HEALTH SCIENCES AUTHORITY

REGULATORY GUIDANCE

For consultation: August 2024

MEDICAL DEVICE GUIDANCE

Guidance on Change Management Program (CMP) for SaMD

HSA Health Sciences Authority

CONTENTS

1. INTRODUCTION

Software as a Medical Device (SaMD), including those incorporating Machine Learning (ML) technology, plays a crucial role in offering innovative solutions to improve medical diagnosis, treatment, and patient care. SaMD Product Owners (PO) are required to adopt Total Product Life Cycle (TPLC) approach to manage and adapt to the ever-changing SaMD while ensuring that the software remains relevant, safe and effective throughout its life cycle.

However, prevailing regulatory framework may not be suited to accommodate the rapid iterative nature of SaMD. POs face the challenges of adhering to regulatory requirements which consist of ensuring compliance and obtaining regulatory approvals which can impact the timeliness of the implementation of SaMD changes. Hence, adoption of modern regulatory framework that embraces agile methodologies and risk-based assessments is necessary to help to expedite the approval process for certain types of changes, especially those aimed at improving the effectiveness and safety of SaMD.

To address this, the Health Sciences Authority (HSA) has initiated a new optional regulatory pathway – **Change Management Program (CMP),** specifically for SaMD that is incorporated into HSA's Premarket Product Registration and Change Notification (CN) processes.

CMP streamlines SaMD TPLC-based regulatory framework to facilitate timely implementation of software changes for SaMD registered on the Singapore Medical Device Register (SMDR), by establishing confidence in PO's good quality management system practices, demonstrated through excellent capabilities in their SaMD development, verification/validation, post-market surveillance/vigilance.

CMP also introduces the concept of **Pre-specified changes**, allowing upcoming anticipated changes (refer Section 5.2) for the SaMD to be implemented in a timely manner. Through this pathway, Product Owners can have better transparency and predictability in regulatory clearance for future software changes.

In addition, with a pre-existing device approval under CMP, this program facilitates leveraging on previously approved CMP documentation if the subsequent device registration is for a similar SaMD with equivalent quality management processes. This reduces redundancy in dossier preparation and allows faster market access for the new SaMD.

1.1 Intended audience

This document is intended for stakeholders who are involved in standalone software medical device development and /or registering such devices in Singapore.

1.2 Objective

This guidance describes the regulatory requirements and procedures for CMP submission during SaMD Product Registration or Change Notification application.

1.3 Scope

This guidance is applicable to all SaMD, including machine-learning (ML) incorporated SaMD (ML-SaMD) with intended use that falls under the definition of a medical device as stipulated in the *Health Products Act (HPA*). This will include SaMD which is intended for medical purposes such as investigating, detecting, diagnosing, monitoring, treating or managing of any medical condition, disease, anatomy or physiological process.

Overall, the following topics will be covered in this document:

- Eligibility criteria to enrol into CMP
- Application process
- Submission requirements
- Post-CMP approval
- Change Notification
- Leveraging on approved CMP
- Turn-Around-Time (TAT) and fees

This document should be read together with the other relevant documents including the Regulatory Guidelines for Software medical Devices – A Life Cycle Approach, other Guidances such as GN-15, GN-17, GN-18 and GN-21.

2. DEFINITION

Definitions that do not indicate they are set out in the *Act* or *Regulations* are intended as guidance in this document. These definitions are not taken verbatim from the above-mentioned legislation and should not be used in any legal context. These definitions are means to provide guidance in layman terms.

ARTIFICIAL INTELLIGENCE (AI): refers to a set of technologies that seek to simulate human traits such as knowledge, reasoning, problem solving, perception, learning and planning.

CYBERSECURITY: a state where information and systems are protected from unauthorized activities, such as access, use, disclosure, disruption, modification, or destruction to a degree that the related risks to confidentiality, integrity, and availability are maintained at an acceptable level throughout the life cycle.

