Will the FDA Precertification Pilot Program Work?

By Scott Thiel and Jason Brooke, MSE, JD, Navigant – May 2019

Digital health products often fall into a class of their own. With the tsunami of Software as a Medical Device (SaMD) products soon to go through the approval process, FDA is proactively looking to redefine how to get an SaMD product to market, before being inundated.

Beyond a series of regulatory shifts already enacted, FDA provided updates to the pre-certification pilot program in January aiming to streamline the approval process for qualifying companies, while better leveraging postmarket data collection for SaMD products.

FDA (or potentially an FDA-accredited third party) will assess an applicant's "culture of quality and excellence." In other words, the regulatory framework will rely on an evaluation of the thoroughness of the company's quality practices as it relates to designing, testing and clinically evaluating its products as well as monitoring real-world performance once the product is on the market. In turn, pre-certified software developers would have, in theory, the option for a reduced review, based upon the trust engendered by being certified.

Currently, nine companies are participating in the pilot program. With initial learnings and results expected near the end of 2019, the rest of the SaMD industry is in a "wait and see" mode—hopeful the program will work but mindful that many questions remain, including as to its practical viability, whether it provides equal opportunity for companies large and small, and whether FDA even has the legal authority to implement the proposed approach.

How the Pilot Works

For the purpose of the pilot, FDA limited the scope to SaMDs and uses the de novo process to review the premarket submission in parallel to the traditional pathway, e.g., 510(k). A de novo petition, meaning those with risk characteristics consistent with Class II medical devices and no viable predicate device, is a review pathway already available to FDA. The main objective of the pilot is to develop the precertification process, identify necessary elements and explore best practices for ongoing monitoring. Through parallel review, FDA supports product submission reviews as they normally would and tests the submission review as though the pre-certification program is active.

FDA's intention is that the program will cover the total product lifecycle and, as such, is divided into the following four, interdependent components.

Excellence Appraisal

The appraisal process is not fully developed but FDA intends to evaluate organizations based on objective and observable evidence. Each organization would determine which processes and Key Performance Indicators (KPIs) best meet the elements to comply with the requirements. According to FDA, the appraisal is not intended to serve as an audit to collect evidence of non-compliance.

In the pilot, excellence is based on demonstrating:

- product quality (i.e., development, testing, and maintenance)
- patient safety (i.e., providing a safe patient experience and emphasizing patient safety as a critical factor in all decision-making processes)
- clinical responsibility (i.e., responsibly conducting clinical evaluations and ensuring that patient-centric issues, including labeling and human factors, are appropriately addressed)
- cybersecurity responsibility (i.e., protecting cybersecurity and proactively addressing cybersecurity issues through active engagement with stakeholders and peers)

- proactive culture (i.e., demonstration of excellence in a proactive approach to surveillance, assessment of user needs, and continuous learning)

Based on the results, a company could qualify for one of two levels. Level 1 allows organizations to develop and market lower-risk software without review, while streamlining review for other types of software. Level 2 allows organizations to develop and market lower and moderate risk software without review while streamlining review for other types of software.

