

The State Of FDA Regulation Of Software As A Medical Device

By **Nicholas Diamond** (January 7, 2022, 5:24 PM EST)

The global market for software as a medical device, or SaMD, products, is projected to grow at over 4% compound annual growth rate from 2020-2027, reaching approximately \$9.8 billion by 2027. Continued growth will be influenced by how the evolving regulatory environment is shaped moving forward.

For the U.S. market, the U.S. Food and Drug Administration has accelerated its activities relating to software, especially for SaMD. This has included, among others, various nonbinding guidance, commenting opportunities, public workshops and the Artificial Intelligence and Machine Learning-Based Software as a Medical Device Action Plan.



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This article briefly surveys this landscape and focuses on where gaps remain that may affect how SaMD developers commercialize new products. In particular, it considers unique challenges for AI/ML-enabled SaMD, such as transparency and change management, which are likely to be the focus of future FDA activities.

Pre-2021 Foundations

The FDA has a long history of regulation at the intersection of medical devices and software. In the late 1980s, the FDA first considered whether certain computer products fell under its regulatory purview as medical devices. The resultant policy statement in 1989 would later be withdrawn in 2005 because, in the FDA's view, the technological evolution had outpaced its content.

In subsequent years, rather than taking a comprehensive approach to products in this space, the FDA took a stepwise approach by classifying certain types of software applications that met the definition of a device under the Federal Food, Drug and Cosmetic Act and, in turn, identifying corresponding regulatory requirements for such products.

In 2013, the FDA returned to so-called device software functions with new guidance, which coincided with International Medical Device Regulators Forum efforts to establish a globally harmonized vocabulary for such products.

Subsequently, in 2017, the FDA adopted the IMDRF's approach to clinical evaluation, marking an important step toward global harmonization of requirements. In 2019, the FDA updated its 2013

guidance on device software functions, now encompassing both SaMD and software in a medical device, or SiMD, with a particular focus on mobile platforms.

Despite these activities, the emergence of new technologies invited further clarification from the FDA on certain issues. For example, as SaMD products evolved, certain products had both device and nondevice software functions, which was not accounted for in the FDA's approach to classification at that time.

Accordingly, in 2020, the FDA released guidance, "Multiple Function Device Products: Policy and Considerations," to assist developers and reviewers with premarket submission requirements for such products.

As another example, the FDA's approach at the time did not easily account for post-market modifications — common for SaMD products — instead requiring a new clearance or approval, even for small coding updates. The FDA's 2017 announcement of the software precertification pilot program was intended to address this challenge. Recent lessons learned and inclusion in the 2021 action plan suggest a continued focus on the program.

The emergence of AI/ML-enabled SaMD further challenged existing approaches to change management. In 2019, the FDA released a discussion paper, "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning-Based Software as a Medical Device," requesting feedback on an optimal approach for regulating such products, given that they require frequent modifications.

2021 at a Glance

In January, the FDA released its 2021 action plan, where it responded to feedback received to the 2019 discussion paper and established a road map for future years. During the remainder of 2021, the FDA implemented several parts of this road map.

First, in October, the FDA released "Good Machine Learning Practice for Medical Device Development: Guiding Principles," developed in concert with regulators in Canada and the U.K.

While an important step toward harmonization, it remains to be seen how these principles will be implemented as specific policies and procedures moving forward.

Also in October, the FDA held a public workshop to discuss key issues relating to transparency in AI/ML-enabled medical devices. Discussions at this public workshop were far-reaching, covering, among other things, product labeling, data quality, bias and equity, change management, and data privacy.

Finally, in November, the FDA issued draft guidance, "Content of Premarket Submissions for Device Software Functions," which, once finalized, will replace previous 2005 guidance. This new draft guidance applies to both SaMD and SiMD products, and is intended to clarify and streamline submission requirements.

In part, it introduces two new documentation categories — basic and enhanced — the criteria for which moves away from the prior, questions-based approach for levels of concern. Notably, devices that are a constituent part of a combination product default into enhanced, which will be important for pharmaceutical innovators to consider.

Looking Ahead

In 2022, the FDA is likely to continue its focus on AI/ML-enabled medical devices. If prior activities are any indication, future developments are likely to come in the form of guidance, rather than regulation.

While stakeholders have queried whether the FDA would issue proposed regulations that comprehensively address the varied issues relating to SaMD or AI/ML-enabled medical devices specifically, the current regulatory agenda for the U.S. Department of Health and Human Services contains no such proposed regulations.

However, there is always the possibility that the regulatory agenda could be subsequently updated to reflect new activities from the FDA, but that remains less likely than continued issuance of guidance in 2022.

Stakeholders should leverage the 2021 action plan as a road map for likely future activities. The FDA hewed closely to the 2021 action plan in implementing various activities in 2021, which suggests a directionally similar trend in 2022.

Indeed, stakeholders should welcome this consistency as they identify their strategic priorities for the year ahead. Issues in the 2021 action plan that have yet to be significantly addressed include, for example, algorithm bias and robustness, and real-world performance monitoring.

The former has of course received significant attention, including during the October 2021 public workshop. It should be noted that AI and bias issues have also been focal areas elsewhere in the federal government, notably the Federal Trade Commission.

The latter reflects a crucial opportunity for stakeholders to collaborate with the FDA to specify how real-world data collection and monitoring can be leveraged for AI/ML-enabled SaMD, especially for purposes of modifications.

The 2021 action plan also identifies a draft guidance on change management for AI/ML-enabled SaMD, which would build on prior feedback received by the FDA via the discussion paper. Stakeholders have been generally supportive of the FDA's focus on the principle of a predetermined change control plan.

As the 2021 action plan underlines, the FDA remains focused on further iteration on change management in a collaborative dialogue with stakeholders.

A particularly crucial issue will be aligning expectations on the details included in the SaMD prespecifications and the algorithm change protocol, given that both the SPS and ACP will be increasingly important for commercialization of new AI/ML-enabled SaMD products.

Finally, given the multiregulator collaborative development of the good machine learning practice principles, there may be further similar efforts in 2022 oriented toward harmonization.

Several activities on the global stage may motivate further collaborative efforts. In September 2021, regulators in the U.K. released a comprehensive public consultation opportunity on the future of medical device regulation which, among other things, included a substantive focus on SaMD.

Moreover, as with the FDA, regulators in the U.K. have also had a specific focus on AI/ML-enabled

medical devices. Also in September 2021, the IMDRF released a consultation focused on key terms and definitions for ML-enabled medical devices. Among other topics, it discusses bias, further suggesting a continued global focus on the issue.

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