END OF SUPPORT (EOS): Life cycle stage of a product starting when the manufacturer terminates all service support activities and service support does not extend beyond this point.

PRODUCT OWNER (*as set out in the Regulations*): in relation to a health product, means a person who:

- supplies the health product under his own name, or under any trademark, design, trade name or other name or mark owned or controlled by him; and
- is responsible for designing, manufacturing, assembling, processing, labelling, packaging, refurbishing or modifying the health product, or for assigning to it a purpose, whether those tasks are performed by him or his behalf.

INTENDED PURPOSE/INTENDED USE (*as set out in the Regulations*): in relation to a medical device or its process or service, means the objective intended use or purpose, as reflected in the specifications, instructions and information provided by the product owner of the medical device.

MACHINE LEARNING ENABLED SaMD (ML-SaMD): A SaMD that uses machine learning, in part or in whole, to achieve its intended medical purpose.

RECOGNIZED STANDARDS: Standards deemed to offer the presumption of conformity to specific essential principles of safety and performance.

REFERENCE STANDARD / GROUND TRUTH: An objectively determined benchmark that is used as the expected result for comparison, assessment, training, etc

REGISTRANT *(as set out in the Act)*: in relation to a registered health product, means the person who applied for and obtained the registration of the health product under this *Act*.

STANDALONE SOFTWARE (also known as SOFTWARE AS MEDICAL DEVICE, (SaMD) in IMDRF context): a software and/or mobile application that is intended to function by itself and are not intended for use to control or affect the operation of other hardware medical devices.

TEST DATASET: A set of data that is never shown to the machine learning training algorithm during training, that is used to estimate the machine learning model's performance after training.

TRAINING: Process intended to establish or to improve the parameters of a machine learning model, based on an machine learning training algorithm, by using training data.

TRAINING DATASET: A set of data that is used to train the machine learning model, which is not part of the Test Dataset

3. ELIGIBILITY CRITERIA TO ENROL INTO CMP

The two pre-requisites to enrol into CMP are as follow:

Conformance with the following standards*:	**Documentary requirement**
ISO 13485	SaMD product owner shall possess a valid ISO 13485 certificate, with approved scope of activity applicable to the SaMD and related development activities. ***Note:*** *For Original Equipment Manufacturer (OEM) SaMD, ISO 13485 certificate is to be provided by OEM.*
IEC 62304	SaMD product owner may either possess IEC 62304 certificate issued by accredited third-party certification body or in-house assessed summary report conforming to IEC 62304, etc

** NOTE: SaMD product owners are required to conform to the latest standard version and conformance shall remain valid throughout the SaMD total product life cycle (TPLC).*