Review Determination

Pre-Cert Program Overview: Review Pathway Determination

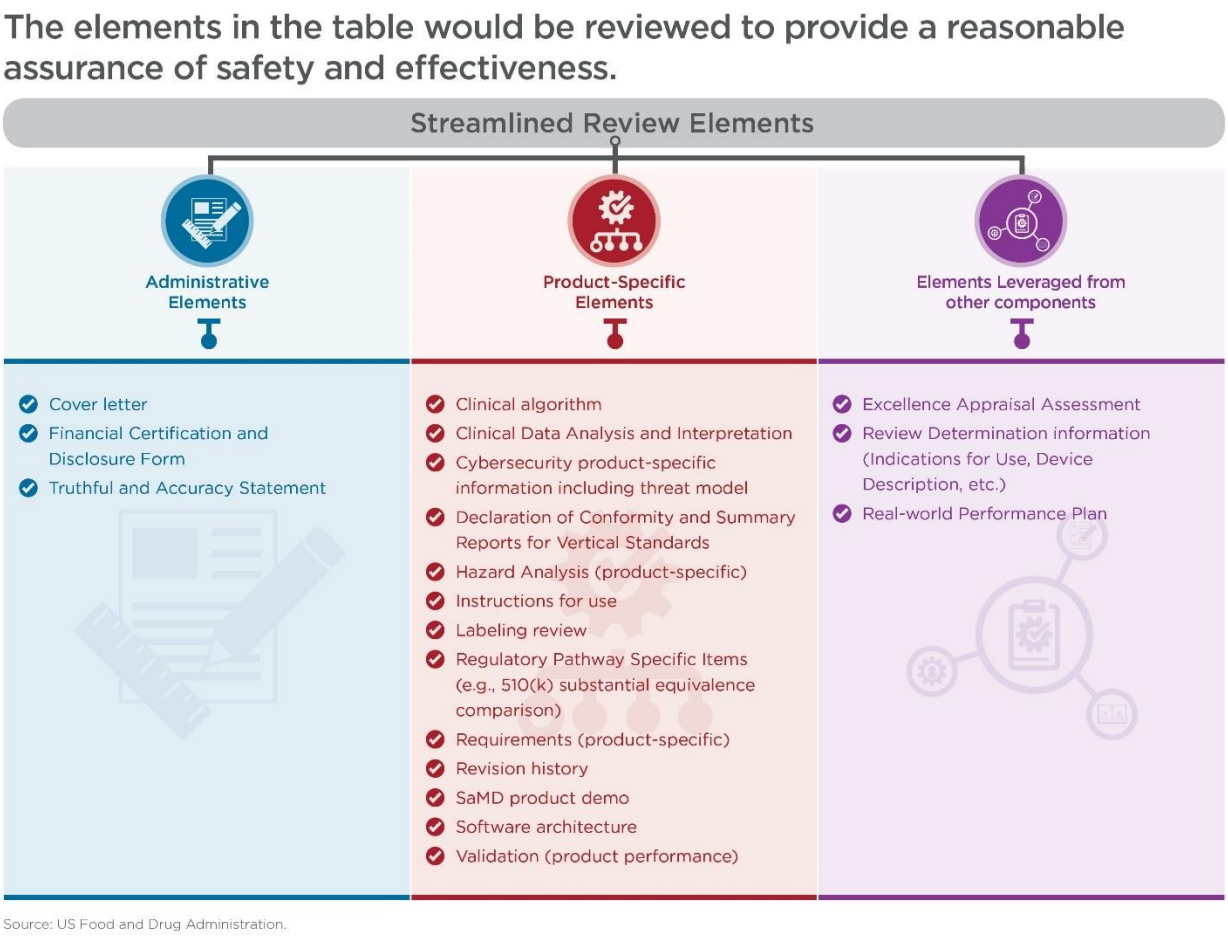
IMDRF Risk Categorization		Level of Review for Level 1 and Level 2 Precertified Organizations' SaMD		
Type	Description	Initial product	Major changes	Minor changes
Type IV	Critical x diagnose/ treat	SR	SR	No Review
Type III	Critical x drive		L1 – SR L2 – No Review	
Type III	Serious x diagnose/ treat			
Type II	Serious x drive	L1 – SR L2 – No Review	No Review	
Type II	Non-serious x diagnose/treat			
Type II	Critical x inform			
Type I	Non-serious x drive	No Review		
Type I	Serious x inform			
Type I	Non-serious x inform			

Table describes a proposal for when the precertification of organizations and commitment to leverage real-world performance might allow for no premarket review ("No Review" in table above) or streamlined premarket review ("SR" in table above), according to the IMDRF type of the SaMD and the Pre-Cert Level of the organization (Level 1 or Level 2).

Source: American College of Radiology.

The principal objective of the review determination is to apply a risk-based framework so pre-certified organizations can determine the premarket review pathway for their SaMD products. In concept, the risk category framework will be informed by work from the International Medical Device Regulators Forum and product-level elements, including core functionality, device description and performance, and intended use.

Streamlined Premarket Review Process



Products considered for streamlined review would be from organizations that successfully went through the excellence appraisal and received a certification level.

In concept, an interactive review of administrative, product-specific and other component elements would be conducted, supported by automated analysis, to gauge a reasonable assurance of safety and effectiveness, and inform a decision on a pre-certified organization's new product within a shorter timeframe than traditional premarket review processes. Repeated unsuccessful streamlined reviews would trigger a reassessment of the organization's precertification determination.

Real-World Performance

During the excellence appraisal, all organizations would demonstrate the capability and commitment to collect and analyze readily available post-launch safety, effectiveness and performance data of the product.

Currently, FDA intends to focus its post-launch product monitoring efforts on trends and summary analytics rather than on raw data.

Precertification Challenges in Practice

As the pilot moves forward, several questions and concerns must be addressed by FDA before a full-blown program can be initiated and institutionalized.

