FDA U.S. FOOD & DRUG ADMINISTRATION

CENTER FOR DEVICES & RADIOLOGICAL HEALTH

Developing the Software Precertification Program:
Summary of Learnings and Ongoing Activities

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2020 Update

Summary

Software is increasingly used in healthcare in connection with treatment and diagnosis of diseases and conditions, including aiding clinical decision making and managing patient care. The ability to access software programs through a variety of platforms allows them to be used in the hospital and in the home, by clinicians and patients. FDA's traditional approach for the regulation of hardware-based medical devices is not well suited for the faster and more iterative design, development, and validation techniques used to develop high quality, safe and effective software, including Software as a Medical Device (SaMD). Rather, today's software development techniques and lifecycles offer unique opportunities and benefits that are not fully realized under the FDA's traditional pathways for regulating medical devices. Modern software development and deployment techniques can allow developers to address malfunctions quickly and efficiently to reduce adverse events, to understand and capture information about product performance outside of traditional clinical trials, and to measure and improve patient engagement and outcomes with iterative deployment of software improvements.

To address these challenges and opportunities, the FDA proposed a new framework and approach in the Working Model v1.0 (WOMO 1.0) of the Software Precertification (Pre-Cert) Program. FDA also launched the Pre-Cert Pilot Program test phase in 2019 and issued two companion documents: the Test Plan and the Regulatory Framework for Conducting the Pilot Program within Current Authorities. The Test Plan explained how the FDA intended to test the proposed framework in the WOMO 1.0 to assess whether the Excellence Appraisal and Streamlined Review components together produce an equivalent basis for determining reasonable assurance of safety and effectiveness as compared to the traditional paradigm. The Regulatory Framework explained how FDA planned to implement the WOMO 1.0 through the De Novo classification process (section 513(f)(2) of the FD&C Act).

The current COVID-19 public health emergency further underscores the need to enable rapid access to safe and effective devices of public health importance. The public health emergency has highlighted the utility of deploying flexible regulatory approaches that can be tailored to suit situational needs.

The development roadmap (see Figure 1) of the Pilot Program is comprised of several phases to help the FDA iteratively test and build the framework of the program before moving into larger scale beta-testing. As the FDA continues to identify, evaluate, and improve on Pre-cert Pilot Program approaches to assure safety and effectiveness of products that require marketing authorization, the FDA's marketing authorizations for these products will continue under the FDA's existing regulatory pathways. FDA continues to develop the Pre-Cert Pilot Program using a transparent and open approach to provide continuous notice and solicitation of public input by means of an open public docket throughout the program development.

