June 3, 2019

Norman Sharpless, MD
Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Dr. Sharpless:

On behalf of the Healthcare Information and Management Systems Society (HIMSS) and the Personal Connected Health Alliance (PCHAlliance), we are pleased to provide written comments in response to the Discussion Paper and Request for Feedback entitled, "Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)," (hereinafter "Proposed Framework"). We appreciate this opportunity to utilize our members' expertise in offering feedback on this Proposed Framework and innovative approach to modification of the existing regulatory oversight, with a goal of realizing the iterative improvement power of AI/ML software as a medical device, while assuring that patient safety is maintained.

HIMSS is a global advisor and thought leader supporting the transformation of health through information and technology. As a mission-driven charitable organization, HIMSS offers a unique perspective with deep expertise in health innovation, public policy, workforce development, research, and analytics to advise global leaders, stakeholders, and influencers on best practices in health information and technology. Through our innovation companies, HIMSS delivers key insights, education, and engaging events to healthcare providers, governments, and market suppliers, ensuring they have the right information at the point of decision.

As an association, HIMSS encompasses more than 76,000 individual members and 660 corporate members. We collaborate with hundreds of providers, academic institutions, and health services organizations on strategic initiatives to advance the use of innovative information and technology. Together, we work to improve health, access, as well as the quality and cost-effectiveness of healthcare. Headquartered in Chicago, Illinois, HIMSS serves the global health information and technology communities with focused operations across North America, Europe, United Kingdom, the Middle East, and Asia Pacific.

PCHAlliance, a non-profit membership association, works to advance evidence-based two-way digital communications between patients, their caregivers, and providers through the development of open technical standards, real-world testing, and health plan coverage of evidence-based connected care.

The Proposed Framework is a positive step towards the advancement of medical device technology because it proactively addresses a regulatory gap for advanced AI/ML that has the potential to have a distinct impact in healthcare. The current regulatory paradigm was not designed to account for the rapid adaptation potential of ML technologies and thus this update, is both timely and desirable to keep pace with the rate of change in technology, while ensuring that quality assurances are maintained by the software developer community.

I. The FDA Software Pre-Certification Pilot Program

In July 2017 FDA announced the Software Pre-Cert Pilot Program to aid in developing a new regulatory approach that would focus on the assessment of organizations that perform high-quality software design, testing, and monitoring. We recognize that a fair portion of the Proposed Framework is built upon concepts described in the Pre-Cert Program design. While we support the intentions and direction both proposals present, it is significant to recognize that the Pre-Cert Program is still in progress, with components still being developed and assessed. We applaud the FDA on the coordination between both the Pre-Cert Program and this Proposed Framework. However, we do have concerns that the interdependence of the two make the success of the Proposed Framework contingent on the final version and success of the Pre-Cert Program. As the Proposed Framework complements what the Pre-Cert Program hopes to achieve, we are interested in learning, if and how this Proposed Framework would evolve, should more resources be put towards the Pre-Cert Program.

HIMSS and PCHAlliance suggest that FDA and industry members focus on clarifying types of changes that clearly require review and oversight from FDA prior to placing products on the market. Furthermore, we recommend that this industry and FDA focus efforts on developing methodologies for verifying and validating adaptive AI/ML algorithms in a manner that supports assurance of reasonably safe and effective algorithms in the market. These two topics alone are likely to take enough effort and time to allow for the Pre-Cert Program to settle into a more finalized form.

II. The meaning of artificial intelligence in the context of machine learning technology

Currently, it is clear to us that the term “artificial intelligence” serves to mean something different to a variety of stakeholders in the health information and technology community. FDA must provide more distinct examples of both locked and adaptive AI/ML to improve clarity on what it is that we should be looking for in terms of this Proposed Framework. For example, there is still an unproven assumption that AI/ML manufacturers can create AI/ML that is always controllable or changes in a predictable fashion. In addition, it’s uncertain whether the trigger that causes the software to act is always realistic or reliable. Overall, we believe that there is a lot more that needs to be investigated and better deciphered before finalizing a definition of AI/ML for the medical field/medical community.

III. Security and privacy issues

We have several concerns regarding security and privacy. Despite assuming initial anonymity in data collection and use, we find it is unclear as to what happens with the data following its usage for purposes of creating test training sets. We suggest FDA delve into this inquiry further upon official comment development.

This area of concern also runs into the sphere of protected intellectual property of software developers and how that implicates what could be shared with the FDA for testing purposes. As

the quality of data tested is an integral component of the success of these technologies operating to its fullest intended capacity, this topic flows directly into the majorly imperative discussion of quality assurance.

