U.S. FOOD & DRUG ADMINISTRATION

Developing a Software Precertification Program: *A Working Model*

(v0.1- April 2018)

Introduction

The Software Precertification Program is envisioned as a voluntary pathway that embodies a regulatory model more tailored than the current regulatory paradigm to assess the safety and effectiveness of software technologies without inhibiting patient access to these technologies. The program is envisioned to provide a more streamlined and efficient regulatory oversight of software-based medical devices from manufacturers who have demonstrated a robust culture of quality and organizational excellence (CQOE) and committed to monitoring real world performance. The current vision for this regulatory model is described in this paper. This paper also sets out challenge questions for public comment, which will be incorporated into future updates of this working model that FDA will continue to periodically release for public input. This pilot precertification program is an important first step to help us explore and evaluate the program model to inform how we establish the precertification program. Once we determine the elements for a future precertification program, we will then consider appropriate mechanisms for establishing the program, including FDA's current statutory and regulatory authorities.

Software is increasingly used in healthcare to promote wellness, treat and diagnose disease, aid clinical decision making, and manage patient care. The ability to download these software programs onto ubiquitously connected mobile platforms allows them to be used in the hospital and in the home, by clinicians and patients. Historically, healthcare has been slow to implement technology tools that have transformed other areas of commerce and daily life. One factor that has been cited, among many, is the regulation that accompanies medical products. But momentum toward a digital future in healthcare is advancing. FDA oversees most mobile apps that are intended to treat, diagnose, cure, mitigate, or prevent disease or other conditions as medical devices under Federal statute. These software-based technologies, including mobile medical apps, are what FDA and other regulators call “Software as a Medical Device” (SaMD).

FDA’s traditional approach for the regulation of hardware-based medical devices is not well-suited for the faster, iterative design, development, and type of validation used for SaMD. SaMD products offer unique opportunities, such as addressing malfunctions quickly and efficiently to minimize adverse events, understanding and capturing patient performance outside of the clinical setting, and enabling patient engagement. Unlike manufacturers of hardware devices who modify their products every few months to years, developers of SaMD modify their products in response to real world performance and user feedback every few weeks to months. Furthermore, evaluating software code alone may not provide a full understanding of the safety and effectiveness of a SaMD product, in part because the impact on patients is often indirect. As a result, the application of FDA’s longstanding regulatory framework to SaMD can impede access to new and improved software-based medical products. An agile regulatory paradigm is necessary to accommodate the faster rate of development and potential for innovation in software-based products. It is important for public health to address these distinctive aspects of

digital health technology -- its clinical promise, unique user interface, ability to facilitate patient engagement with the developer, and compressed commercial cycle of new product introductions – while ensuring that existing standards of safety and effectiveness are met or exceeded.

To address these challenges, in July 2017 FDA announced the Software Precertification Pilot Program to develop a new regulatory paradigm that would focus first on the assessment of organizations that perform high-quality software design, testing, and monitoring. This proposed approach, based on demonstration of a culture of quality and organizational excellence and a commitment to monitor ongoing performance, is intended to drive market competition to higher standards of safety and effectiveness. Because SaMD products can be adapted to respond to glitches, adverse events, and other safety concerns quickly, FDA is working to establish a regulatory framework that will allow efficient responses to software issues, and thus continue to ensure that consumers have access to safe and effective products. The Software Precertification Program is envisioned to evaluate a firm's capability to respond to real world performance, and FDA intends to work with precertified firms to quickly and effectively address software issues.

As part of the development process, FDA is publishing this initial working model of the Software Precertification Program to gather public input. There are nine SaMD manufacturers participating in the pilot, but FDA considers the public to be the "tenth participant" and values stakeholder input in the development of the program. FDA will continue to build and refine this program by incorporating comments received, as appropriate, and will regularly seek additional public input throughout the development of this program.

Software Precertification Program

Scope

The current scope of the program is limited to FDA-regulated Software as a Medical Device (SaMD), as defined in the International Medical Device Regulators Forum (IMDRF) guidance documents and the recently adopted finalized SaMD clinical evaluation guidance document.

> *"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.*[1]

Program Goal

The goal of the program is to have tailored and pragmatic regulatory oversight that ***trusts*** organizations with a demonstrated culture of quality and organizational excellence to develop high quality products, leverages ***transparency*** of organizational excellence and product performance across the entire lifecycle of SaMD, utilizes a tailored streamlined premarket review, and leverages unique postmarket opportunities available in software to ***verify*** the continued safety, effectiveness, and performance of SaMD in the real world.