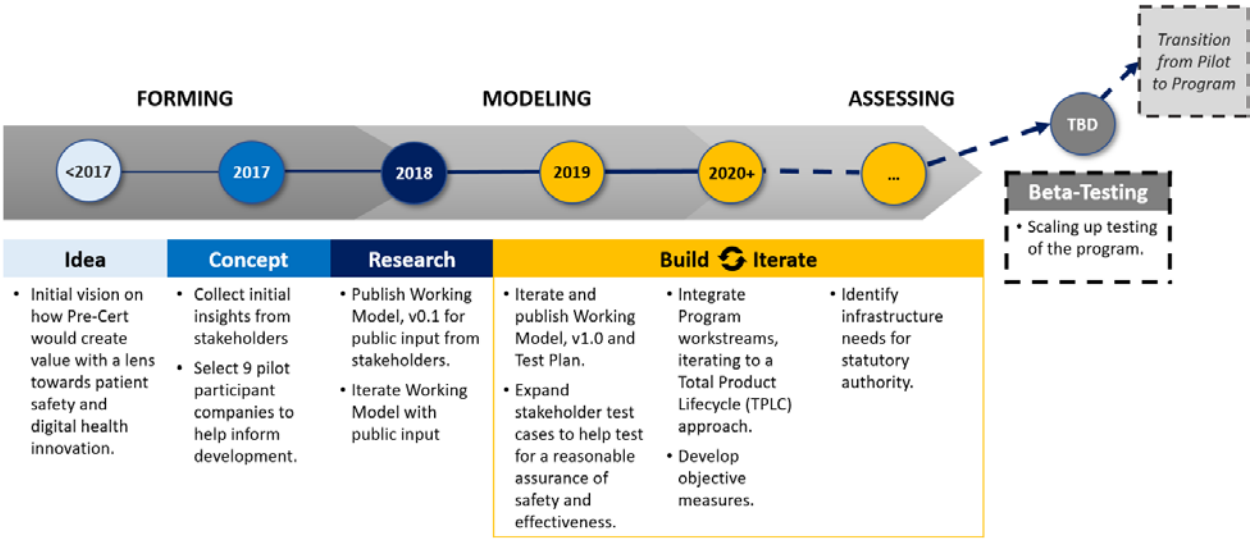


Figure 1. Software Pre-Cert Pilot Program Development Roadmap

This document highlights learnings[1] to date from the building and testing of the Pre-Cert Pilot Program and how the pilot program is leveraging its learnings for the next iteration of testing. Specifically, this document highlights the following findings:

- A mock Excellence Appraisal[2] reliant on remote pre-work and objective evidence appears to be a viable alternative to a multi-day on-site visit;
- Additional exploration and testing is needed to inform Streamlined Review[3]; and
- Collection of Real-World Performance[4] data allowed for the observation of several important measures, including Human Factors Usability and Engineering and metrics that provide assurance that safety risks are managed and mitigated in a timely way. More testing is needed to understand how health benefits may be observed in Real-World Performance data.

Based on public comments and other information collected in support of program development, the FDA is working with pilot participants and test case[5] companies to define structured data models for the information and objective evidence needed to make key decisions at each stage of the product lifecycle under the future Pre-Cert Program. As we learn and iterate, these data

[1] These learnings are generalized and do not refer to any confidential commercial information from a particular test or pilot participant.
[2] See section "About Excellence Appraisals" in the Midyear 2019 Update available at https://www.fda.gov/media/129047/download
[3] See section 6 Streamlined Premarket Review Process of the WOMO 1.0, available at https://www.fda.gov/medical-devices/digital-health/digital-health-software-precertification-pre-cert-program
[4] See section 7.2 Real World Performance Collection Plan of the WOMO 1.0.
[5] In 2019, FDA announced an opportunity for software organizations to volunteer to participate in the 2019 Test Plan. The test case companies referred to in this document are those who were selected from the companies who volunteered in response to this announcement, as described on our webpage "Participate in the 2019 Test Plan" available at https://www.fda.gov/medical-devices/digital-health-software-precertification-pre-cert-program/digital-health-software-precertification-pre-cert-program-participate-2019-test-plan

