ConnectedHealth

June 3, 2019

ATTN: Bakul Patel, Associate Director for Digital Health
Food and Drug Administration
Center for Devices and Radiological Health
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

RE: *Comments of the Connected Health Initiative on the Food and Drug Administration's* Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning Based Software as a Medical Device: Discussion Paper and Request for Feedback *(FDA-2019-N-1185)*

The Connected Health Initiative[1] (CHI) appreciates the opportunity to provide input on the Food and Drug Administration's (FDA) *Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning Based Software as a Medical Device: Discussion Paper and Request for Feedback*.[2]

I. About the Connected Health Initiative and its Health AI Task Force

CHI is the leading multistakeholder consensus policy advocacy effort driven by the consensus of a diverse stakeholders across the connected health ecosystem that seeks to advance the responsible availability and use of digital health innovations in both prevention and treatment. CHI's advocacy reaches across the Department of Health and Human Services (HHS), as well as other relevant agencies, in seeking to advance policies that will provide the infrastructure and policy environment to support, as well as incentives to use, cutting-edge digital health products and services. Additionally, CHI is an appointed member of the American Medical Association's (AMA) Digital Medicine Payment Advisory Group, an initiative bringing together a diverse cross-section of 15 nationally recognized experts that identifies barriers to digital medicine adoption and proposes comprehensive solutions revolving around coding, payment, coverage, and

[1] For more information, see www.connectedhi.com.

[2] FDA, Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning Based Software as a Medical Device: Discussion Paper and Request for Feedback (April 2019), *available at* https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device.

more.[3] CHI is also a board member of Xcertia, a collaborative effort develop and disseminate mHealth app guidelines that can drive the value these products bring to the market and the confidence that physicians and consumers can have in health apps and their ability to help people achieve their health and wellness goals.[4] In addition, CHI is a member of the Consumer Technology Association's standardization effort on Artificial Intelligence in Health Care.[5]

Artificial/augmented intelligence (AI), powered by streams of data and advanced algorithms, have incredible potential to improve healthcare, prevent hospitalizations, reduce complications, and improve patient engagement. Yet, applications of AI in healthcare have also given rise to a variety of potential effects and challenges for U.S. policymakers to consider, including notice/consent, bias, inclusion, transparency and digital due process, and law enforcement access to data, among others. Representing the leading developers of AI, we recognize that, as healthcare AI innovations continue to be developed and even start to enter today's regulatory processes, policymakers at the legislative and regulatory levels are considering whether policy changes are needed. Based on this assessment, the CHI assembled a Health AI Task Force in the Summer of 2018. Consisting of a range of innovators and thought leaders, the CHI Health AI Task Force was formed with the goals of:

(1) Advancing policymaker understanding by providing an authoritative voice from the connected health tech community to policymakers to provide a baseline taxonomy as well as to help them understand the foundations of healthcare AI;

(2) Providing thought leadership through the development of healthcare AI policy principles that address the range of opportunities and challenges associated with AI in healthcare and advocate for the appropriate role of government regulation; and

(3) Building stakeholder community consensus through convening inclusive stakeholder roundtables that will feature presentations from and dialogue with policymakers.

[3] https://www.ama-assn.org/delivering-care/digital-medicine-payment-advisory-group

[4] http://www.xcertia.org/

[5] https://www.cta.tech/News/Press-Releases/2019/April/CTA-Brings-Together-Tech-Giants,-Trade-Association.aspx.

As a result of its work throughout the second half of 2018, in early February 2019, the CHI unveiled its AI Task Force's deliverables during a public-private multistakeholder dialogue in Washington, DC.[6] These deliverables included a position piece supporting AI's role in healthcare, policy principles addressing how policy frameworks should address the role of AI in healthcare, and a terminology document targeted at policymakers.[7] Since the release of its deliverables, CHI has actively advocated for the development of frameworks that will responsibly support the development, availability, and use of AI innovations.