[1] http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-131209-samd-key-definitions-140901.docx

Program Overview

The program concept is based upon precertification of trusted SaMD manufacturers and will leverage data from all appropriate sources. This approach is intended to enable more efficient and streamlined oversight without compromising safety and effectiveness of SaMD products. Under this program, SaMD developers would be assessed by FDA or an accredited third party for the quality of their software design, testing, clinical practices, real world performance monitoring, and other appropriate capabilities to qualify for a more streamlined premarket review while better leveraging postmarket data collection on the device's safety and effectiveness.

This new, organization-based approach enhances the ability to assure the safety and effectiveness of software products by using the precertification framework in addition to some aspects of the Agency's traditional reliance on individual product-based oversight. FDA will evaluate organizational excellence based on five culture of quality and organization excellence (CQOE) principles (hereafter referred to as "excellence principles"):

- Product Quality
- Patient Safety
- Clinical Responsibility
- Cybersecurity Responsibility
- Proactive Culture

Leveraging the data gleaned from the precertification process, FDA would seek to adopt a risk-based, streamlined regulatory approach to SaMD review to either replace the need for a premarket submission or, for higher risk products, to allow for streamlined premarket review that maximizes efficiency and engagement. The premarket review determination will apply principles of premarket-postmarket balance by uniquely leveraging real world performance data. Similar to FDA's current regulatory system under which not all devices require premarket review (e.g., 510(k) exempt devices), this program envisions exemptions from premarket review for lower risk SaMD products or faster review of higher risk SaMD products that are developed, delivered, and maintained by precertified organizations.

In addition to demonstrating excellence, as established through the five excellence principles, precertified organizations will also have a robust mechanism to collect, monitor, and analyze real world performance of their organization and the products they deliver. FDA also intends to bolster postmarket monitoring by more effectively leveraging real world data from device registries and other electronic health information sources. The collection of real world performance data on precertified companies' SaMD products is anticipated to enable improvements of the Software Precertification Program itself.

The Software Precertification Program is intended to build stakeholder confidence that participating organizations have demonstrated capabilities to build, test, monitor, and proactively maintain the safety, efficacy, performance, and security of their SaMD products, so that they meet or exceed existing FDA standards of safety and effectiveness. FDA also recognizes the need for transparency so that end users of SaMD products from precertified companies can understand the premarket review and postmarket monitoring conducted for these products. Table 1 below shows anticipated benefits for various stakeholders.

Table 1. Example of Anticipated Program Benefits

	End user	Business	FDA	Payor	Investor
	Patients, Providers, Caregivers	*SaMD Developer*	*Agency Reviewer*	*Insurance Provider*	*Venture Capitalist*
Enhanced trust in organizations developing SaMD products	+		+	+	+
Improved quality/safety/proactiveness to address known and emerging risks	+	+	+	+	
Timely availability of solutions to patients	+	+	+	+	+
Enhanced regulatory simplicity and experience		+	+	+	+
Business simplicity - faster/timely market access	+	+	+		+

Challenge questions for the Precertification Program:
FDA proposes the following challenge questions for public input.

0.1 FDA recognizes stakeholder perspectives and priorities as important inputs into the development of the Precertification Program. How should anticipated stakeholder benefits in Table 1 above be revised, and what additional stakeholder perspectives should be included?

0.2 As a stakeholder, what would you want to know about the organizations that have been precertified and about the SaMD products that they manufacture?

Outline

To deliver the goals of the program as outlined above, we have divided the program into four key program components, depicted below in Figure 1.

1) Excellence appraisal and precertification,
2) Review pathway determination,
3) Streamlined premarket review, and
4) Real world performance (postmarket surveillance of SaMD products and feedback into the precertification program)

