AMA
AMERICAN MEDICAL ASSOCIATION

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March 8, 2019

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

Re: Software Precertification Program: Current Working Model, Regulatory Framework and Pre-Cert Pilot Program, and 2019 Test Plan

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 software as a medical device (SaMD) Precertification Program Working Model (PPWM) (v1.0, January 2019), the Regulatory Framework for Conducting the Pilot Program within Current Authorities, and the 2019 Test Plan. We appreciate the Food and Drug Administration's (FDA) efforts to develop an alternative oversight model(s) for SaMD that provides 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 safe and efficacious SaMD.

The AMA recognizes that the rapid iterative nature of software and increase in new SaMD developers strain the resources and capacity of the FDA to safeguard safety and efficacy without chilling innovation. While we support thoughtful and well-vetted measures and applaud the FDA's methodical approach, we continue to have several outstanding questions about and concerns with the current PPWM. In particular, we reiterate our previous concerns about the PPWM elements that would undermine FDA efforts to promote the PPWM as an excellence model and erode physician trust that products developed through this pathway are safe and efficacious.

Application of Precertification Program Working Model to Certain AI Systems

The AMA does not support the application of the current PPWM to certain augmented intelligence (AI) systems and methods. The FDA has not yet established the necessary foundation to apply this proposed new pathway to certain AI systems particularly those that utilize machine learning. The AMA supports the use of existing FDA regulatory pathways for such systems as demonstrated by the FDA's *de novo* market authorizations for a number of AI-enabled products in 2018. While a precertification program could be appropriate for AI-enabled systems at some point, the FDA has not established foundational definitions, risk frameworks, or excellence categories for AI-enabled systems, particularly those utilizing machine learning. The AMA urges the FDA to establish accepted nomenclature and definitions and appropriate risk stratification for AI systems.

The source documents relied upon by the FDA to establish definitions and risk stratification for the PPWM from the International Medical Device Regulators Forum (IMDRF) do not address AI systems generally nor machine learning in particular. The AMA has actively facilitated and participated regularly in meetings for the past two years with subject matter experts in AI systems and health care applications. It is evident that many individuals, including those considered experts, do not use the same definition of AI and many do not understand the risk profile presented by machine learning systems that employ continuous learning in contrast to those that utilize locked models for clinical applications. The particular risks (and benefits) associated with machine learning systems are detailed in the Current State and Near-term Priorities for AI Enable Diagnostic Support Software in Health Care report recently issued by the Duke Margolis Center for Health Policy. In addition, the AMA is involved in two separate efforts to address the particular challenges and benefits of AI systems for clinical applications that remain ongoing, including those sponsored by XavierHealth's AI Initiative and the Association for the Advancement of Medical Instrumentation (AAMI) and British Standards Institution (BSI) initiative to address AI and machine learning in health care.

The AMA is concerned that both AI and machine learning are referenced in the PPWM without definitions, but even more concerning is the lack of careful consideration of the novel risk dimensions that machine learning systems may pose, particularly if the FDA does not specify that only locked model machine learning systems would be eligible to utilize the PPWM. (It is not ethical nor compliant in many cases with federal laws, including the Food, Drug, and Cosmetic Act as amended to utilize continuous machine learning systems directly for clinical care without first locking such models and testing for clinical efficacy and safety unless done so after complying with laws governing human subject research.) The IMDRF model of risk that the FDA has utilized for PPWM was developed without any consideration or discussion of the particular and novel risks posed by machine learning. Therefore, the FDA's use of the IMDRF risk model, even as modified by the FDA, is not appropriate for machine learning. The AMA strongly urges the FDA to strike all references to AI systems and machine learning specifically until these issues have been fully considered and a clear set of definitions and appropriate adjustments are made to address risk.

Precertification Levels

In our prior AMA comment letter, we outlined our concern with the proposed two levels of precertification. To clarify more fully, the AMA opposes two levels of precertification and specifically does not support the creation of a Level 1 precertification. The FDA states that Level 1 precertification:

> Would be awarded to an organization that has objectively demonstrated excellence in product development in all five Excellence Principles, *with a limited track record in developing, delivering and maintaining products*. This level of certification may benefit an organization with limited or *no experience in delivering software products*, but with established organizational elements and strategies in place that indicate they have or can acquire the capability to deliver and maintain high-quality lower-risk SaMD that are safe and effective.

As many innovators in health care will report along with clinicians and health care administrators, appropriate and safe use of new digital technologies is not only related to the technology, but human factors, organizational workflows and complexity, along with a range of factors that are not anticipated by first-time innovators. The AMA does not support an excellence model where entities with precertification

do not have experience or a track record of developing and deploying SaMD. Beyond the clear risks posed to patients such an approach presents, it undermines the FDA's intention to promote this model to physicians as one that is based on excellence which suggests a track record of proven performance—not just policies and processes. While the AMA appreciates that the level 1 certification would incentivize new developers to adhere to the excellence standards, the risk and trade off are too pronounced and invites degrading the value of the "quality" designation since it will not be based on an actual track record of demonstrated excellence.

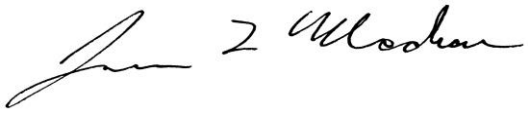
FDA Appraisal and Third-Party Appraisers: Initial and Ongoing Adherence to Excellence Principles

The AMA strongly supports both the FDA's Excellence Appraisal and the proposed accreditation of third-party appraisers with the capacity and expertise to conduct an Excellence Appraisal as well for organizations seeking precertification. However, additional information is needed with regard to the scope and rigor of the initial appraisal provided by the FDA and third-party accreditors as well as ongoing assessments that the FDA and accreditors would provide to ensure patient safety and efficacy. The AMA has previously expressed concern that self-reported adherence to the Excellence Principles was not sufficient and continues to have questions related to ongoing adherence to the Excellence Principles as well as active post-market assessments of specific product performance and safety that would be relevant to consistent adherence to such Excellence Principles.

Conclusion – Ongoing Dialogue

The AMA appreciates the engagement of the FDA with stakeholders on SaMD. The AMA, however, urges the FDA to convene a separate meeting to specifically address the unique risks and benefits presented by AI systems and machine learning. The foregoing should include developers that have utilized the existing FDA pathways, as well as experts deploying such systems in health systems along with physician organizations, such as the AMA and national medical specialty societies. We would also welcome the opportunity to discuss in greater detail additional elements and others not raised in the documents offered for comment. We look forward to a continued discussion and ask that you contact Shannon Curtis, Assistant Director of Federal Affairs at shannon.curtis@ama-assn.org or 202-789-8510, to schedule a meeting or a conference call.

Sincerely,



James L. Madara, MD