IMDRF International Medical Device Regulators Forum

Software as a Medical Device (SaMD)

Clinical Evaluation

IMDRF/SaMD WG (FD1)/N41: 2017

Bakul Patel, USA FDA

Chair – SaMD Working Group

NWIE Proposal - Software as a Medical Device (SaMD): Clinical Evaluation

Scope

The document describes a converged approach for planning the process for clinical evaluation of a SaMD.

Rationale

Though current clinical guidance are intended to be relevant across a broad spectrum of technology, SaMD operates in a complex socio-technical environment heavily influenced by the inherent nature of software that enables a highly interactive and iterative technological environment. A majority of the respondents (from the IMDRF survey) either believe current clinical guidance needs to be revised with criteria specific for SaMD, or don't know whether it applies to SaMD.

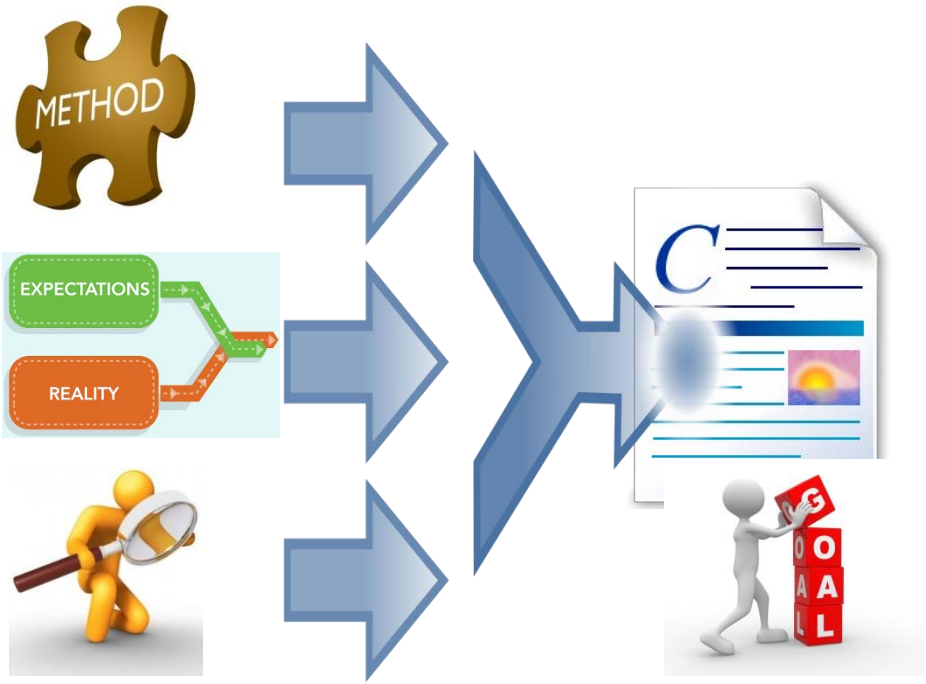
Alignment with Goals/Objectives

A common understanding on the application of clinical evaluation and clinical evidence processes and the need for clinical data to support market authorization will lead to increased transparency and promoting a converged thinking on this topic.

Goal

International Guidance -- Based on "SaMD category" (level of impact on public health) and unique aspects of software

- Relevant clinical evaluation methods and processes which can be appropriately used for SaMD to generate clinical evidence
- The necessary level of clinical evidence for SaMD and the continuous gathering of evidence through continuous learning from real world performance data
- SaMD categories where independent review is more or less important.



Project Summary Timeline

1. Discuss and create working draft document *(Feb-Mar 2016)*
2. WG member solicit input from mirror groups *(April 2016)*
3. Create formal draft document from input *(May 2016)*
4. WG member solicit feedback from mirror groups *(June 2016)*
5. Submit WD to IMDRF MC for public consult *(July 2016)*
6. Consolidate public comments *(Dec-Feb 2017)*
7. Draft preliminary final document *(Mar-April 2017)*
8. WG member solicit input from mirror groups *(May 2017)*
9. Create formal final document from input *(June 2017)*
10. **Submitted FD to IMDRF MC *(June 23, 2017)***

100+ comments from 22 entities and individuals

500+ comments from 36 entities and individuals

1400+ comments from industry (21), academia (5), regulators (9), trade associations (9) and others (18) (legal, consultants, individuals)