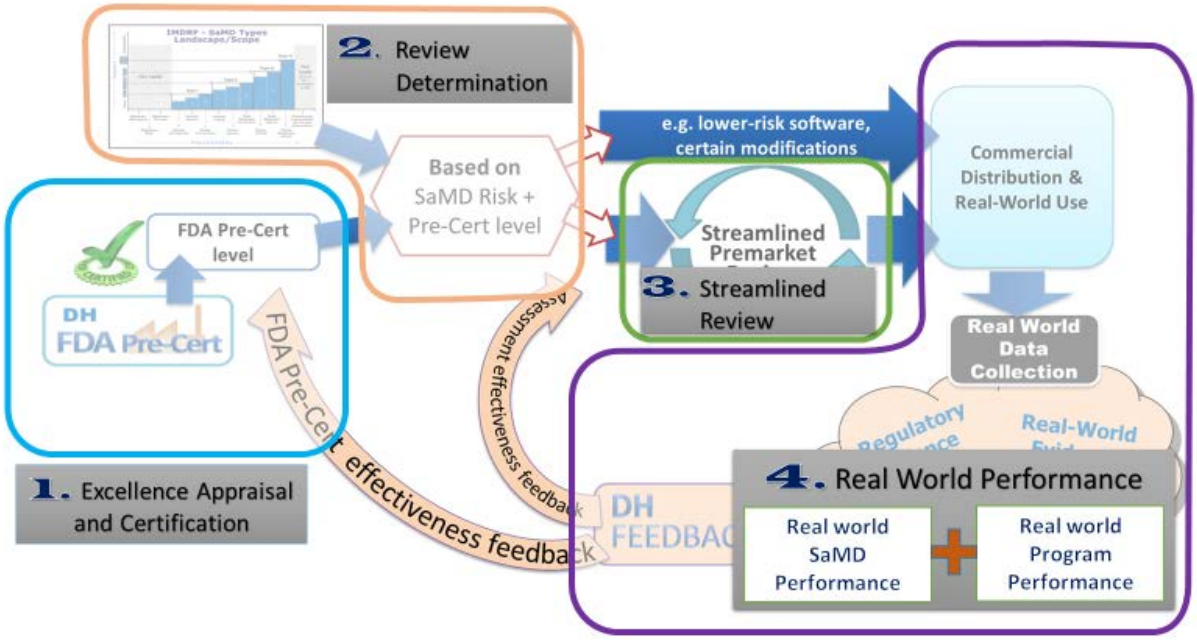

Figure 1. Software Precertification Program Components

Component 1: Excellence appraisal and precertification

The principal objective of the excellence appraisal and precertification component is to develop the process of company precertification, including eligibility and application, evaluation against precertification criteria, and precertification status determination.

Eligibility

Any organization that intends to develop or market a regulated SaMD in the United States would be eligible for the program. This could include organizations that are developing SaMD and organizations that are planning to develop SaMD. FDA recognizes the potential for significant variability in the culture and internal processes of different business units within a single organization; in the case of large organizations that are multinational or include multiple business units, therefore, FDA anticipates precertifying at a business unit or center of excellence level, rather than at a corporate level.

Initial Precertification

An organization will be appraised based on objective demonstration of its ongoing commitment to the five excellence principles:

- Product Quality – Demonstration of a commitment to the development, testing, and maintenance necessary to deliver SaMD products at the highest level of quality.
- Patient Safety – Demonstration of a commitment to providing a safe patient experience, and emphasizing patient safety as a critical factor in all decision-making processes.
- Clinical Responsibility – Demonstration of a commitment to responsibly conduct clinical evaluation and ensure that patient-centric issues including labeling and human factors are appropriately addressed.

- Cybersecurity Responsibility – Demonstration of a commitment to protect cybersecurity, and to proactively address cybersecurity issues through active engagement with stakeholders and peers.
- Proactive Culture – Demonstration of a commitment to a proactive approach to surveillance, assessment of user needs, and continuous learning.

This is an important first step to help us explore and evaluate the program model to inform how we establish the Precertification Program. Once we determine the elements for a future Precertification Program, we will then consider the appropriate mechanisms for establishing the program, including FDA's current statutory and regulatory authorities. While the FDA has not yet determined the appropriate method for determining appraisal and initial precertification, the information in this box reflects current thinking subject to public feedback and iteration.

We expect the method and process used to appraise an organization applying for precertification will include:

- **Application** - Eligible companies and business units apply to the Precertification Program; FDA confirms their eligibility and acceptability, and initiates process for precertification determination.
- **Appraisal** - The applicant collects objective indicators related to the excellence principles and makes available information that demonstrates their capabilities and maturity.
- **Determination** - The FDA evaluates evidence and makes a determination on approval and level of precertification.
- **Maintenance** - Precertification status is maintained, changed, or lost by automated and manual analysis of relevant indicators of organizational excellence, including real world performance.

The FDA will collect and evaluate objective indicators of an applicant's capabilities and maturity to determine the organization's precertification level and status. A requirement for precertified organizations will include the capacity and commitment to collect real world performance data of marketed SaMD products related to safety, effectiveness, and performance. The appraisal process is intended to be a least burdensome approach.