Additionally, we wish to highlight concerns around the vulnerabilities regarding AI/ML in terms of "poisoning" the data upon which it may rely to function and/or tampering with the means by which the algorithms may adapt or change, as the case may be. While AI/ML is somewhat of a nascent endeavor, so too is our understanding of the malicious use of AI/ML. Essentially, every advancement in the state of the art may potentially have a vulnerability which may be exploitable today or tomorrow. Thus, today's advancement could be ultimately a limitation due to the exploitation of the vulnerability. Accordingly, we urge FDA to carefully examine the vulnerabilities that could be presently existing and/or that may develop and/or be discovered in the future.

IV. Total Product Lifecycle (TPLC) Approach and Quality Assurance

HIMSS and PCHAlliance are pleased to see and greatly support the fact that the outlined proposal clearly identifies the necessity of quality systems in place, manufacturer's practices, and training sets within its TPLC approach. It does not come as a great surprise that the Pre-Cert Program also goes to extreme lengths to ensure quality amongst software developers and their corresponding quality standards.

FDA indicates that the TPLC approach "enables the evaluation and monitoring of a software product from its premarket development to post-market performance, along with continued demonstration of the organization's excellence." While we appreciate the proposed potential, the TPLC approach is conceptual at this point and has not yet been proven to enable the goals identified. That said, we would recommend adjusting the language to clearly articulate that the proposed TPLC approach is meant to enable the goals and quality system responsibilities identified, but still needs to be proven out before it can be relied upon.

In terms of the data being utilized for testing purposes, we have concerns about what is being considered as "good" data and whether the data being utilized may only be applicable to certain populations. We would be interested in learning how FDA is determining validity and the determinative comparison variable. Overall, we are left asking if we can ultimately trust how accurate and reliable the test results are for the intended use of software as a medical device – to diagnose, interpret, and treat.

What safeguards are in place now or should be in place to ensure these algorithms are being implemented properly and risks are mitigated? As AI/ML can change its function to varying degree and autonomously, this issue should always be stressed at the forefront. The focus of the development of the AI/ML algorithms are not different in that they need a quality process applied to ensure testing and consistency. Once an AI/ML routine is trained there needs to be guardrails for supervision put in place in the event that further tuning can be added with additional data sets while deployed in real time. It is for this reason that unsupervised AI/ML situations may pose a risk to patient safety and therefore be too dangerous for healthcare.

To re-emphasize, while HIMSS and PCHAlliance support the FDA bringing proposals such as this Proposed Framework and the Pre-Cert Program to the forefront of a discussion today, we believe adaptive mechanisms should have a supervised quality review since this is all based on human input.

VI. When is this Proposed Framework's logic triggered?

The Proposed Framework presumes that manufacturers can (1) predict the changes an algorithm will undergo when exposed to data in the field, (2) know when those changes occur, and (3) be in control of when the changes take place. These presumptions do not seem consistent with a true adaptive algorithm. The same adaptive algorithm hosted on multiple servers could change in different ways if exposed to different real-world evidence, which in turn could lead to multiple "versions" of the algorithm that the manufacturer cannot predict if the changes are due to real-world data (i.e., unknown inputs).

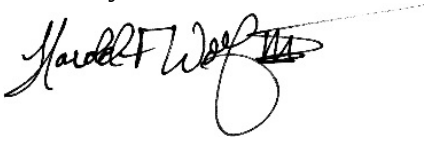
In sum and to further refine the discussion for the Proposed Framework, we recommend that FDA clarify that the framework is intended for addressing changes to an AI/ML algorithm that is predictable and or/controllable by the manufacturer.

VII. Final considerations going forward

We recommend using other industries who have been involved in the discussions and regulatory review of AI/ML, as an example for the health care industry. FDA should also consider convening a technical expert panel of stakeholders from multiple areas that would have material involvement in future frameworks such as the one represented in this paper, or in the alternative, leverage the experience of participants in the Pre-Cert Program, to participate on an expert committee. FDA should consider establishing an ongoing program – such as Smart and Connected Health - that focuses on the interface between research and industry domains to identify and maintain key issues and share learnings. Concerns with the proposal do err on the issue of whether the healthcare industry is ready to take to on additional risk.

We appreciate the opportunity to provide input on the Discussion Paper and Request for Feedback. HIMSS and PCHAlliance look forward to working with FDA on this and other future frameworks that embrace the iterative improvement power of AI/ML software as a medical device, while assuring that patient safety is maintained. IF you have any additional questions, please do not hesitate to contact Eli Fleet, Director for Federal Affairs for HIMSS at efleet@himss.org, or Robert Havasy, Senior Director for PCHAlliance at rhavasy@pchalliance.org.

Sincerely,



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