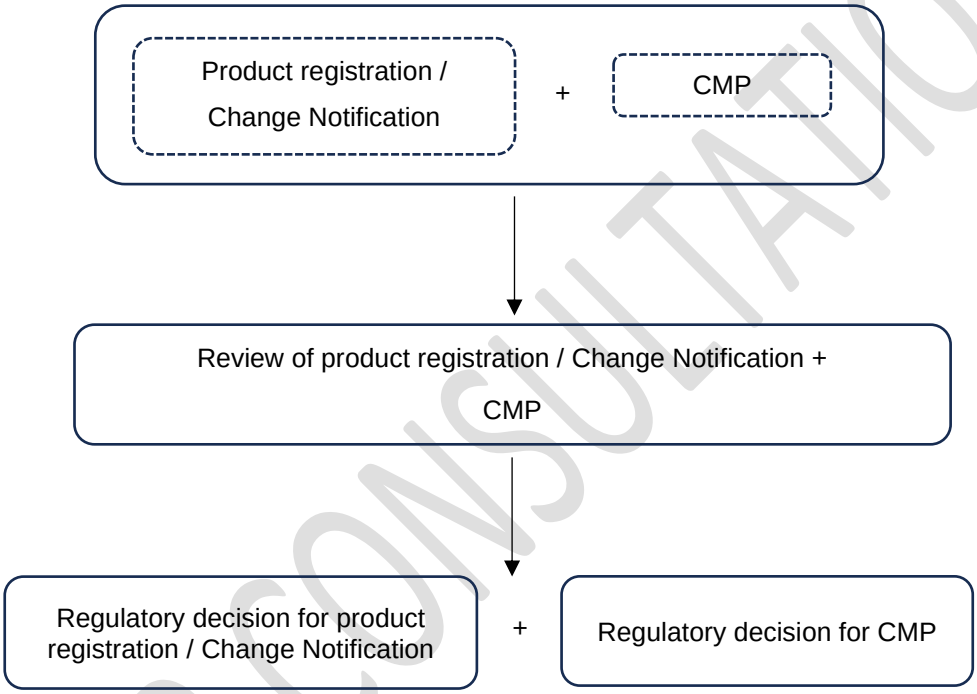
4. APPLICATION PROCESS

Registrant can enrol into CMP through either a premarket product registration or Change Notification* (CN) application for an existing registered medical device.

** Note: Review change for class B SaMD; Technical change for Class C SaMD*

The CMP and product registration/CN application will be reviewed concurrently. Regulatory outcome for product registration/CN and CMP will be determined independently (i.e. the CMP regulatory decision does not affect the outcome of the product registration/CN).

The application process for the assessment of product registration or Change Notification application, with CMP submission is summarised as below:



5. SUBMISSION REQUIREMENTS

Product Owners shall demonstrate that good quality management system practices have been established through excellent capabilities in SaMD development, verification/validation, post-market surveillance/vigilance to ensure the safety, effectiveness and cybersecurity of the SaMD throughout their TPLC.

By demonstrating that robust quality assurance processes are in place, it provides assurance that the SaMD is designed, developed, and maintained in a manner that ensures its safety and effectiveness. Besides, it also instils confidence in the proactive management of changes to the SaMD (as outlined in the Pre-specified changes), ensuring that any updates or alterations are made in a controlled and systematic manner, without compromising its safety or performance.

To demonstrate this, the following documentations shall be submitted as part of the CSDT for CMP submission during product registration or Change Notification application. You may also refer to Annex 1 for the summary of submission requirements.

Note: Product Owner (PO) shall provide justification or alternative information, as applicable, if any of the following outlined information is not available.

5.1 Quality assurance processes

By using Annex 2 template, describe how current quality assurance processes applicable to your SaMD can demonstrate the following:

a) Timely review of recognized standards throughout SaMD TPLC.
   - Demonstrate that processes are in place to enable timely review or perform gap analysis to assess whether the SaMD conforms to the latest standard version applicable to your SaMD.

b) SaMD versioning and traceability processes
   - Demonstrate the following processes are in place throughout the SaMD TPLC to enable identification and post-market traceability / follow-up in the event of software changes and / or field safety corrective actions:
     - SaMD software versioning: how the different levels of software version numbers are designated (e.g: version x.y.z, whereby x = major software change; y = minor software change; z = internally assigned build number).
     - 3rd party and / or open-source software, if applicable: Processes for record-keeping and monitoring of these components (e.g: Software bill of material , etc).

c) Cybersecurity and data safety management

Either (if SaMD PO conforms to IEC 81001-5-1)

- Conformance to IEC 81001-5-1 (Health Software and health IT systems safety, effectiveness and security). This can be demonstrated through certificate issued by accredited third-party certification body or in-house assessed summary report;
- Demonstrate on-going plan and/or processes in-place to address cybersecurity risks when current operating system is reaching End of Support (EOS);

Or (full set of cybersecurity requirements)

