AMA
AMERICAN MEDICAL ASSOCIATION

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Scott Gottlieb, MD
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: Software Precertification Program: Working Model–Version 0.2–June 2018

Dear Commissioner Gottlieb:

On behalf of the physician and medical student members of the American Medical Association (AMA), I appreciate the opportunity to provide comments on the most recent version of the proposed Precertification Program for software as a medical device (SaMD) and to respond to questions posed by the U.S. Food and Drug Administration (FDA). As outlined in previous correspondence, the AMA understands the compelling need to develop alternative oversight model(s) for SaMD that provide a strong incentive for developers to cultivate and maintain a culture and practice of excellence in order to ensure the design, development, validation, deployment, and modification of a safe and efficacious SaMD. This is an important effort in light of the large and rapidly growing volume of SaMD and the finite FDA resources available to provide oversight. The AMA has a number of recommendations in response to the specific questions posed by the FDA concerning the Precertification Program, as well as additional comments related to a subset of software and computer science methods and systems variously referred to as continuous machine learning, deep learning, or continuous learning systems.

The AMA urges the FDA to be very cautious with regard to the speed with which the Precertification Program is being developed. While we appreciate the efforts to engage physician organizations over the last several months, industry has been steeped in the complexities of this proposal for an extended period of time. The AMA, physician organizations, and the broader health care provider community would benefit from obtaining additional information on the experiences of the companies participating in the Precertification Program pilot as there are no public examples of how this program operates in practice to provide context since the January 2018 Workshop meeting.

SaMD Precertification Program[1]

The FDA has sought the AMA's feedback on a number of questions. The responses to the questions are contained below in the format presented by the FDA.

[1] The following comments apply to all SaMD except for "continuous learning" systems.

| Q | Work stream | Question / Input | Desired Output |
|---|---|---|---|
| 1.1 | Excellence Appraisal | What attributes should organizations who have not developed medical devices have so they can adequately demonstrate a track record of excellence in the principles of patient safety and clinical responsibility, in particular clinical effectiveness? | As outlined in the AMA's prior comment letter, we do not support the establishment of two levels of precertification—one for organizations that have developed software and one for organizations that have not. In short, the risks and challenges associated with deploying SaMD into the health care ecosystem is challenging and rife with unanticipated and unexpected challenges. Organizations that have not successfully deployed SaMD should first demonstrate that they are able to deploy such software safely through the existing oversight product specific process. The Precertification Program will only engender the trust of SaMD end-users if it is understood that Precertification organizations have not only met and demonstrated adherence to the excellence principles, but also have a track record of having done so with SaMD. It might be appropriate at a future date to test a second level of precertification for organizations that do not have a track record, but there is a much higher risk that such organizations may market SaMD that could cause harm. This would degrade trust in the Precertification Program and fails to provide the requisite documented track record of performance that should be part of the Precertification Program. |
| 1.2 | Excellence Appraisal | Should the FDA consider weighing Patient Safety and Clinical Responsibility more heavily than the other Excellence Principles? | The AMA strongly supports weighting Patient Safety and Clinical Responsibility more heavily than the other Excellence Principles. Again, this is essential to engender trust among end-users that the Precertification Program is designed to incentivize best practices and quality that consistently and reliably drive SaMD performance anchored in patient safety and clinical factors (validity, analytical validity, reliability, etc.). |
| 1.3 | Excellence Appraisal | What "clinical standards" can be leveraged as part of the Excellence Appraisal? | The AMA supports the use of standards as long as the process is open and transparent and the AMA supports standard development organization standards, such as ISO and HL7. |
| 4.1 | Real World Performance | Should the three proposed data domains for real world health analytics be tailored to the type or risk level of SaMD product? (The three proposed data domains include: | The AMA agrees with the FDA that organizations can show excellence per the Pre-Cert Excellence Principles by taking user-centric steps toward continuous improvement through proactive monitoring of Real World Performance (RWP) data related to their SaMD products. In general, it would be reasonable to tailor the real-world health analytics to the type and risk level of the SaMD product. However, the AMA encourages the |

