BILL CASSIDY, M.D.
LOUISIANA

WASHINGTON, DC OFFICE:
SUITE SH-520
HART SENATE OFFICE BUILDING
WASHINGTON, DC 20510
(202) 224-5824

United States Senate

COMMITTEES:
FINANCE
HEALTH, EDUCATION, LABOR, AND PENSIONS
ENERGY AND NATURAL RESOURCES
VETERANS' AFFAIRS
JOINT ECONOMIC COMMITTEE

February 10, 2020

Jeffrey Shuren, M.D., J.D.
Director, Center for Devices and Radiological Health
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Director Shuren:

I write to gain a better understanding of how and when the Food and Drug Administration (FDA) plans to develop and finalize a regulatory framework for Artificial Intelligence/Machine Learning-based (AI/ML-based) software as a medical device (SaMD), as well as inquire about the safeguards the agency envisions establishing to adequately protect patient safety. AI/ML-based SaMD has the potential to radically transform the delivery of high quality health care for both patients and providers. It cannot reach its revolutionary potential, however, if it is not safe and effective. Manufacturers urgently need guidance to navigate the current regulatory environment, especially as many technology companies entering the field are not accustomed to interacting with the FDA and the unique factors surrounding development of such medical products. Consumer confidence in the burgeoning field is also critical to its development and would be advanced by a regulatory framework that provides for reliable guarantees that AI/ML-based SaMD produces the results claimed. Recent well-publicized missteps and actions by companies like Theranos and 23andMe remind us that medical product development has distinct ethical considerations and may require more validation than technologies in other sectors.

The Medical Device Amendments of 1976 (Act), which established the current medical device regulatory framework, was not designed with AI/ML-based SaMD in mind. Stakeholders and other interested parties have long warned FDA that the Act is not adaptable to increasingly novel digital technologies. AI/ML-based SaMD and Software in a Medical Device (SiMD) pose highly complex regulatory questions that challenge the FDA's traditional review methods. FDA clearly agrees, having reiterated on numerous occasions that the framework is "not well-suited" for software-based medical technologies. FDA explained as early as 2011 that it never published an "overarching software policy" because "the use of computer and software products as medical devices grew exponentially and the types of products diversified and grew more complex." That exponential growth has only continued in the intervening decade, and FDA is now at risk of being dangerously behind the curve.

Given these concerns, I appreciate the FDA's release of the "Artificial Intelligence/Machine Learning Software as a Medical Device Action Plan" on January 12, 2021. The Action Plan signals that FDA views it as a priority to clearly define this regulatory paradigm, which will help bring certainty and clarity to manufacturers interested in this sector.

3600 JACKSON STREET
SUITE 115A
ALEXANDRIA, LA 71301
(318) 448-7176

5555 HILTON AVENUE
SUITE 100
BATON ROUGE, LA 70808
(225) 929-7711

101 LA RUE FRANCE
SUITE 505
LAFAYETTE, LA 70508
(337) 261-1400

1 LAKESHORE DRIVE
SUITE 1155
LAKE CHARLES, LA 70629
(337) 261-1400

3421 N. CAUSEWAY BOULEVARD
SUITE 204
METAIRIE, LA 70002
(504) 838-0130

1651 LOUISVILLE AVENUE
SUITE 123
MONROE, LA 70201
(318) 324-2111

6425 YOUREE DRIVE
SUITE 415
SHREVEPORT, LA 71105
(318) 798-3215

The Action Plan announces FDA's intent to further develop a regulatory framework for AI/ML SaMD that was first proposed in discussion paper form in 2019. It also commits to developing long-awaited draft guidance on a Pre-Determined Change Control Plan that will enable the AI/ML-based SaMD to make certain anticipated modifications in response to new data inputs without necessitating additional FDA review. Such guidance will be a critical part of enabling the marketing of safe and effective medical devices that learn from data, adapt, and change over time.

FDA has indicated an interest in new statutory authority to support this proposed regulatory framework when fully developed. Based on preliminary specifications, it is clear the approach will represent a major departure from longstanding FDA precedent and is not specifically authorized in the Act. Despite this, the Action Plan is largely a preview of future policy changes that FDA anticipates enacting through guidance. Numerous stakeholders have raised concerns that the Action Plan uses inconsistent terminology that confuses the proposed regulatory framework, and that its reliance on the International Medical Device Regulators Forum framework – while generally reasonable – does not directly map to the regulatory paradigm established under the Act and our existing medical device classification system. Moreover, the proposed framework leverages numerous concepts that FDA is still testing under the Software Pre-Certification Pilot Program. Launched as a voluntary pilot, the program has only accepted a limited number of participants and has not publicized examples of participants successfully meeting pre-certification organizational excellence criteria or submitting satisfactory real world evidence to the agency. In fact, FDA has indicated that it still needs to engage stakeholders to further develop viable approaches to major components of the program, leading some onlookers to project that full implementation could be years away. It is understandable that FDA test these new approaches before scaling up or finalizing the concepts, but the scope and unprecedented nature of this project, as well as the lack of clarity on its timeframe or results to date, pose serious challenges for congressional oversight of the agency.