- Cybersecurity vulnerabilities (known and foreseeable), risk analysis focusing on assessing the risk of patient harm and mitigation measures implemented.
- On-going plans, processes or mechanisms for surveillance, timely detection and management of those identified and future cybersecurity-related threats including operating system reaching EOS and emerging vulnerabilities throughout the useful life of the device.
- Evidence that the security of the device/ effectiveness of the security controls have been verified. It should contain the following information where applicable:
    - Descriptions of test methods, results, and conclusions;
    - A traceability matrix between security risks, security controls, and testing to verify those controls; and
    - References to any standards and internal SOPs/documentation used.

d) Safety issues management, including effective adverse events (AE) and Field Safety Corrective Action (FSCA) reporting

- Demonstrate PO's proactivity and efficiency in responding to safety-related issues, including but not limited to
    - robust AE and FSCA reporting;
    - corrective software roll-out;
    - recovery software roll-back process or in-built mechanism to roll back to previous software version if an unexpected safety issue is found in the current software version.

e) For SaMD with third-party and open-source software
(E.g: commercial or 3rd party operation and communication systems):

Processes related to risk management of third-party and open-source software throughout the SaMD TPLC (E.g: monitoring potential hazards and risks; isolation of identified hazards and risks; implementation of the respective risk control measures, etc), including analysis

of the frequency of updates necessary to ensure SaMD receives timely cybersecurity support (E.g: network security updates, pushdowns, patches)

f) Post-market data analysis

- Processes related to how post-market data is collected, analysed, fed back into SaMD TPLC to consistently improve the SaMD, or mitigate newly identified risks (E.g: post market surveillance / real world data on cyber threats, technology update and risk assessments, etc).

g) Change management

- Processes to ensure potential safety risks are identified and mitigated upon implementation of changes, and all relevant deliverables are updated after a change (e.g.: software change history, release notes, etc)

5.2 Pre-specified changes

For SaMD with upcoming anticipated-changes (e.g: improvement in existing features / specifications, bug fixes, etc) that would otherwise require a new Change Notification application.

Exclusion: Changes resulting in change in SaMD intended use, indication for use and method of use (e.g: Existing approved workflow includes a review the final output by a nurse and specialist. New workflow will exclude the review of the result by a specialist), changes to device particulars which are published on SMDR.

Documentary requirements:

a) Change description

Information provided should include, but not limited to:

- List of the anticipated SaMD changes, including references to any associated proposed changes in labeling relevant to each modification. For each anticipated modification, please also specify the corresponding software version on a best effort basis. We understand that the software versions provided may be subject to change in the future.
- Information on expected update frequency or implementation timeline on a best effort basis.
- Description on factors or triggers for implementation to take place (e.g: user feedback, performance thresholds, etc)

b) Implementation protocol

Describing how the changes will be implemented and managed. Information provided should include, but not limited to:

- Deployment plan - description on how each change will be implemented (e.g: automatically or manually by users, service engineers, etc)
- User communication plan - Description on how users can be informed when each change is implemented (e.g: communication note, release note, etc)
- Description of verification instructions (e.g. instructions to determine the current installed software version) for users to ensure successful implementation takes place, Description of the planned updated user training (if applicable)
- Draft labelling update plan - Description of expected labelling changes resulting from the implementation
- Post-update corrective action plan (E.g: Description of mechanisms put in place to detect and revert / stop the implementation of a change if the SaMD does not perform as intended after change is implemented, etc)
- Information on post-implementation surveillance plan, including real world performance monitoring (if applicable)

c) Performance verification & validation protocol

The protocol should describe the process that will be followed to demonstrate that the changed SaMD will meet the new identified specifications as part of a specific change, as well as maintain existing specifications (i.e: regression testing) . Information provided should include, but not limiting to:

- Description of test methods to support planned changes, including test objective
- Pre-defined acceptance criteria / specifications
- Management of potential safety risks identified from unresolved anomalies

d) For ML-SaMD* only:

**Note: not including continuous learning (CL) & generative AI*

1) Training test dataset selection / collection

New data input data and features/ attributes used to generate the corresponding output. Information should include:

