Asian Harmonization Working Party
WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

PROPOSED FINAL DOCUMENT

Title: Guidance document on Risk Categorisation of Software as a Medical Device

Authoring Group: Work Group 3, Pre-Market: Software as a Medical Device

Date: 25 November 2016

Dr. SETHURAMAN Rama

Chair, Work Group 3

Contents

1. Objectives

This document was drafted by Work Group 3 of AHWP Technical Committee to provide guidance and information to Regulatory Authorities (RAs) and the Medical Device Industry (Industry) on the Risk Categorisation of Software as a Medical Device (SaMD) taking reference from the IMDRF/SaMD WG/N12FINAL:2014. This document is based on the IMDRF/SaMD WG/N12FINAL:2014 document with inclusion of additional examples and explanation to clarify the risk categorization for SaMDs.

The main aim of this document for medical device software categorisation is to provide information to AHWP member economies' RAs and industry in establishing a consistent approach to determine the risk categorisation of SaMD based on its intended purpose. 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;

- 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.

1.1 Application of this document

- This document focuses on the SaMD irrespective of software technology and/or the platform (e.g., mobile app, cloud, server).
- 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 does not address software that drives or controls a hardware medical device.

2. Relationship to other regulatory classification and standards[1]

- 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.

[1] Additional details can be found in Section 8.

- 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.

This guideline is based on currently available IMDRF documents on Software as a Medical Device, AHWP-WG3-SaMD-001 guidance document, AHWP white paper on medical device software regulation – Software Qualification and Classification and published guidelines from global agencies including European Union, Health Canada and US FDA, and IEC 62304, with focus on the recent developments in regulation of SaMD.

3. 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.[2]
- "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.

[2] "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.

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.

3.2 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 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.

4. 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[3]. Although many of the aspects may affect the performance of the SaMD, only some of these aspects can be identified by the intended use of a SaMD. The following are the 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 (e.g. diagnose, treat, clinical management), and;
B. State of the healthcare situation or condition (e.g. critical condition, non-serious condition).

3 AHWP-WG3-SaMD-001; Guidance document on Qualification of Medical Device Software

When these factors are included in the manufacturer's description of intended use[3], they can be used to categorize SaMD.

The other aspects influencing patient safety not included in the above two factors, although important, do not influence the determination of the category of SaMD. However, appropriate considerations of all these aspects by the manufacturers, users and other stakeholders can significantly reduce patient safety risks. For example, the core functionality of the software (e.g., properly identify and prompt healthcare providers of potential arrhythmia episodes in cardiac patients based on their ECG recording) can be very instrumental in preventing harm to patients.

5. 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 related to the subsequent action taken.

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 or qualified 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. 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.

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[4], e.g. supplying information for diagnosis, prevention,

[4] IMDRF key definitions Final document "medical purposes" also repeated here in Section 3.3.

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

Description of the SaMD's core functionality[5], i.e., the critical features/ functions of the SaMD can contribute 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.

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

7. SaMD Categorization

7.1 SaMD Categories

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] 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, 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.

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

7.2 Criteria for Determining SaMD Category

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.

Examples of 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.
- SaMD that collects data from peak-flow meter and symptom diaries to provide information to anticipate an occurrence of an asthma episode**.**
- SaMD that analyzes images, movement of the eye or other information to guide next diagnostic action of astigmatism.
- 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).
- 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.
- SaMD that stores historical blood pressure information for a health care provider's later review.
- SaMD intended for image analysis of body fluid preparations or digital slides to perform cell counts and morphology reviews.
- 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.
- SaMD that uses hearing sensitivity, speech in noise, and answers to a questionnaire about common listening situations to self-assess for hearing loss.
- SaMD that collect data from individuals for daily pain score for pain management.
- SaMD that collects fetus movement or development.
- SaMD that collects information for control of conception, in IVF.
- SaMD that functions as a electronic patient record systems.
- SaMD that automates reporting of a Parkinson’s disease patient’s movements for treatment optimization.
- SaMD such as mobile-based cognitive assessment software tool.

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.

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.

Examples of Category II:

- SaMD that analyzes heart rate data intended for a clinician as an aid in diagnosis of arrhythmia.
- 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.
- SaMD that uses data from individuals for predicting risk score for developing stroke or heart disease for creating prevention or interventional strategies.
- 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.
- 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.
- SaMD that uses scores to determine current density of electrical stimulation for pain relief, eg in pain management.

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.

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

- 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.
- SaMD that uses data from individuals for predicting risk score in high-risk population for developing preventive intervention strategies for colorectal cancer.
- SaMD that uses data from individuals for predicting risk score in high-risk population for developing breast cancer
- 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.
- SaMD that compares images over a period of time and monitor growth of a lesion
- SaMD embedded in contact lens with Glucose Monitoring functions

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.

Examples of 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.
- 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.
- SaMD that performs analysis of cerebrospinal fluid spectroscopy data to diagnose tuberculosis meningitis or viral meningitis in children.
- SaMD that combines data from immunoassays to screen for mutable pathogens/pandemic outbreak that can be highly communicable through direct contact or other means.
- SaMD that functions as a heart monitor with Atrial Fibrillation diagnostic capability

8. SaMD Categorization and its overall purpose

The categorize framework in this document is not a regulatory classification, nor implies a convergence of classification rules.

There are different classification schemes for medical device software that serve different purposes. This includes for example,

- To assign a safety class to the medical device software during its development and maintenance for efficient management of the software lifecycle processes including risk management based on international standards
- To determine or calibrate the appropriate levels of regulatory oversight for the devices such as requirements for conformity assessment, quality system etc. based on the Medical Device Risk Classification

Most of the existing classification systems are applicable to Medical Device Software that is SaMD and also when the software is an embedded or integral part of the final hardware medical device.

The categorisation criteria in this document introduces a fundamental approach in terms of general and specific considerations for manufacturers, regulators and users alike to identify the generic risks for SaMD. This sets a path towards common harmonised vocabulary and convergence in risk management processes to enable a more efficient management of the life cycle of SaMD.

9. References

[1] AHWP/WG1/F001:2014: White Paper on Medical Device Software Regulation – Software Qualification and Classification

[2] AHWP-WG3-SaMD-001:2015: Guidance Document on qualification of medical device software

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

[4] IEC 62304:2006 – Medical device software – Software life cycle processes

[5] GHTF/SG1/N71:2012: Definition of Terms Medical Device and In Vitro Diagnostic Medical Device

[6] GHTF/SG1/N77:2012: Principles of Medical Device Classification

[7] IMDRF/SaMD WG/N12FINAL:2014: "Software as a Medical Device": Possible Framework for Risk Categorization and Corresponding Considerations

[8] GHTF/SG1/N70:2011: Label and Instruction for Use for Medical Devices