Finally, I am concerned that while federal privacy laws are enforced by the HHS Office for Civil Rights and Federal Trade Commission, FDA has not discussed any mechanisms or considerations to ensure patient privacy is protected throughout the total product lifecycle of any AI/ML-based SaMD, including its potential iterations or updates. Data is essential to technology development and continuous learning algorithms require massive amounts just to be trained. This fact combined with a plan to continually evaluate real world evidence and real world performance data to assure safety and efficacy drastically complicates the security and data privacy considerations surrounding use of these products. Moreover, traditional strategies for protecting patient privacy, like notice and consent, may not be sufficient protections. De-identifying data also may not be sufficient in the context of a massive, complex dataset in an era where re-identification can easily be achieved.

I respectfully ask that FDA answer the following questions by March 15, 2021:

1. What internal deadlines has FDA set for completion of each component of the AI/ML-based Action Plan?
2. What guidance documents does FDA currently intend to publish regarding AI/ML-based SaMD regulation, and on what schedule?

   a. Please provide the anticipated time frame for publication as well as whether FDA intends to publish the document in draft or final form.
3. Does FDA expect that the parameters of the AI/ML-based SaMD regulatory framework under development could be extrapolated for AI/ML-based SiMD?
   a. Under what circumstances and on what schedule?
4. What guidelines are FDA staff members currently following in reviewing AI/ML-based SaMD applications or pre-submission requests?
   a. Are review teams trained on FDA's digital health policies and do they interact with the Agency's Center of Excellence for Digital Health to ensure Center-wide consistency in the application of FDA's policies?
   b. If so, by what metrics are FDA review teams measured to ensure consistent application of FDA's policies?
5. Are there any continuous learning systems without locked algorithms currently in use that have received FDA approval, clearance, or de novo authorization?
   a. If so, does this represent human subjects research?
   b. If so, how is FDA ensuring protection of patient data in the field and in any real world performance analysis?
6. Does FDA plan to hold workshops or other educational opportunities to further explore concepts related to the proposed regulatory framework like the SaMD Pre-Specifications and Algorithm Change Protocol? If so, please describe FDA's plans.
7. Does FDA have a consistent format for manufacturers to describe SaMD Pre-Specifications and the Algorithm Change Protocol in the premarket review submission or application?
   a. If so, please provide such format.
8. Have any organizations that successfully met organizational excellence criteria under the Software Pre-Certification Pilot Program with appropriate explanatory key performance indicators? Please provide the total number of submissions under the Pilot program and the total number of submissions that have successfully met the criteria.
9. How many organizations have submitted sufficient real-world performance data under the Software Pre-Certification Pilot Program?
   a. How does FDA continue to work with organizations that have submitted insufficient real-world performance data?
10. How can FDA and manufacturers ensure protection of patient data in accordance with federal laws governing health privacy throughout the AI/ML-based software's total product lifecycle?
11. How will FDA balance expectations for real world performance analysis with data privacy considerations?
   a. How does FDA envision handling scenarios in which an organization is unable to obtain patient consent for data sharing? Will FDA provide clear guidelines for such scenarios?
   b. Has FDA considered mechanisms to ensure patients can withhold their data from use in training or developing AI/ML-based software?
12. What information has FDA gathered from industry regarding how manufacturers control and clean real world evidence data?

13. What methods is FDA considering to ensure that providers can quickly inform patients if AI/ML-based SaMD becomes a safety risk? Will FDA provide clear guidelines for such scenarios?
14. How is FDA taking into account the potential for data to influence algorithm bias, which might exacerbate existing health disparities?
15. How does FDA intend to harmonize its AI/ML policies with other global medical device regulators? If so, please describe in which ways.

Thank you for your prompt attention to this request. If you have any questions, please reach out to Amanda Lincoln with my staff at (202) 224-5824.

Sincerely,

Bill Cassidy, M.D.

Bill Cassidy, M.D.
United States Senator