200+ comments from 15 entities and individuals

FD informed by 2200+ comments from global stakeholders

Key Feedback and Changes to Final N41

- Simplify architecture of document
- Streamline content and flow

Final Document:

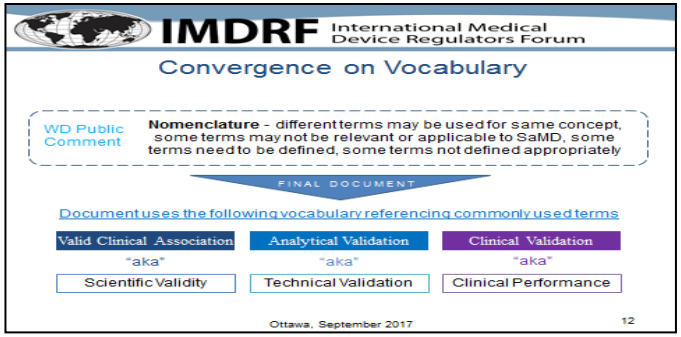
- ✓ Is 29 pages down from 45 pages
- ✓ Eliminates repetition of concepts
- ✓ Points to prior SaMD documents, GHTF

- Explicitly state that it is not a regulation

Document states:

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

- Adopt familiar terms and define them



Final Document Overview

- The document describes a converged approach for planning the process for clinical evaluation of a SaMD to establish that:
  - There is a valid clinical association between the output of a SaMD and the targeted clinical condition; and
  - The SaMD provides the expected technical and clinical data.
- The document recommends that certain SaMD may require independent review of the results of the clinical evaluation to ensure that the SaMD is clinically meaningful to users.
- The document encourages the use of technology to continuously monitor a SaMD to understand and modify software based on real-world performance data.

Clinical Evaluation & Evidence Gathering

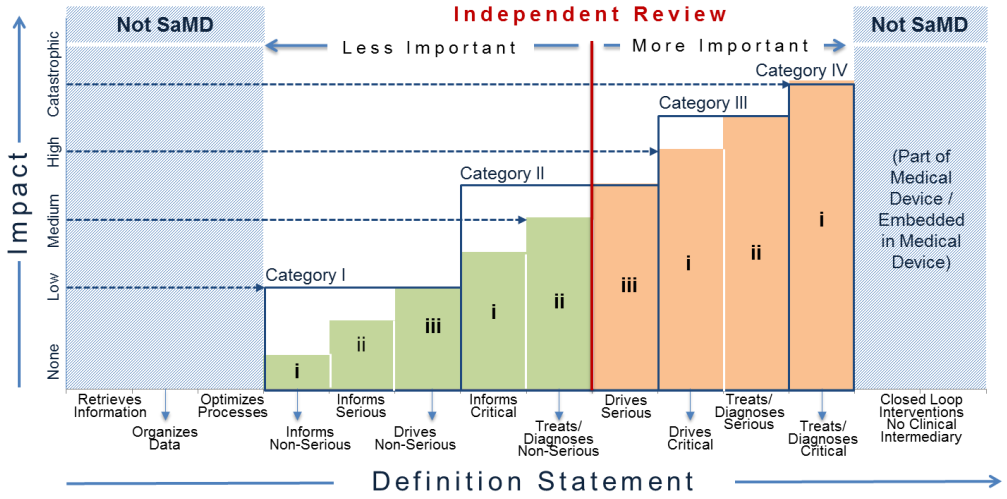
Clinical Evaluation

① Valid Clinical Association aka "Scientific Validity"	+	② Analytical Validation aka "Technical Validation"	+	③ Clinical Validation aka "Clinical Performance"
Generate evidence to demonstrate a valid clinical association between a SaMD output and a SaMD's targeted clinical condition		**Generate evidence** to demonstrate that the SaMD correctly processes input data to generate accurate, reliable, and precise output data		**Generate evidence** to demonstrate that the SaMD's accurate, reliable, and precise output data achieves its intended purpose in its target population in the context of clinical care

• **Use existing evidence** (e.g., literature searches, original clinical research, professional society guidelines), or
• **Generate new evidence** (e.g., secondary data analysis, perform clinical trials)
		• Generate evidence as part of **quality management system** or **good software engineering practices**		• Generate evidence that shows:
				  • **The SaMD has been tested for its target population and for its intended use;**
				  • **Users can achieve clinically meaningful outcomes through predictable and reliable use.**

Importance of Independent Review

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.