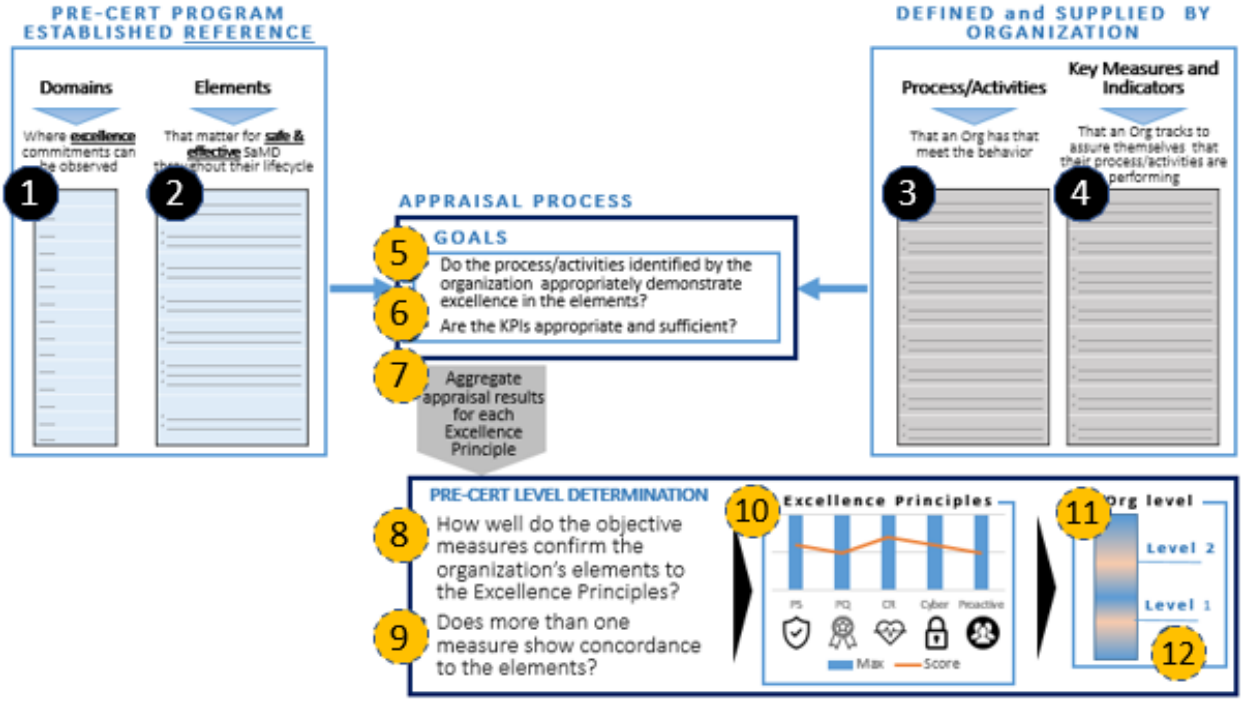
models will inform how components of the future Pre-Cert Program interact to support a determination that marketed products are safe and effective.

The learnings from building and iterating the structured data models to support the Pre-Cert Pilot Program will also inform the FDA as to specific regulatory authorities needed to implement a more effective, proactive, and efficient regulatory framework for software-based medical devices.

Summary of Activities and Learnings

In Section 4 of the WOMO 1.0, the FDA included a conceptual framework for the Excellence Appraisal. FDA has built out and tested several pieces of this framework. Figure 2 below depicts the conceptual framework and denotes the parts the FDA built and tested to date (see parts 1-4 in Figure 2).

Figure 2. Conceptual Framework for Excellence Appraisal (with Numbering) from the WOMO 1.0



The following is an overview of the testing the FDA has conducted with the help of pilot participants and test case companies:

- Conducted mock Excellence Appraisals to test different methods and approaches of collecting objective evidence that aligns to the Pre-Cert Excellence Principles[6];
- Explored the usability of the information gathered during the mock Excellence Appraisals; and

[6] See section 3.4 Software Precertification Program Overview of the WOMO 1.0 available at https://www.fda.gov/medical-devices/digital-health/digital-health-software-precertification-pre-cert-program

- Aggregated activities, processes, and Key Performance Indicators (KPI) observed during mock Excellence Appraisals and other sources—metrics identified during the Pre-Cert Public Workshop, initial site visits with pilot participants, the public docket, and literature reviews—as part of creating a library of activities, processes, KPIs.[7]

FDA took an iterative approach when conducting mock Excellence Appraisals. The intent of these mock appraisals was to create and test a structured approach to collecting objective measures and evidence indicative of the organization's culture of quality and organizational excellence and product performance. The testing process started with a three- to four-day site visit, and currently the FDA is testing an approach reliant on remote pre-work, in part driven by the current restrictions related to COVID-19. As communicated in the 2019 Software Precertification Program Mid-Year Update[8], the FDA confirmed that the elements identified in the Pre-Cert Program model can be demonstrated and provide a comprehensive view of an organization's capabilities.

As described in Section 4.4 of the WOMO 1.0, one of the tools envisioned for the program is to develop a library of activities, processes, and KPIs used by high performing organizations. A draft framework for the library has been created and draft content added to the KPI library from information collected during the mock Excellence Appraisals. The draft library also includes relevant information from the Pre-Cert Public Workshop, initial site visits with pilot participants, the public docket, and literature reviews.