Precertification levels

The Precertification Program will distinguish between differing levels of excellence and experience in developing, maintaining, and marketing safe and effective SaMD. Organizations seeking precertification will have different levels of maturity in the medical device space. Some organizations have no or limited experience in delivering medical devices, but they have the culture, processes, systems, and other demonstrable characteristics that support the potential to create safe and effective SaMD. Other organizations have a demonstrated track record in creating safe and effective SaMD and/or other medical devices. Excellence and maturity models assess an organization's current performance on a well-established spectrum of practices and behaviors that drive success. The goal of establishing levels of certification is to allow organizations at different stages in achieving excellence to afford the advantages of the program that is commensurate with their level.

Among companies that have objectively demonstrated capabilities in all five excellence principles, the working model distinguishes between those companies that have successfully marketed and maintained medical devices, and those that have not.

Level 1 Pre-Cert – The FDA envisions this level would be awarded to an organization that has objectively demonstrated excellence in all five excellence principles, without a track record in delivering SaMD. This level of certification may benefit an organization with limited or no experience in delivering SaMD, but with established organizational elements and strategies in place that indicate the capability to deliver high quality SaMD that are safe and effective.

Level 2 Pre-Cert – The FDA envisions this level would be awarded to an organization that has objectively demonstrated excellence in all five excellence principles with a demonstrated track record in delivering SaMD and/or medical devices.

Benefits of the two levels are described below under "Component 2: Review Pathway Determination."

Maintenance and Monitoring of Pre-Cert Status

In the finalized state, the FDA expects that maintaining Pre-Cert status will be automatable, through objective evidence generated by approved organizations and made available to FDA. Organizational leadership will track and monitor its adherence to the excellence principles, and ensure safe and effective operation of their devices by responding appropriately to postmarket indicators, including adverse events. These details will be developed in a future version of the Software Precertification Program and made available for public comment.

Challenge questions for appraisal models:
FDA proposes the following challenge questions for public input. Although these questions are specific to excellence appraisal models and precertification status, they should be considered in coordination with the other aspects of the Precertification Program. The questions should also be considered with the objectives of establishing an excellence appraisal model, including identifying the evidence SaMD manufacturers can provide that ensure product safety and effectiveness, harmonizing FDA regulatory review with SaMD manufacturer timelines, and creating clear and straightforward FDA requirements.

1.1. How might an existing excellence or maturity appraisal framework used by a SaMD manufacturer be leveraged to demonstrate an organization's performance and success as outlined by the five excellence principles?

1.2. How might the appraisal process consider the track record demonstrated through an organization's objective Key Performance Indicators (KPIs) as part of the evaluation?

1.3. Does it matter if the track record is in medical device products or in consumer products and why? How long, and how detailed of a track record would be needed to demonstrate an organization's sustainable performance? Why?

1.4. When looking at past performance, how should negative events be evaluated to provide an accurate assessment of responsiveness, responsibility, and improvement?

1.5. FDA is anticipating establishing two levels of precertification. Please advise whether and why the same appraisal model should be used to assess all organizations applying for precertification, or whether separate appraisal models should be used for each level of precertification and why?

1.6. How might an appraisal framework reconcile the requirement for precertified organizations to demonstrate a consistent threshold of excellence with the recognition

that different organizations are likely to use performance measures specific to their operations and product lines?

1.7. How might an excellence or maturity assessment balance the FDA's "least burdensome" approach with the obligation to assure stakeholders that SaMD are safe and effective?

1.8. When considering large organizations that are multinational or include multiple business units, what defines a "unit" for purposes of FDA precertification? If FDA precertifies a "unit" within a corporation or multinational, how should FDA factor in corporate processes during appraisal?

1.9. Should there be two levels of Pre-Cert? What should be the differentiating factors between Pre-Cert levels?

1.10. Are there specific approaches to developing SaMD, such as machine learning and artificial intelligence, that raise different considerations with respect to the excellence principles, e.g., such that the appraisal would be different and/or precertification for the company based on processes/culture using one technology should not apply to other SaMD development methods? Why or why not?

Component 2: Review pathway determination

The principal objectives of establishing the review pathway determination component of the Software Precertification Program are to develop a risk-based framework to determine the need for premarket review and to clearly communicate to stakeholders how different premarket and postmarket requirements apply to each category of SaMD products. The FDA is exploring a paradigm for determining the premarket review pathway for a precertified organization's product. This pathway for premarket review for a precertified organization's product will be informed by the organization's precertification status, precertification level, and the SaMD's risk-category. The FDA envisions leveraging the risk-category framework for SaMD developed by the International Medical Device Regulatory Forum (IMDRF) to inform the risk category (see Table 2 below). The review pathway for initial product availability, major changes, and minor changes may differ.