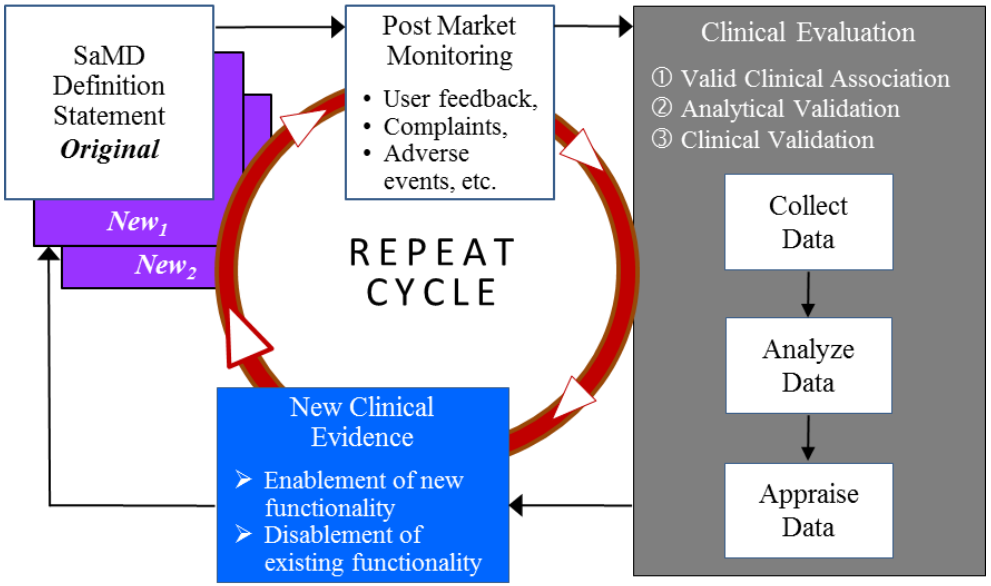


Independent review is more important for SaMD that 'Treats/Diagnoses Serious and Critical' health care situations and conditions and SaMD that 'Drives Critical' health care situations and conditions..

- The level of clinical evaluation and importance of independent review should be commensurate with the risk posed by the SaMD.
- Independent review does not necessarily imply regulatory review but instead demonstrates the concept where independence in review of the results is important.
- Less important independent reviews can be conducted by individuals within the company or by utilizing outside experts.
- 'More important' independent review may be conducted by outside experts, but may also be conducted by "non-conflicted" internal expert reviewers without significant involvement in the development of the SaMD.

Pathway for Continuous Learning Leveraging Real World Performance Data

SaMD manufacturers are encouraged to leverage SaMD's technology 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.



1. Additional clinical data is gathered.
2. The data may create and support new intended use(s).
3. The SaMD manufacturer will update the clinical evaluation and generate a new definition statement.
4. Cycle repeats for future iterations.

Recommended Next Steps

For the global healthcare community to see the full potential of digital health technologies, individual jurisdictions must lean forward, re-examine current regulatory tools, and adopt the principles set forth in this SaMD clinical evaluation document and in previous documents.

Benefits Realization:

- Encourage clinically focused good software engineering practices
- Global consistency and clarity on SaMD regulatory expectations
- Drive efficient and effective regulatory practices for SaMD
- Focus on higher risk SaMD functionality and attributes
- Enable patient's with access to safe and effective technology and innovation
- Build global trust and confidence in SaMD

Building blocks in place for individual jurisdiction's regulatory implementation

Goal - A Converged SaMD Framework and Associated Controls

Prioritized Building Blocks

Strategy – Create building blocks that contribute to the goal

SaMD Definition

(IMDRF N10)

SaMD Risk Framework

(IMDRF N12)

SaMD Controls

Quality Management System

(IMDRF N23)

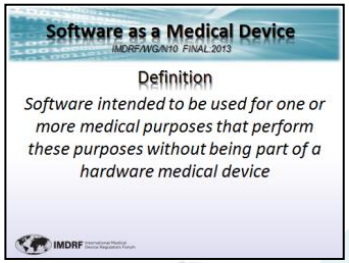
Clinical Evaluation

(IMDRF N41)

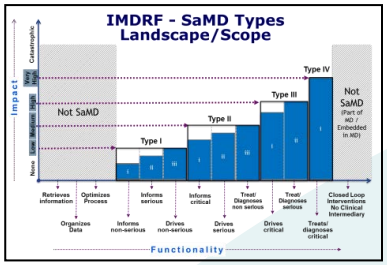
Each regulatory jurisdiction implements using converged IMDRF principles