CHI is a longtime supporter of the FDA's efforts to develop a total product lifecycle-based regulatory framework for these technologies that would allow for modifications to be made from real-world learning and adaptation, while still ensuring that the safety, efficacy, and equity of the AI/ML SaMD is maintained. The open and collaborative approach taken by the FDA is consistent with the CHI Health AI Task Force's recommendations, however, we provide some recommendations for clarity to the proposed framework which are provided below.

[6] https://actonline.org/2019/02/06/why-does-healthcare-need-ai-connected-health-initiative-aims-to-answer-why/

[7] The CHI Health AI Task Force's deliverables are appended to this comment.

II. Artificial/Augmented Intelligence and Machine Learning's Role in the Future of Healthcare

Today, there are already many examples of AI systems, powered by streams of data and advanced algorithms, improving healthcare by preventing hospitalizations, reducing complications, decreasing administrative burdens, and improving patient engagement. AI offers the promise to rapidly accelerate and scale such results and drive a fundamental transformation of the current disease-based system to one that supports prevention and health maintenance. For example, AI-driven digital therapeutics that deliver clinically-backed interventions to treat patients where they are, saving the patient, provider and others throughout the healthcare value chain immense time and expense.

The CHI finds that one of the most helpful ways to see the value of AI in healthcare is to view the proposition through the lens of the "quadruple aim" framework. Built on the Institute for Healthcare Improvement's "triple aim,"[8] a widely accepted compass to optimize health system performance,[9] the quadruple aim focuses on four key areas where health systems need to be improved and acknowledges concerns of key stakeholders. The four areas are (1) enhancing population health; (2) improving patient experience, satisfaction, and health outcomes; (3) better clinician and healthcare team experience and satisfaction; and (4) lowered overall costs of healthcare.

> **Improving Population Health Management:** AI-enabled tools offer great promise in overcoming the challenges faced by clinicians, health systems, health plans, and public health officials working to advance population health management and public health. AI-enabled tools, for example, can process massive and disparate data sources to provide public health officials, health care systems, and providers essential and actionable data rapidly related to assist with more timely and accurate population level disease surveillance and assessments of disparities and health care resource distribution.
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> Population health[10] management has long been viewed as the essential ingredient to improve overall health outcomes and arrest rising health care costs. Population health management involves aggregation and analysis of huge amounts of data from divergent sources, something that can be potentially streamlined through robust and powerful AI systems. AI-powered tools can collect patient generated health data and also deliver clinically-backed interventions to treat patients where they are.

[8] http://www.ihi.org/engage/initiatives/tripleaim/pages/default.aspx.

[9] Thomas Bodenheimer, MD and Christine Sinsky, MDFrom Triple to Quadruple Aim: Care of the Patient Requires Care of the Provider, Ann Fam Med November/December 2014 vol. 12 no. 6 573-576.

[10] Defined as "an approach [that] focuses on interrelated conditions and factors that influence the health of populations over the life course, identifies systematic variations in their patterns of occurrence, and

As more systems are created and deployed, the opportunity for AI to help improve healthcare outcomes is significant, with estimates suggesting outcomes could be improved by 30-40 percent.[11]

Improving Patient Experience, Satisfaction, and Outcomes: One of the more significant critiques of healthcare systems around the world is that they fail in many respects to meet patients' expectations around access to care, ease of use, and care continuity and coordination.

All too often, patients are forced to make multiple visits, shuffling between a general practitioner and a specialist. With the ability to replicate specialist-level expertise at the frontlines of care, AI-enabled tools will reduce paperwork burdens, center care around where the patient is located, and enhance the ability to manage and understand how to sustain health or manage a disease. Services that increasingly can be enhanced and improved with AI systems will provide patients and their health care teams with timely, essential information, and ongoing support that is not currently available.

With people over the age of 65 representing an increasing percentage of the population, AI systems will be essential for human caregivers and clinicians to extend their reach and coverage of an ever-growing population of patients.