We anticipate that the trust gleaned from the precertification process and commitment to robust postmarket oversight will mitigate residual risk for certain low risk devices from precertified device manufacturers enabling such devices to be introduced to market without a premarket review. Software instrumentation permits greater visibility into real world performance, and higher confidence in collected data, allowing companies and the FDA to react more quickly in cases where devices prove unfit for market under manufacturer's claims.

The IMDRF issued a framework for risk-based clinical evaluation of the safety and effectiveness of SaMD, which FDA adopted as a guidance document.[2] That framework includes Table 2,[3] designed to facilitate harmonized risk categorization of SaMD, based on intended use.

Table 2. IMDRF type (I to IV) and subtype (1 to 9) of SaMD products by state of healthcare condition and significance of information provided by the products to healthcare decision.

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 *(9)*	III *(7)*	II *(4)*
Serious	III *(8)*	II *(6)*	I *(2)*
Non-serious	II *(5)*	I *(3)*	I *(1)*

In order to determine where a SaMD falls in the IMDRF risk-categorization table, a SaMD manufacturer should characterize the SaMD's intended use as a "SaMD definition statement" (see box below) as defined in the "Software as a Medical Device": Possible Framework for Risk Categorization and Corresponding Considerations IMDRF N12 document.[4]

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 of the IMDRF N12 Framework document.***

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 of the IMDRF N12 Framework document.*

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.*

[2] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM524904.pdf.

[3] The table was first introduced by IMDRF in http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf.

[4] http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf, p. 12.

[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.

This is an important first step to help us explore and evaluate the program model to inform how we establish the Precertification Program. Once we determine the elements for a future Precertification Program, we will then consider appropriate mechanisms for establishing the program, including FDA's current statutory and regulatory authorities. While the FDA has not yet determined the appropriate method for determining review pathway, the detailed information in this box reflects current thinking subject to public feedback and iteration.

The table below lays out an initial model for determining premarket review pathway for SaMD from precertified companies, depending on (1) the IMDRF risk category of the SaMD, (2) the level of precertification of the organization, and (3) whether the SaMD is a new device or an iteration of an existing device, as follows:

Table 3. Level of Review for Level 1 and Level 2 Precertified Organizations' SaMD

IMDRF Risk Categorization			Level of Review for Level 1 and Level 2 Precertified Organizations' SaMD		
Type	**Sub type**	**Description**	**Initial product**	**Major changes**	**Minor changes**
Type IV	*(9)*	Critical x diagnose/treat	SR	SR	No Review
Type III	*(8)*	Critical x drive	SR	L1 – SR L2 – No Review	No Review
Type III	*(7)*	Serious x diagnose/treat	SR	L1 – SR L2 – No Review	No Review
Type II	*(6)*	Serious x drive	L1 – SR L2 – No Review	L1 – SR L2 – No Review	No Review
Type II	*(5)*	Non-serious x diagnose/treat	L1 – SR L2 – No Review	No Review	No Review
Type II	*(4)*	Critical x inform	L1 – SR L2 – No Review	No Review	No Review
Type I	*(3)*	Non-serious x drive	No Review	No Review	No Review
Type I	*(2)*	Serious x inform	No Review	No Review	No Review
Type I	*(1)*	Non-serious x inform	No Review	No Review	No Review

This table describes when the precertification of organizations and commitment to leverage real world performance replaces the need for a premarket submission (no review) or allows for streamlined premarket review (SR), according to the IMDRF type/subtype of the SaMD and the Pre-Cert Level of the organization (L1, Level 1; L2, Level 2).

Challenge questions:

FDA proposes the following challenge questions for public input. Although these questions are specific to the review pathway determination, they should be considered in coordination with the other aspects of the Precertification Program. The questions should also be considered with the objectives of establishing the review pathway determination component of the Software Precertification Program, including developing a risk-based framework to determine the need for premarket review and clearly communicating to stakeholders how different premarket and postmarket requirements apply to each category of SaMD products.

2.1 Given the definition of SaMD, what additional information is needed to help stakeholders clearly differentiate between software as medical device (SaMD), software in a medical device (SiMD), and other types of software and hardware?

2.2 The IMDRF definition statement is intended to provide a structure towards defining intended use. Should other components be included, and if so, what, or should the current components be modified in order to provide clarity around the function of the SaMD and if so, how?

2.3 The IMDRF risk categorization framework uses and defines "inform," "drive," and "diagnose/treat" to identify the "significance of information provided by SaMD" of how the SaMD is intended to be used. What additional clarity or modifications are necessary within these definitions that will enhance the use of this risk categorization framework?