In Section 6 of the WOMO 1.0, the FDA also explained how Streamlined Review would work at a high-level, including identifying the elements necessary for safety and effectiveness in a premarket review, which of these elements would be included in a Streamlined Review Pre-Cert package, and how the depth of review would change for certain elements depending on the risk. The model also outlined specific testing objectives for 2019. FDA built on the high-level concepts included in the WOMO 1.0 and tested several parts of the Streamlined Review framework, and this work is continuing.

In accordance with the Test Plan, the FDA also completed the following activities:

- Conducted staged reviews of select traditional premarket submission packages and of mock Streamlined Review packages for which the FDA extracted elements from the Excellence Appraisal, Review Determination Pre-Sub, and the traditional premarket submission (as described in the WOMO 1.0[9]) and compared the outcomes of the two processes. *(Note that this testing did not impact the final market authorization decision—all premarket submissions proceeded through the traditional review pathways)*; and
- Explored potential product demo options for conducting Streamlined Review including interactive engagements with a focus on risk-based approaches.

The staged reviews highlighted that the premarket software documentation used to demonstrate the alignment between clinical evaluation, intended use, indication for use, and performance is essential for the review of these products. The software development and validation information evaluated during mock Excellence Appraisals provided additional context to the Streamlined Review process. However, the FDA found that there was variability regarding the specific information needed from the masked software review elements to achieve a comparable outcome to current review practices. As further work is conducted to build and test the Pre-Cert

[7] See section 4.4 Key Performance Indicators of the WOMO 1.0,

[8] For learnings related to mock Excellence appraisals see section Prospective Testing available at https://www.fda.gov/media/129047/download

[9] See section 6.1 Elements Necessary for Assuring Safety and Effectiveness in Premarket Review of the WOMO1.0

approach for Streamlined Review, the FDA continues to explore the sources of the variability encountered to identify opportunities to standardize. This activity will also inform, using least burdensome principles, what Excellence Appraisal information could best support the review of SaMD products.

Additionally, the FDA explored the following:

- Structured ways for manufacturers to define their SaMD products consistently while leveraging the International Medical Device Regulators Forum (IMDRF) framework to ensure a globally harmonized approach.
- Methods for collecting ongoing Real-World Performance data—both organizational and product level data—that can be integrated into a total product lifecycle approach to continuously monitor and verify ongoing excellence following the Excellence Appraisal, identify emerging safety and cybersecurity risks, provide critical feedback to the other components of the Program, and support the appropriate use of postmarket data in clinical evidence generation.

Learnings from the Streamlined Review testing, and from engagement with external stakeholders and the FDA's review staff, suggested that a question-based approach will lead to a structured and consistent SaMD definition in alignment with the IMDRF framework. During the mock Excellence Appraisals, numerous product measures in use by the pilot participants and test case companies related to Real-World Performance were observed—especially in the subcategories related to User Experience Analytics and Product Performance Analytics[10]. In the Real-World Health Analytics subcategory, measures related to Human Factors Usability and Engineering and measures that provide assurance that safety risks are managed and mitigated in a timely way were also widely seen. However, it was more challenging to identify measures to support Health Benefits, so additional work to identify these measures is needed. The collection of Health Benefit information is important to provide reasonable assurance of safety and effectiveness, which is one of the tenets of the Pre-Cert Program. The current FDA approach contains mandatory requirements for manufacturers, importers, and device user facilities to report certain device-related adverse events and product problems to the FDA under the Medical Device Reporting (MDR) regulation (21 CFR Part 803).[11] FDA is exploring optimal approaches for gathering SaMD product performance information from Pre-Cert companies to understand and monitor the ongoing benefit-risk profile of SaMD products once marketed.