Improving Clinician and Healthcare Team Experience and Satisfaction: Among clinicians and the extended health care team, the growing administrative and paperwork demands coupled with compounding rates of new medical knowledge and data generation are driving records levels of burn-out and dissatisfaction. AI-enabled tools can and should be deployed to drastically improve clinician and healthcare team satisfaction using tools that help clinicians and the health care team to more quickly screen, diagnose, treat, and monitor effectively patients and remove time-consuming and often mundane tasks.

applies the resulting knowledge to develop and implement policies and actions to improve the health and well-being of those populations." Kindig, D. and Stoddart, G. What Is Population Health? American Journal of Public Health, 93, 380-383 (2003).

[11] Nicole Lewis, Artificial Intelligence to play key role in population health, Medical Economics (2017) (available at http://www.medicaleconomics.com/medical-economics-blog/artificial-intelligence-play-key-role-population-health).

Reducing Healthcare Costs: Countries around the world struggle with both rising costs and absolute costs of providing healthcare to their citizens. Nations spend between roughly 6 percent and 18 percent of their gross domestic product (GDP) and many have seen the share of GDP devoted to healthcare costs sharply rise over the last three decades.[12] The situation is unsustainable, and, in many countries, the problem will only get more acute as populations age and average life expectancy continues to rise. A huge amount of data is available today for collection and utilization in timely prevention and treatment decisions that would result in massive cost savings, but that data currently usable, but can be found in electronic health record (EHR) systems.

Healthcare experts see enormous promise in AI to more accurately capture and leverage the range of health data available, with estimates suggesting AI applications can create $150 billion in annual savings for the United States healthcare economy by 2026.[13] This savings estimate includes only the top 10 AI scenarios, such as assisted surgery, virtual nursing assistants, and administrative workflow assistance, etc.

On a worldwide basis, healthcare administrative costs (e.g., billing) are a continuing challenge. The administrative costs of the U. S. health care system are estimated to be 31 percent of total healthcare expenditures.[14] AI's potential to help us address spiraling costs in healthcare is very real, and it is already showing returns today.

These are all areas where we are already seeing the potential AI systems have to positively impact the current healthcare system. Any future FDA framework addressing AI SaMD should advance the quadruple aim.

[12] Henry J Kaiser Family Foundation, Snapshots: Health Care Spending in the United States & Selected OECD Countries (2011); Bradley Sayer and Cynthia Cox, How does health spending in the U.S. compare to other countries?, Kaiswer Family Foundation (2018).

[13] Accenture, Artificial Intelligence: Healthcare's New Nervous System (2017).

[14] http://www.pnhp.org/publications/nejmadmin.pdf.

III. General Comments of the Connected Health Initiative on the Proposed Framework

CHI reiterates its strong support for the FDA's efforts to develop a total product lifecycle-based regulatory framework for these technologies that would allow for modifications to be made from real-world learning and adaptation, while still ensuring that the safety and effectiveness of the SaMD is maintained. We applaud the FDA's forward thinking and collaboration, which we believe will lead to eased American patients' access to medical device innovation. Further, through this effort the FDA is ensuring that it remains a global leader for other medical device regulators around the world.

Initially, we note our concern with the FDA's key terminology in the draft framework. Across policymaking communities, CHI has observed that much confusion rests in different understanding of key terminology related to AI. For example, FDA must avoid using AI and ML as interchangeable terms. AI with an algorithm learns and changes without being programmed when exposed to new data, where knowledge can either be static (data sources that do not change frequently over time) or continuous (continually learning, accumulating, and building on previously learned knowledge in part by generating new algorithms which may be unknown to the original designer or trainer). A term falling under AI, ML allows inferencing—the ability of an AI model to infer or draw conclusions on data it has never seen before—and can happen in a data center, in the cloud, or on the device (edge computing). CHI strongly encourages the FDA to leverage definitions brought forward through cross-stakeholder consensus efforts, including but not limited to that the of CHI's Health AI Task Force,[15] the Duke Margolis Center for Health Policy's *Current State and Near-term Priorities for AI Enable Diagnostic Support Software in Health Care*,[16] BSI, IEEE, and others. CHI has numerous concerns with key definitions in the draft framework, including for locked versus continuous learning AI (for example, FDA's discussion initially raising TPLC appears to conflate continuous learning systems that may utilize a locked algorithm with autonomous systems.