2.4 The IMDRF risk categorization framework uses and defines "non-serious," "serious," and "critical" to identify the "state of health care situation and condition" where the SaMD is intended to be used. What additional clarity or modifications are necessary within these definitions that will enhance the use of this risk categorization framework?

2.5 How should FDA think about a major change versus a minor change for SaMD, and about how these changes should be handled?

2.6 Should the current software modifications guidance be enhanced with the added assurance of a precertified organization and if so, what are some proposed enhancements and what concepts should be considered for the guidance?

2.7 Should FDA be informed about new products, major changes, and minor changes from precertified organizations that do not undergo premarket review, and if so, how?

2.8 Cybersecurity issues often circumvent intended use. How can/should this be considered when determining risk level?

Component 3: Streamlined premarket review process

The principal objectives of establishing the streamlined premarket review process component of the Software Precertification Program are to establish the scope of the review of a precertified company's SaMD, what information will be reviewed, how modifications affect marketing authorization, and how to leverage existing SaMD community standards. Organizational capabilities demonstrated by precertified companies give SaMD manufacturers, FDA reviewers, and consumers greater insight and confidence in SaMD products. These SaMD products merit a streamlined review process that takes advantage of the information available to reviewers from precertification and recognizes the demonstrated maturity against the five excellence principles. The content, method, and process for premarket review can be streamlined to account for these factors.

The FDA envisions reviewing an organization's clinical evaluation results (per final SaMD IMDRF guidance N41) and risk management for safety for the device's intended use, as appropriate. The FDA intends to conduct an interactive review supported by automated

analysis, where appropriate, and to provide a decision on the marketing of the precertified company's SaMD product within a shorter timeline than other premarket review processes.

If FDA does not authorize the marketing of the product, the organization and FDA will complete an after-action review to determine gaps in the evidence supporting the submission and determine a plan for future submission. The FDA expects repeated unsuccessful streamlined reviews of a precertified organization's SaMD to trigger a process to reassess the organization's precertification determination. FDA and the precertified organization will review the basis of the precertification to address any systematic issues within both the organization and the precertification program.

This is an important first step to help us explore and evaluate the program model to inform how we establish the Precertification Program. Once we determine the elements for a future Precertification Program, we will then consider appropriate mechanisms for establishing the program, including FDA's current statutory and regulatory authorities. While the FDA has not yet determined the appropriate method for determining review pathway, the information in this box reflects current thinking subject to public feedback and iteration.

1. In a streamlined review, the precertified organization will provide the SaMD Definition Statement (as defined by IMDRF N12) and an overview of the intended use of the SaMD during an interactive review with FDA. FDA is considering options for how the organization could describe the SaMD and its intended use, such as an interactive demonstration or submission of a wireframe of the SaMD.

2. In a streamlined review, the FDA interactively reviews supporting information. FDA is considering options for the supporting information, which could include evaluating product performance, the clinical association between the SaMD output and a clinical condition, and appropriate safety measures. For instance, this review may be conducted through screensharing, access to development environment, and testing logs – using freeform audit of test results.

3. FDA makes a premarket decision, documents a summary, and communicates the decision to the organization.

Challenge questions:

FDA proposes the following challenge questions for public input. Although these questions are specific to the streamlined premarket review process, they should be considered in coordination with the other aspects of the Precertification Program. The questions should also be considered with the objectives of establishing the scope of the review of a precertified company's SaMD, what information will be reviewed, how modifications affect marketing authorization, and how to leverage existing SaMD community standards.

3.1 Given that one goal of this program is to significantly reduce the average premarket review timeline, what would be the best way for precertified companies to share product review information with us? Specifically:

3.1.1. What specific elements of review could be shifted to the company-specific excellence appraisal (as opposed to the product-specific review)?

3.1.2. What are the features of a SaMD product that need to be assessed during device review?

3.1.3. What product-specific content would be expected to be reviewed premarket?

3.1.4. What specific postmarket real world data could be collected to support the assurance of safety and effectiveness for each product if an element is not reviewed premarket?

3.1.5. What updates should FDA require, and at what interval, to provide continuous assurance of safety and effectiveness?

3.1.6. Should there be a phased market authorization, where some elements are reviewed premarket and other elements are gathered through real world evidence to support full market authorization? What should happen to products that receive "preliminary" market authorization but fail to provide adequate evidence in the agreed upon timeframe?