| Q | Work stream | Question / Input | Desired Output |
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| | | Human Factors and Usability Engineering, Clinical Safety, Health Benefits) | FDA to consider whether this would create confusion, particularly where such information is provided to end-users related to clinical safety and health benefit. Careful consideration should be given to cognitive burden to regulators, end-users, and other stakeholders (such as researchers) created by lack of standardization. |
| 4.2 | Real World Performance Analytics (RWPA) | Where is transparency important in the RWPA process? | The AMA urges the FDA to not use the term "transparency" in this context; it creates confusion as this term is used to address a different set of concepts in the context of continuous learning systems (which concerns data and algorithmic transparency, for example). Real world performance analytics disclosure should be required (or minimally available): (1) when an organization seeks Precertification status; (2) when a SaMD product is introduced into the market; (3) at regular established intervals after market entry, based on risk, but generally not longer than monthly; (4) when a major modification is made; and (5) when there is an adverse event. |

The FDA has also sought feedback on specific real-world performance analytics (RWPA) metrics important to physicians and patients. The FDA has identified three RWPA domains including:

- Real world health analytics: human factors and usability engineering, clinical safety, and health benefits;
- User experience analytics: user satisfaction, issue resolution, user feedback channels, and user engagement;
- Product performance analytics: cybersecurity and product performance.

As a threshold matter, to the extent that developers need flexibility on metric selection within each of the above domains based on intended use, functionality, and risk classification of the SaMD product, the AMA strongly urges the FDA to consider the cognitive burden such flexibility places on end-users where there is a lack of standardization and there is not an ability to make apples-to-apples comparisons due to significant variation in selected metrics. The AMA also urges the FDA to provide stakeholders examples of how the metrics would be shared with the end-users. Metrics under all three domains should be provided to end-users based on the specific SaMD product. While organizations should provide overall performance of all products for purposes of Precertification designation to the FDA, end-users generally should have readily available relevant performance metrics that are product specific. The AMA continues to engage physicians and national medical specialties in order to provide additional feedback with regard to specific metrics.

Continuous Learning Systems and Transparency

The AMA does not support the inclusion of continuous learning systems in the Precertification Program as currently proposed. While certain machine learning systems that are static (locked) may be appropriate for the Precertification Program, there remain a wide array of additional risks and unanswered questions with regard to the safety of continuous learning systems. The concern is heightened as there is not a widely accepted methodology taxonomy and set of definitions to characterize different augmented intelligence (AI) (commonly referred to as artificial intelligence) methods. The AMA is working with experts within our organization, along with a number of other health care stakeholder organizations, to facilitate a convergence that would be consistent with the terms and method descriptors used by the broader community of AI stakeholders. For example, the most recent SaMD products that the FDA authorized and identified as utilizing AI methods do not utilize continuous learning systems. Instead, these are static (locked) systems where the algorithm does not change once subject to FDA authorization and introduction into the market. The AMA recognizes the importance of the consistent use of terms and method identification and is concerned that continuous learning systems do not fit within the current risk level identification laid out in the Precertification Program. We urge the FDA to develop a separate proposal that captures the additional risks associated with continuous learning systems and the additional controls that may need to be standard to ensure safety and efficacy. In addition, the AMA will provide additional comments under separate cover concerning transparency in the context of continuous learning systems. The concept of transparency for these types of systems is one that concerns a broad group of stakeholders as different types of transparency may be required depending on the product. In addition, specific requirements may vary over the life cycle of the continuous learning system.

We appreciate the opportunity to continue an ongoing discussion on these important reform models and concepts. If you have questions, please contact Shannon Curtis, Assistant Director, Division of Federal Affairs, at shannon.curtis@ama-assn.org or 202-789-8510.

Sincerely,

James L. Madara, MD