Regulatory implementation according to the regulatory process in application in the respective jurisdictions

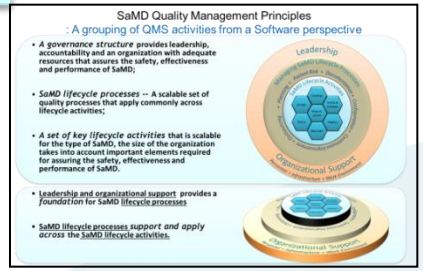
On a path towards global convergence



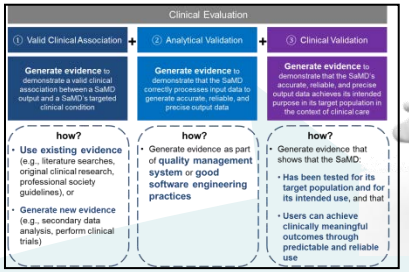
2013 Foundational vocabulary



2014 – Risk framework based on impact to patients

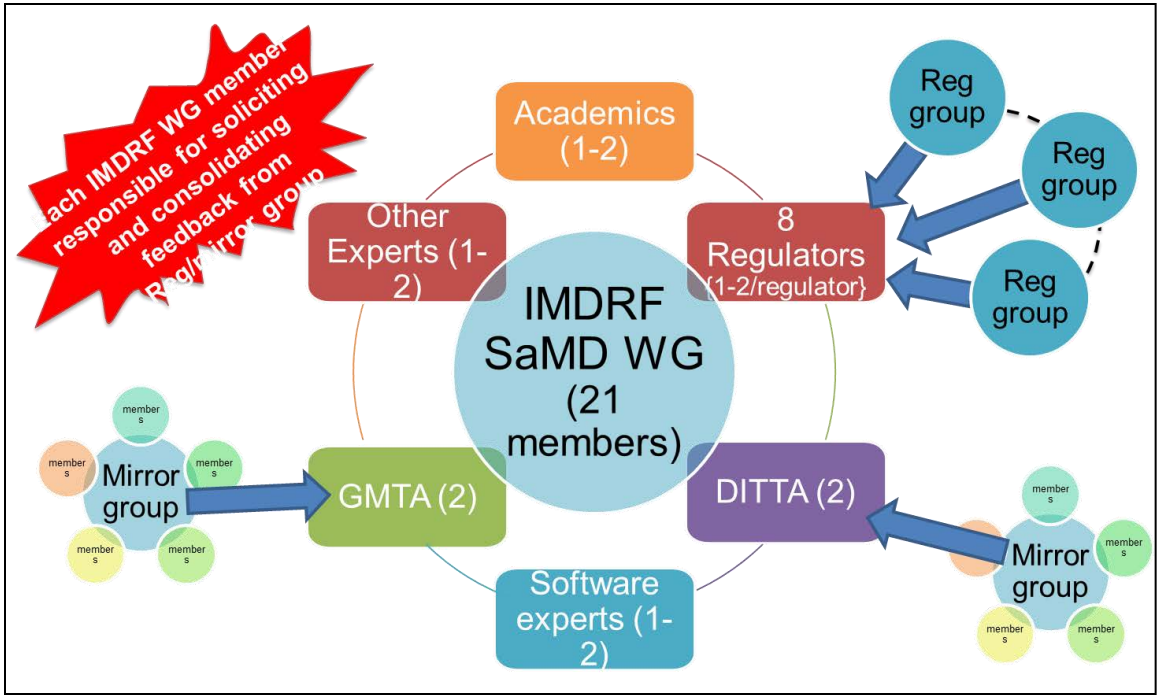


2015 – QMS control ➔Translating Software development practices to regulatory QMS



SaMD – Clinical Evaluation ➔Generating evidence for clinically meaningful SaMD

Thank you to all who contributed to this and prior SaMD documents



"We would like to express our appreciation to the IMDRF Working Group for their consideration and responsiveness to the comments submitted by AdvaMed and others. The guidance has been dramatically improved in clarity, content, graphical representation, and general organization. With the multitude of comments submitted, it is obvious that the Working Group expended a tremendous amount of effort to review and respond to the many suggestions. The addition of examples throughout the document is very helpful in understanding the intent of the guidance."