Authority?
When FDA first began exploring the concept for a precertification path for qualifying companies, the US Congress pushed back, questioning whether FDA had the authority to initiate such a program. As a result, FDA determined to focus on SaMD products that qualify for the de novo petition because this category is meant for products that do not have a comparison or an associated regulation. So, theoretically, even if the program launches upon pilot completion, the scope might require an act of Congress to go beyond this niche product segment.

That's because FDA draws its authority from the US Federal Food, Drug, and Cosmetic Act and amendments to that act. If FDA aims to work outside of the established act and its amendments, FDA must get approval from Congress to do so in the form of another amendment. At present, it is unclear whether the pre-certification pilot program will or will not require new or amended authorities from the FDA, but many insiders believe it will. This in turn likely would trigger further delays and/or modifications to the program.

Equal Opportunity?
In principle, the precertification program is meant for interested applicants from companies of all sizes. However, considering the user fee to file a de novo petition, the time and effort to host an excellence appraisal, and having the ability to demonstrate KPIs aligned with the appraisal categories, the precertification program appears to favor larger companies that can afford the price tag. As a result, in practice, a fully launched precertification program could disproportionately benefit resource-rich corporations by enabling them to get to market even faster over competing cash-strapped startups and small companies. In the long-term, this could potentially impact innovation if for no other reason than by resulting in reduced investment in innovative companies.

Excellence?
As mentioned above, the criteria for excellence appraisal is loosely defined and being tested and vetted in the pilot. Assuming FDA determines the KPIs for companies to use, then another host of questions must be sorted, including how should that information be stored, what pieces are most useful for the admission process, and how should participating companies maintain that information? There are additional considerations of who the information will be shared with in a manner that meets data privacy requirements yet provides sufficient context for the reader to appropriately understand the information.

A few factors to keep in mind: the current benchmark for the excellence appraisal is the quality management system as defined under 21 CFR Part 820. FDA is hinting that compliance to Part 820 may not be the only way to satisfy the excellence appraisal, but have not provided any particulars. FDA is contemplating whether to accept ISO 13485 certification as an alternative to the Part 820 quality system regulations, but the close alignment between the two makes them seem to be two sides of the same coin. Given that compliance to Part 820 is a requirement and the current law of the land, FDA will need to either see a traditional quality system or be convinced a surrogate method is sufficient to meet the expectations of Part 820.

Time-Savings?
As part of the pilot, FDA is timing the process to gauge the streamlined vs. traditional review paths. At this stage, it is difficult to know whether the program will indeed save time for companies seeking precertification. Presumably, with precertification in place, the review of the de novo petition will go faster because the FDA already knows and trusts the manufacturer from the excellence appraisal and the product design from the pre-submission meeting.

However, the first time through this chain will likely take longer than the current submission approach because the manufacturer has to prepare for and host FDA for the excellence appraisal and likely file a pre-submission meeting request. These steps will be in addition to the de novo petition being used in the 2019 pilot. In the future, FDA envisions using it for other marketing submissions, e.g., 510(k), as well. As such, it is unlikely a company will save time on their first submission or for subsequent and different product designs. So, in practice, time savings might only occur on submissions for modifications to a product design that already completed the process.

Even if the streamlined review process proves to save companies time once qualified, there is still the issue of the time it takes to collect and share post-market real-world data. Some product design decisions also may be impacted in order for the company to collect or receive information from the devices. The concept of real-world information sharing is meant to support transparency, which is a good thing when done well. However, if the

information is shared without appropriate context or the recipient is not versed in how to interpret the information, the transparency could lead to confusion or fear. In addition, companies will need to find the balance between being transparent and complying with data privacy and security requirements.

Moving Forward: Cautious Optimism
Until the results of the pilot are known, stakeholders should monitor the program's progress and, as relevant and appropriate, provide feedback and perspective to FDA. Just as importantly, interested companies with products in development that might qualify for such a future pre-certification program should be proactively implementing quality systems or at least parts of 21 CFR Part 820, especially around design controls (21 CFR 820.30).

As the pre-certification pilot program progresses, much will be learned to inform future review processes and regulations for market authorization. From inception, the pilot has been meant to be an iterative and collaborative process. As such, it is highly unlikely the pilot will go into effect exactly as currently outlined.

Still, the pilot itself provides reason for cautious optimism, namely because it indicates FDA seeks to evolve processes and regulations to meet the needs of advancing technology. This alone bodes well for the future of digital health, and healthcare as a whole, because it effectively encourages—and potentially incentivizes—innovators to do what they do best.

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Cite as: *Thiel S and Brooke J. "Will the FDA Precertification Pilot Program Work?" Regulatory Focus. May 2019. Regulatory Affairs Professionals Society.*