Work continues with the pilot participants and test case companies on outlining the framework and mechanics for collecting Real-World Performance. This effort includes exploring less reliance on solely manual collection of information and more focus on ways to use technology, such as automated remote access to digital data, to collect SaMD product information once it is on the market. FDA is also continuing to explore how to leverage and use information and data from available external sources that would allow the FDA and Pre-Cert companies to be more efficient and streamlined without compromising product safety and effectiveness.

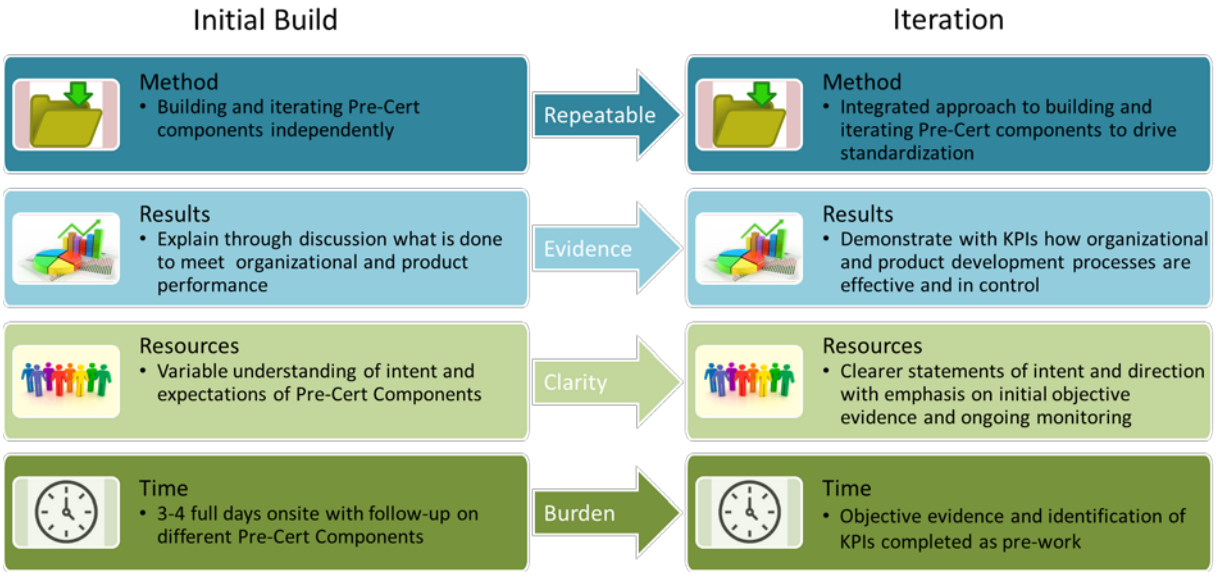
[10] See Appendix 12 – Proposed Organizational Elements to Demonstrate Excellence Principles and Appendix 13 – Real-World Performance Analytics for Product Monitoring in the WOMO 1.0 for examples of KPIs that were observed during mock Excellence Appraisals

[11] Medical Device Reporting for Manufacturers – Guidance for Industry and Food and Drug Administration Staff, November 2016 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/medical-device-reporting-manufacturers

Next Steps

Using the Pre-Cert development method of building, testing, and iterating, the FDA is evaluating learnings from the testing activities and will iterate and revise the testing approach. FDA learned that refinements are needed across the program to drive repeatability of the processes, improve the quality and quantity of information, provide clarity to internal and external stakeholders, and reduce the time burden on both internal and external stakeholders (see Figure 3).

Figure 3. Iterating from Lessons Learned



The FDA will continue to build on the framework highlighted in Figure 2, with focus on Parts 5-12 that need further development and testing, including using the draft KPI library to model and test scenarios for Pre-Cert excellence thresholds. FDA also intends to outline scenarios to test least burdensome approaches to establish a safe and effective total product lifecycle approach to SaMD products. This will help to identify the appropriate level of data necessary from pilot participants and test companies, and to compile examples of how different organizations' processes and measures of performance track and fulfill the program's specified elements, performance measures, and ultimately, the Excellence Principles (see Figure 2). In addition, the FDA will explore least burdensome methods for collecting organizational and product performance metrics to reduce variability and identify how the FDA will ensure that Excellence Appraisals are consistently interpreted across different SaMD developers.