Further, as it further develops its AI SaMD framework, FDA is encouraged to utilize the wide range of resources available to it regarding AI development concepts. There are many resources publicly available to the FDA today that should be considered, including those developed by the CHI's Health AI Task Force, as well as other important efforts including but not limited to the Partnership for AI, Xavier Health, the American Medical Association, and the Association for the Advancement of Medical Instrumentation and that of the British Standards Institute.

[15] https://actonline.org/wp-content/uploads/Artificial-Intelligence-in-Health-Appendix.pdf.

[16] https://healthpolicy.duke.edu/sites/default/files/atoms/files/dukemargolisaienableddxss.pdf.

CHI generally supports the FDA's framework utilizing risk-based approaches that align the use of AI with recognized standards of safety, efficacy, and equity. Providers, technology developers and vendors, health systems, insurers, and other stakeholders all benefit from understanding the distribution of risk and liability in building, testing, and using healthcare AI tools. The FDA's AI SaMD framework should ensure that those in the value chain with the ability to minimize risks based on their knowledge and ability to mitigate should have appropriate incentives to do so. CHI also supports the FDA's AI SaMD framework providing that:

- AI in healthcare is safe, efficacious, and equitable;
- Developers tie AI/ML systems to clinical outcomes research;
- The framework is based on a standardized nomenclature and terminology;
- Algorithms, datasets, and decisions are auditable and when applied to medical care (such as screening, diagnosis, or treatment) are clinically validated and explainable;
- AI developers consistently utilize rigorous procedures, documenting their methods and results;
- Those developing, offering, or testing healthcare AI systems provide truthful and easy to understand representations regarding intended use and risks that would be reasonably understood by those intended, as well as expected, to use the AI solution; and
- Adverse events should be timely reported to relevant oversight bodies for appropriate investigation and action.

CHI also highlights its support for the FDA's AI SaMD framework including the concept of thoughtful design. The FDA's framework should require the design of AI systems in health care that are informed by real-world workflow, human-centered design and usability principles, and end-user needs. Also, AI systems should help patients, providers, and other care team members overcome the current fragmentation and dysfunctions of the healthcare system. AI systems solutions should facilitate a transition to changes in care delivery that advance the quadruple aim. The design, development, and success of AI in healthcare should leverage collaboration and dialogue between caregivers, AI technology developers, and other healthcare stakeholders to have all perspectives reflected in AI solutions.

CHI notes that the FDA's AI/ML SaMD framework and FDA's Software Precertification Program use the International Medical Device Regulators Forum (IMDRF) risk framework for SaMD. We believe this framework does not entirely account for issues unique to AI/ML. For example, the IMDRF risk tables do not account for the added dimensions of autonomy level and whether a system is "locked" or "continuous," which have significant impacts on the design and validation to ensure safe, effective, and equitable AI/ML systems. We urge FDA to further consider defining these terms using standardized terminology and adding these categories to its risk classification framework.

CHI also notes that the FDA's Software Precertification Program total product lifecycle (TPLC) concept is included in this draft AI SaMD framework. The TPLC concept, however, is not fully developed in the context of the Software Precertification Program, and therefore difficult to assess in the FDA's draft AI SaMD framework at this time, and CHI is unclear as to how the FDA's AI SaMD framework would apply to companies that do not participate in the Software Precertification Program. We believe it would be very helpful for the FDA to provide as much clarity as possible on these questions, and the relationship between future AI SaMD guidance and the Software Precertification Program generally. Likewise, it would be beneficial for the FDA to clarify this AI SaMD guidance's relationship to existing FDA guidance documents (e.g., addressing software changes in existing medical devices).

