needed to allow a manufacturer to demonstrate conformity with the Essential Principles.
Additional resources: see Section 7.5 in *SaMD N23*[3] , and *GHTF SG5 N8:2012*[16], *GHTF SG5 N6:2012*[11], *GHTF SG5 N1R8:2007*[7]

Clinical Performance -- the ability of a device to yield results that are correlated with a particular clinical condition/physiological state in accordance with target population and intended user.
(Also see Clinical Validation)
Additional resources: see Section 4.0 in *GHTF SG1 N68:2012*[12]

Clinical Research -- use of clinical data generated through clinical use.

Additional resources: see Section 6.2 in *GHTF G5 N2R8:2007*[8]

Clinical Trials -- A properly conducted clinical investigation, including compliance to the clinical investigation plan and local laws and regulations, ensures the protection of human subjects, the integrity of the data and that the data obtained is acceptable for the purpose of demonstrating conformity to the Essential Principles.
Additional resources: see Section 6 in *GHTF SG5 N3:2010*[9]

Clinical Usability -- the means by which the user and a computer system interact, in particular the use of input devices and software and the evaluation of safety considerations for device users, use environments and user interfaces.
Additional resources see *ISO/IEC 62366-1:2015*[20], *SaMD N12*[2] Section 4.0, *SaMD N23*[3] Section 7.2 and 8.4
(Also see Usability, User Interface)

Clinical Validation -- measures the ability of a SaMD to yield a clinically meaningful output associated to the target use of SaMD output in with the target health care situation or condition identified in the SaMD definition statement.
(Also see Clinical Performance)

Continuous Monitoring -- collecting post-market information.
Additional resources: see Section 7.5 in *SaMD N23*[3]

Confidence Interval -- An interval about a point estimate that quantifies the statistical uncertainty in the true value being estimated (e.g. an accuracy metric) due to variability in the subject/sample selection process. A $1 - \alpha$ level confidence interval contains the true value in $100(1 - \alpha)$ % of applications, but in any given application either contains it or does not.
Additional resources: see Section 7.4 in *GHTF SG5 N8:2012*[16]

Critical (situation or condition) -- situations or conditions where 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.
Additional resources: see Section 5.2.1 in in *SaMD N12*[2]

Definition Statement -- clear and strong statement about intended use that explains how the SaMD meets one or more of the purposes described in the definition of a medical device and describes the SaMD's core functionality.
Additional resources: see Section 6.0 in in *SaMD N12*[2]

Diagnose (SaMD output to) -- information provided by the SaMD will be used to take an immediate or near term action.
(Also see Treat (SaMD output to))
Additional resources: see Section 5.1.1 in in *SaMD N12*[2]

Drive Clinical Management (SaMD output to) -- the information provided by the SaMD will be used to aid in treatment, aid in diagnoses, to triage or identify early signs of a disease or condition will be used to guide next diagnostics or next treatment interventions.
Additional resources: see Section 5.1.2 in *SaMD N12*[2]

Effectiveness -- when it can be determined that a device, based upon valid scientific evidence, that in a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results.
(Also see Safety, Performance)

Functionality -- identifies the critical features/functions of the SaMD that are essential to the intended significance of the information provided by the SaMD to the healthcare decision in the intended healthcare situation or condition.
Additional resources: see Sections 6.0, 7.3, 8.2, 9.1, and 10.1 in *SaMD N12*[2]

Global Harmonization Task Force -- was a voluntary group of representatives from national medical device regulatory authorities and industry representatives. GHTF was disbanded in 2012 and its mission has been taken over by the IMDRF.

Hypothesis -- a supposition or proposed explanation made as a starting point for further investigation. Evidence is not necessary to form a hypothesis.

Independent Review -- the process of subjecting a work, research, or ideas to the scrutiny of others who are experts in the same field.

Inform Clinical Management (SaMD output to) -- Informing clinical management infers that the information provided by the SaMD will not trigger an immediate or near term action.
Additional resources: see Section 5.1.3 in in *SaMD N12*[2]

Input (SaMD) -- one or several defined numeric tables or models accepted by an algorithm.
(Also see Basic Programming Model, Outputs)

Intended (Medical, Purpose, Use) -- the objective intent of the manufacturer regarding the use of a product, process or service as reflected in the specifications, instructions and information provided by the manufacturer.
(Also see Claim)

International Medical Device Regulatory Forum -- a voluntary group of medical device regulators from around the world who have come together to build on the strong foundational work of the Global Harmonization Task Force on Medical Devices (GHTF), and to accelerate international medical device regulatory harmonization and convergence.

Labeling -- the label, instructions for use, and any other information that is related to identification, technical description, intended purpose and proper use of the medical device, but excluding shipping documents.
Additional resources: see Section 4.0 in *GHTF SG1 N70:2011*[14]

Least Burdensome -- addressing a premarket issue that involves the most appropriate investment of time, effort, and resources.

Likelihood Ratio Negative (LR-) -- (1 – sensitivity) / specificity = ratio of the probabilities of testing negative in patients with and without disease or clinical condition. It can be

interpreted as the increase in the odds of disease given a test negative result relative to the pretest odds.
Additional resources: see Section 7.2 in GHTF SG5 N7:2012[13]

Likelihood Ratio Positive (LR+) -- sensitivity / (1 – specificity) = ratio of the probabilities of testing positive in patients with and without disease or clinical condition. It can be interpreted as the increase in the odds of disease given a test positive result relative to the pretest odds.
Additional resources: see Section 7.2 in GHTF SG5 N7:2012[13]

Literature Search -- use of published clinical data that establishes a valid clinical association.
Additional resources: see Section 6.1 in GHTF SG5 N2R8:2007[8]

Machine Learning Software (Incremental) -- software device for which input data is continuously used to automatically extend the existing device's knowledge i.e. to further train the device after it has been released into the market.