3.2. Beyond number of days, what are additional key factors important for a successful streamlined review?

3.3. Once a review decision is made:

3.3.1. How should the FDA share that information with the company? With the public?

3.3.2. Should the public know that a product comes from a precertified company and if so, what is the best way to share that information?

3.4. Imagining that there is an initial, automated part of the review – what information can be provided so an initial automated review can add value?

3.5. A key element for streamlined review will be the communication between precertified companies and FDA. What technologies can be leveraged to support bi-directional communication?

3.6. How should FDA handle an organization that submits an unsuccessful submission for premarket review? Should there be a limit on the number of unsuccessful submissions a precertified organization can submit before their precertification status is affected?

3.7. Could FDA conduct a premarket review without requiring a premarket submission and if so, how, e.g., by accessing and interactively reviewing information internal to the precertified organization about the SaMD?

3.7.1. What are possible methods to facilitate FDA access to necessary information?

3.7.2. Is there information other than risk management, technical evaluation, and clinical evaluation necessary for such a review to assure safety and effectiveness of the SaMD?

3.7.3. How should the reviewed information relevant to the marketing authorization decision be documented for administrative purposes?

3.8. Is premarket clinical performance necessary to assess SaMD safety and effectiveness? Please explain your answer and provide your rationale.

3.9. Should FDA be informed about new products, major changes, and minor changes from precertified organizations that do not undergo premarket review, and how?

Component 4: Real world performance

The principal objectives for the real world performance component of the Software Precertification Program are to develop real world performance data (RWPD) elements and analytic methodologies needed for Pre-Cert Program activities. The scope of this program component is to identify and address all requirements and expectations for use of RWPD by both precertified organizations and FDA in the Pre-Cert Program. These details will be developed in a future version of the Software Precertification Program and released for public comment.

SaMD manufacturers have the capacity to continuously improve by leveraging knowledge obtained through the ongoing monitoring, collection, and analysis of SaMD product performance. To verify the ongoing safety and effectiveness of SaMD products marketed through the Pre-Cert Program, all precertified organizations will be required to demonstrate a robust program for monitoring real world performance data related to their SaMD devices, and for sharing such data with FDA.

Terminology

For the purposes of this document, real world performance data (RWPD) is defined as all data relevant to the safety, effectiveness, and performance of a marketed SaMD product from a precertified manufacturer. FDA anticipates that RWPD may be generated efficiently by leveraging not only data collected from appropriately instrumented SaMD products, but also real world data from device registries, and other electronic health information sources including the National Evaluation System for health Technology (NEST), which is currently under development.

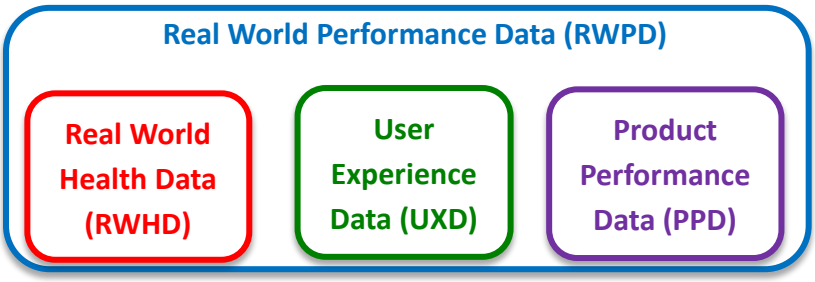

Figure 2. Relationship between various types of SaMD RWPD outputs and outcomes

FDA considers RWPD to encompass at least three types of data (Figure 2), as defined below.

- Real world health data (RWHD) are outputs and outcomes related to the SaMD Definition Statement. RWHD can inform changes to the intended use of a SaMD product, support expanded functionalities and use in broader target populations, and monitor the continued safety and effectiveness of a marketed SaMD product.
- User experience data (UXD) are outputs derived from user experiences related to the real-world use of a SaMD product. UXD facilitate timely identification and correction of user issues, and improve utilization and effectiveness of the software.
- Product performance data (PPD) are outputs and outcomes demonstrating the accuracy, reliability, and security of a SaMD product. PPD monitoring allows for timely patches and updates to correct software bugs and security vulnerabilities.

Framework for Use of RWPD

FDA intends to use RWPD for monitoring and feedback at product, organizational, and program levels. FDA proposes the following key objectives for use of RWPD and has identified the bulleted elements requiring development:

1. *Monitoring ongoing safety, effectiveness, and performance of marketed SaMD products.*

    - Expectations for instrumentation of SaMD products to collect and analyze RWPD;
    - Identification of data sources external to SaMD manufacturers for information about RWPD of SaMD products;
    - Framework for analyses of RWPD to be performed by precertified organizations; and
    - Mechanism and frequency of RWPD sharing between FDA and precertified organizations.