- Data selection / collection protocols including clinical study protocols (as applicable) with inclusion/exclusion criteria;
- Quality assurance process related to the data consistency and completeness
- Processes to ensure training and test datasets are independent of one another

2) Re-training protocol. Information should include:
   - Description on how the planned re-training protocol is relatable to respective Change.
   - Objective of the re-training process (ie: how the re-training can achieve the Change described)
   - Plans to ensure the other software functions remain unaffected by the re-training process
   - Information on how re-training process is initiated (e.g., planned timeline, when new data reaches a certain size, etc).
   - Description on potential safety risks posed by re-trained AI model and their respective planned mitigations

e) Traceability table (for multiple changes only).
Relevant protocols (i.e: as described in part b – d) should be stated for respective change (i.e: as outlined in the change description).

Example:
To facilitate the review process, kindly cite the pertinent section or document file name for the corresponding change

Changes per described in section 5.2 a)	**Performance validation protocol**	**Implementation protocol**	**For ML-SaMD only**	
			Dataset protocol	**Re-training protocol**
Change 1	See section W	See section X	See section Y	See section Z
Change 2				
Change 3				
Change 4				

f) Post-implementation impact analysis
Analysis of the risks and benefits of implementing the pre-specified changes, as well as the mitigations of the identified risks. The information should include:

- Description on effects of the changes on device (e.g: comparison between initial baseline device performance vs post-change implementation device performance)
- Assessment of risks and benefits of respective changes and discuss how the activities proposed within the described performance validation and implementation protocols (i.e: section 5.2b and c) are able to reasonably ensure the safety and effectiveness of the device.

- Assessment on how the implementation of one change impacts the implementation of another change
- Overall collective impact analysis of implementation of all the proposed changes.

6. POST-CMP APPROVAL

Approved Pre-specified changes under CMP may be implemented without Change Notification submission. These approved changes are still subject to relevant post-market regulatory oversight. The Registrant shall be required to submit a Declaration on the implementation records within 1 year after approval of CMP application. Subsequent Declaration on the implementation records shall be submitted within 1 year from the last declaration submission.

Companies are to ensure that appropriate mechanisms are in place to differentiate and identify the changed SaMD from the original version (e.g. through software version, change implementation date, etc), and maintain relevant inventory records on file to ensure traceability of the different SaMD versions, as part of their quality management system (QMS). All relevant records on file shall be made available to the Authority upon request.

7. CHANGE NOTIFICATION

A software medical device undergoes a number of changes throughout its product life cycle. The changes are typically meant to (i) correct faults, (ii) improve the software functionality and performance to meet customer demands and / or (iii) ensure safety and effectiveness of the device is not compromised (e.g. security patch).

The following type of changes require Change Notification submission:

Type of changes	Categories of change	Submission requirement
Change to previously approved Pre-specified changes	Notification change	1) Annex 2 to GN-21: Summary Table of Change Notification 2) Updated relevant section 5.2, with changes highlighted/identified.
Addition of new Pre-specified changes		1) Annex 2 to GN-21: Summary Table of Change Notification 2) Section 5.2
All other changes (ie: not described above)	Please refer to **GN-21: Guidance on Change Notification for Registered Medical Devices** For changes to registered ML-SaMD, please refer to **Regulatory Guidelines for Software medical Devices – A Life Cycle Approach**	

Notification Changes may be implemented immediately upon receipt of the acknowledgement email from HSA after submission via MEDICS.

Changes under Notification change type may be bundled and notified to HSA in one change notification application. Alternatively, such changes could be submitted together with the next Review/Technical change of the registered software (whichever comes first). While bundling Notification changes, any such change shall be submitted within a maximum of 6 months from the point of first implementation, globally. Prior to implementation of notification changes in Singapore, companies shall maintain relevant inventory records on file to ensure traceability of the changes as part of their QMS requirements.