Negative Predictive Value (NPV) -- proportion of test negative patients who do not have the disease or clinical condition.
Additional resources: see Section 7.2 in GHTF SG5 N7:2012[13]

Non-Serious (situation or condition) -- situations or conditions where 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.
Additional resources: see Section 5.2.3 in SaMD N12[2]

Number Needed To Harm (NNH) -- number of patients that need to be treated in order have an adverse effect on one patient.

Number Needed To Treat (NNT) -- average number of patients that need to be treated in order to have an impact on one person.

Odds Ratio (OR) -- ratio of the odds of disease or clinical condition given the SaMD test result is S to the odds of disease given the SaMD test result is not S. OR is equivalent to ratio of likelihood ratio positive to likelihood ratio negative.

Output -- results obtained from an algorithm.

Performance (Essential Principles) -- a product's behavior must not cause harm to a person, place or thing if something goes wrong
(Also see Effectiveness, Safety)

Performance (Metrics) -- measures behaviors, activities and performance.

Performance (Real World) -- information on real-world device use and performance from a wider patient population than a more controlled study or pertinent literature, and thus provide information that cannot be obtained through such studies.
(Also see Real World Performance)

Performance (Studies) -- establish or confirm aspects of device performance which cannot be determined by analytical validation, literature and/or previous experience gained by routine testing.
Additional resources: see Section 5.0 in *GHTF SG5 N8:2012*[16]

Positive Predictive Value (PPV) -- proportion of test positive patients who have the disease or clinical condition.
Additional resources: see Section 7.2 in *GHTF SG5 N7:2012*[13]

Post-market Surveillance -- the practice of monitoring the safety of a medical device after it has been released on the market.
Additional resources: see *GHTF Study Group 2*[5] documents; *GHTF SG2 N79R11:2009*[15]

Pre-market -- the period prior to a product being available for purchase.
Additional resources: see *GHTF Study Group 1*[4] documents

Professional Society Guidelines -- practices and documents recommended by leading authorities; use of existing, well-established standards and/or clinical data.
Additional resources: see Section 9 in *GHTF SG5 N2R8:2007*[8]

Real World (SaMD) Evidence -- evidence derived from aggregation and analysis of real world data elements.

Real World Data -- product information generated after a product has been released to the market that can provide insight into the performance of the product used in actual clinical settings, in routine medical practice, and by regular use by consumers.

Real World Performance -- information on real-world device use and performance from a wider patient population than a more controlled study or pertinent literature, and thus provide information that cannot be obtained through such studies.
(Also see Performance (Real World))

Risk Categorization Framework (SaMD) -- a framework to determine the category of a SaMD based on the significance of the information provided to the healthcare decision and on the state of the healthcare situation or condition that the SaMD is intended for.
Additional resources: see Section 7.0 in in *SaMD N12*[2]

Safety -- a product should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training, and the medical and physical conditions of intended users, they will perform as intended.
(Also see Effectiveness, Performance)

Safety Data -- adverse events and other problems with medical devices that impact the health and safety of patients; safety data may be collected in the same activity as performance data; absence of safety issues during clinical performance testing is an indicator of safety.

Scientific Validity -- refers to the extent to which the SaMD's output (concept, conclusion, measurements) is clinically accepted or well founded (existence of an established scientific framework or body of evidence) that corresponds accurately in the real world to the healthcare situation and condition identified in the SaMD definition statement.
(Also see Clinical Association)

Secondary Data Analysis -- use of analyzed data collected for another purpose.

Sensitivity -- effectiveness of a SaMD to correctly identifies patients with the intended clinical disease or condition.
Additional resources: see Section 4.0 in *GHTF SG5 N7:2012*[13]

Serious (situation or condition) -- situations or conditions where accurate diagnosis or treatment is of vital importance to avoid unnecessary interventions (e.g., biopsy) or timely interventions are important to mitigate long term irreversible consequences on an individual patient's health condition or public health.
Additional resources: see Section 5.2.2 in *SaMD N12*[2]

Specificity -- correctly identifies across a range of available measurements patients that do not have the intended disease or condition.
Additional resources: see Section 4.0 in *GHTF SG5 N7:2012*[13]

Treat (SaMD output to) -- information provided by the SaMD will be used to take an immediate or near term action.
Additional resources: see Section 5.1.1 in in *SaMD N12*[2]

Usability -- the means by which the user and a computer system interact, in particular the use of input devices and software and the evaluation of safety considerations for device users, use environments and user interfaces.
Additional resources see *ISO/IEC 62366-1:2015*[20], *SaMD N12*[2] Section 4.0, *SaMD N23*[3] Section 7.2 and 8.4
(Also see Clinical Usability, User Interface)

User Interface -- the means by which the user and a computer system interact, in particular the use of input devices and software and the evaluation of safety considerations for device users, use environments and user interfaces.
Additional resources see *ISO/IEC 62366-1:2015*[20], *SaMD N12*[2] Section 4.0, *SaMD N23*[3] Section 7.2 and 8.4
(Also see Clinical Usability, Usability)

User(s) - includes patients, healthcare providers, specialized professionals, lay users, consumers.

Validation -- confirmation through provision of objective evidence that the requirements for a specific intended use or application have been fulfilled.
Additional resources: see Section 2.8 in *GHTF SG3 N18:2010*[6]

Verification -- confirmation through provision of objective evidence that specified requirements have been fulfilled.

Additional resources: see Section 2.7 in *GHTF SG3 N18:2010*[6]