2. *Supporting modifications of clinical and performance claims for safety and effectiveness.* FDA anticipates that use of RWPD for this purpose will involve defining the following elements:

    - Methodology and processes to evaluate RWPD used to support an initial SaMD product claim; and
    - Methodology and processes to evaluate RWPD used to support a design change, labeling change, or change in intended use; such changes may reflect either increased or decreased functionality of the SaMD product in real world performance, as compared to pre-launch expectations.

3. *Providing input to initial precertification and changes to precertification status.* FDA anticipates that use of RWPD for this purpose will involve defining the following elements:

    - Methodologies and processes for using RWPD as inputs into the initial precertification appraisal; and
    - RWPD-based thresholds that would trigger a need to review and modify the precertification status of an SaMD manufacturer.

4. *Providing feedback to FDA to further refine the Pre-Cert Program appraisal model and streamlined review process.* FDA anticipates that use of RWPD for this purpose will involve defining the following elements:

- Framework for using aggregate RWPD of precertified organizations to inform refinement of the precertification appraisal model; and
- Framework for using aggregate RWPD of precertified organizations to inform refinement of the precertification streamlined review process.

FDA Access to RWPD

All precertified organizations will be required to conduct ongoing monitoring and analysis of RWPD, and to provide access to such data to FDA on a regular basis and at the request of the Agency. FDA expects access to RWPD to both inform FDA decisions on both individual products and the precertification status of SaMD manufacturers.

Challenge questions:

FDA proposes the following challenge questions for public input. Although these questions are specific to real world performance, they should be considered in coordination with the other aspects of the Precertification Program. The questions should also be considered with the objectives of establishing the RWPD component of the program, including developing elements, metrics, and methodology of RWPD and analysis needed for Pre-Cert Program activities and defining RWPD requirements for each component of the program.

4.1 As FDA conducts a landscape assessment of existing RWPD frameworks and use cases, what are important sources of information and stakeholders to include?

4.2 How can RWPD surveillance best be designed to support existing standards of safety and effectiveness?

4.3 What are critical RWPD elements to be monitored by SaMD manufacturers?

4.4 Are the definitions for data types underlying RWPD accurate and comprehensive or do the terms used in this section need to be modified or revised, and if the latter, how?

4.5 From the perspective of a precertified organization, how does RWPD differ from real world evidence (RWE) in supporting pre-launch product clearance and post-launch modification product claims?

4.6 Since the methodology of analyzing RWPD is still evolving, how can we strike a balance between ensuring the scientific rigor in analytic methods and encouraging innovation in collecting and analyzing RWPD for regulatory considerations?

4.7 RWPD can come in different shapes and sizes. Should RWPD requirements depend on the risk level of the intended product claim or modification in claims?

4.8 How can precertified organizations best leverage existing RWPD processes to reduce the submission burden for pre-launch product clearance and post-launch modification product claims?

4.9 How can FDA and SaMD manufacturers ensure that least burdensome principles are applied in collecting real world data? That is, what is the minimum amount of RWPD necessary to adequately determine precertification through the most efficient manner at the right time?

4.10 How can we ensure that the patient or end-user expectations about safety and effectiveness of SaMD are met by the process developed to review and evaluate the use of RWPD in precertification?

4.11 Should an organization that meets a higher level of precertification have the same requirements for RWPD monitoring as an organization at a lower level of precertification and why?

4.12 How can we ensure the methods to review and evaluate RWPD for precertification are robust, applicable, and understandable across different types of organizations?

4.13 With what frequency should FDA assess RWPD as an input into precertification maintenance?

4.14 What RWPD elements should be the most critical inputs for assessing whether precertification status should be maintained or modified?

4.15 What would be an appropriate risk matrix for FDA to use in determining which adverse outcomes should result in a loss of precertification status?

4.16 How can FDA use RWPD surveillance to support SaMD manufacturers in continuous product improvement and maintenance of precertification status?

Next Steps and Public Engagement

FDA is publishing this initial working model of the Software Precertification Program to gather public input on this developing program. FDA will continue to evolve this document by thinking through what is needed to be successful, by incorporating comments received, as appropriate, and will regularly seek additional public input throughout the development of this program.

FDA is seeking public feedback on this version of the working model by May 31, 2018 at https://www.regulations.gov/comment?D=FDA-2017-N-4301-0001. This feedback will be incorporated into future versions of the program model, which will also be disseminated for public input.