Bundled Notification Changes do not apply to:

- Artificial Intelligence (AI) based devices (e.g. machine learning, neural networks and natural language processing); and
- AE/FSCA related changes.

8. LEVERAGING ON APPROVED CMP

As equivalent quality management processes may be applied across similar SaMDs, the same CMP documentation may be applicable across these devices.

To reduce redundancy in CMP dossier preparation and facilitate faster market access for similar upcoming SaMD, Product Owner may leverage on the approved CMP documentation (except Section 5.2) in

i) new Product Registration on similar SaMD; or
ii) CN* for existing registered SaMD (ie: different listing),

if the quality management processes are equivalent for both SaMDs (new SaMD and previously approved SaMD under CMP).

** Note: Review change for class B SaMD; Technical change for Class C SaMD*

The following documents are required to be submitted (refer Annex 1 for summary of submission requirements):

- Evidence of conformity to ISO 13485 & IEC 62304 (Section 3)
- Justification for identified SaMD used as the reference case in previously approved CMP submission remains applicable to the new SaMD intended to be registered / already-listed SaMD.
- Pre-specified changes documents (Section 5.2), if applicable.

  Note: The pre-specified changes for the new SaMD may be different from the pre-specified changes authorized for the previously approved SaMD under CMP.
- Declaration letter from PO stating that the the quality management processes for the new SaMD / already-listed SaMD are equivalent to the one reviewed previously for referenced CMP-approved SaMD (Annex 3).
- Referenced CMP-approved SaMD device name and SMDR listing number

9. TURN-AROUND TIME (TAT) AND FEES

There is no change to target turn-around-time (TAT) for Product registration and Change Notification applications with CMP enrolment. The target TAT for Product registration and Change Notification applications commences from the date of receipt of the application and does not include 'stop-clock time' due to input requests for clarifications and additional information. Information on TAT for respective application types can be found on HSA website.

There is no additional fee chargeable for CMP enrolment. Product registration and Change Notification application fees and evaluation fees can be found on HSA website.

10. ANNEXES

Annex 1: Summary of CMP submission requirements

Documents	New CMP application	With approved-CMP		
		New SaMD registration with equivalent Quality assurance processes	Change of approved Pre-specified changes	Addition of Pre-specified changes
Evidence of conformity to ISO 13485 & IEC 62304 (Section 3)	√	√		
Quality assurance processes (Section 5.1)	√	Justification of relevance only		
Pre-specified changes (Section 5.2)	√	√	Updated sections only	√
Declaration letter from PO on Quality Management Processes (Annex 3)		√		
Referenced CMP-approved SaMD device name and SMDR listing number		√		
Annex 2 to GN-21: Summary Table of Change Notification			√	√

Annex 2: Quality assurance processes checklist template

Quality assurance processes requirements	Description on how the conformity applicable to the SaMD can be demonstrated
Timely review of recognized standards throughout SaMD TPLC	
SaMD versioning and traceability processes	
Cybersecurity and data safety management	
Safety issues management, including effective adverse events (AE) and Field Safety Corrective Action (FSCA) reporting	
Processes related to risk management of third-party and open-source software throughout the SaMD TPLC	
Post-market data analysis	
Change Management	

Annex 3: Declaration letter on Quality Management Processes template

[To be printed on Company Letterhead of Product Owner]

Medical Devices Cluster
Health Products Regulation Group
Health Sciences Authority

[Date]

Dear Sir/Madam,

Subject: Declaration letter of Quality Management Processes

We, *[name of Product Owner (Company Name)]*, as the Product Owner confirm that the Quality Management Processes for *[new SaMD device name]* are identical/equivalent to the one reviewed previously for *[referenced Device name (SMDR listing number), job reference number]*. If not identical, please provide a description of the differences.

Yours sincerely,

[Signature]

[Full name and Title of Senior Company Official]
[Name and address of company]

HEALTH SCIENCES AUTHORITY

Health Products Regulation Group
Blood Services Group
Applied Sciences Group

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