As described above, more work is needed to refine the Streamlined Review Framework. To efficiently explore opportunities for a Streamlined Review, the Agency intends to rely on submissions that were previously authorized to expand access to additional test cases. In this next integrated iteration, the FDA intends to

- Continue to analyze how the information collected during Excellence Appraisals, Review Determination and Real-World Performance monitoring can be leveraged for Streamlined Review by determining the usefulness and relevance of the software

submission content in informing the FDA's determination for a SaMD market authorization; and
- Collaborate with stakeholders and review staff to explore regulatory decision support tools such as relevant hazards and typical mitigations for those hazards, and for product performance data.

As the FDA continues to build out components for the Pre-Cert model, as outlined in the WOMO 1.0[12], the building and iterating of the Pre-Cert Program is shifting towards integrating the four components of Pre-Cert (Excellence Appraisal, Review Determination[13], Streamlined Review, Real-World Performance), while continuing to develop the details of each component. The integration of these components will help the FDA test the interfaces of the different Pre-Cert activities, processes and information, and ensure a more comprehensive understanding of the interdependencies between the components of the Program.

The FDA intends to simulate scenarios to test the interdependencies and to help uncover unknowns to build the program appropriately. More specifically, this will enable the FDA to:

- Evaluate how information at various points of the total product lifecycle can support a reasonable assurance of safety and effectiveness, and address uncertainties at any given point in the lifecycle;
- Support evaluation of an organization-product-user ecosystem that helps identify the benefits and risks of the product through a "What-If" analysis;
- Explore the information manufacturers can provide that is least burdensome and allows them the flexibility to change, modify, and improve software development processes to enhance the quality of the products while also tailoring to their organizational goals;
- Evaluate the ability to leverage structured data for market authorizations while reducing reliance on narrative documentation; and
- Improve the ability to leverage data that creates a knowledge-rich, transparent, performance-related environment that benefits patients and manufacturers.

Simulating a wide variety of scenarios will allow the FDA to build on the learnings of our real-world experience to date while also enabling us to anticipate situations the FDA has not yet encountered to identify regulatory, infrastructure, and resource needs.

FDA will use the learnings and information collected to date and conduct simulations to explore scenarios that will help the FDA develop a structured, objective and repeatable approach to assessing organizational excellence. This information will also help identify and test parameters necessary for ongoing monitoring of SaMD product performance to identify potential post-market product issues. Lastly, this information will also help in determining the criteria for maintaining Excellence Appraisal status, and/or the need for re-appraisals.

The Agency will continuously assess and evaluate the readiness of the Pre-Cert Program before progressing to the next phases of development and will consider obtaining legislative authority to fully implement it as a new pathway for SaMD. As noted in the Program Development Roadmap (see Figure 1), the FDA will continue to build out and iterate on concepts outlined in the WOMO 1.0. FDA's current focus is on assessing how to integrate all four components into a viable total product lifecycle approach, while keeping the model least burdensome. This means the Agency is focusing on translation efforts to understand what

[12] See Section 3.5 Total Product Lifecycle of the WOMO 1.0

[13] See section 5 Review Pathway Determination of the WOMO 1.0

information is optimal to collect/observe to provide a reasonable assurance of safety and effectiveness.

Additional Information

Along with this status update, the FDA is releasing updated Frequently Asked Questions (FAQs) on the Pre-Cert Pilot Program website to provide more insight into the Pilot. The Pre-Cert Pilot Program relies heavily on collaboration to develop an effective model. Please visit the Pre-Cert Pilot Program web pages at www.fda.gov for more details.

For more information:

- FDA's Digital Health Program (https://www.fda.gov/digitalhealth)
- FDA's Pre-Cert Pilot Program
- Contact FDAPre-CertPilot@fda.hhs.gov