Finally, the FDA's draft AI SaMD guidance (like its proposed Software Precertification Program) notes that the FDA may "require additional statutory authority to implement fully" its envisioned approach to AI SaMD. Reiterating our support for the FDA's efforts to address AI to responsibly provide American patients with the most innovative medical devices more quickly, we urge FDA to, in the short term, shape its programs within its existing authority.

IV. Connected Health Initiative Answers to Specific FDA Questions

Building on our support for the FDA's continued work to realize a fully functional Software Pre-Certification Program, we offer the following specific input to questions posed by the FDA:

Do these categories of AI/ML-SaMD modifications align with the modifications that would typically be encountered in software development that could require premarket submission?

CHI agrees that the categories of AI-SaMD modifications generally align with the modifications that would typically be encountered in software development that could require premarket submission. However, we believe that clearly adding defined categories for autonomy level and continuous vs. locked systems as additional considerations to the IMDRF SaMD intended use risk table will provide needed clarity when considering AI/ML modifications.

We also request that FDA clearly address whether future guidance addressing AI SaMD will be a complement to existing guidances, including those addressing the 510(k) process and making software changes to existing medical devices. For example, the FDA should clarify that general performance and cybersecurity software updates made to a medical device do not require a premarket submission. Answering this threshold question will enable CHI and other stakeholders to provide detailed feedback as to whether this draft framework's categories of AI-SaMD modifications align with the modifications that would typically be encountered in software development that could require premarket submission.

What additional categories, if any, of AI/ML-SaMD modifications should be considered in this proposed approach?

In addition to adding autonomy level and locked vs. continuous learning categories, CHI suggests that the FDA add a new category to capture software modifications that are unrelated to intended use and medical device performance. Such updates would include, for example, cybersecurity updates (consistent with the FDA's guidance on cybersecurity updates made to medical devices).

Would the proposed framework for addressing modifications and modification types assist the development AI/ML software?

CHI agrees that the proposed framework for addressing modifications and modification types assist the development AI software. We advise FDA to develop clear and easily-understood resources for its framework (e.g., graphic flowcharts). Further, as we have noted elsewhere in this comment, we request that the FDA clarify this future guidance's relationship to existing guidance documents and the Software Precertification Program.

What additional considerations exist for GMLP?

CHI supports GMLPs reflecting the following consensus priorities developed by the CHI's Health AI Task Force:

- AI in healthcare is safe, efficacious, and equitable;
- Developers tie ML/AI systems to clinical outcomes research;
- AI/ML frameworks are based on a standardized nomenclature and terminology;
- Algorithms, datasets, and decisions are auditable and when applied to medical care (such as screening, diagnosis, or treatment) are clinically validated and explainable;
- AI developers consistently utilize rigorous procedures, documenting their methods and results;
- Those developing, offering, or testing healthcare AI systems provide truthful and easy to understand representations regarding intended use and risks that would be reasonably understood by those intended, as well as expected, to use the AI solution; and
- Adverse events should be timely reported to relevant oversight bodies for appropriate investigation and action.
- That the design of AI systems in health care utilize thoughtful design concepts (are informed by real-world workflow, human-centered design and usability principles, and end-user needs). AI systems solutions should facilitate a transition to changes in care delivery that advance the quadruple aim. The design, development, and success of AI in healthcare should leverage collaboration and dialogue between caregivers, AI technology developers, and other healthcare stakeholders to have all perspectives reflected in AI solutions.

How can FDA support development of GMLP?

CHI urges FDA to consider the variety of important efforts underway today, including but not limited to the Partnership for AI, Xavier Health, the American Medical Association, and the Association for the Advancement of Medical Instrumentation and that of the British Standards Institute.

Further, we strongly encourage the FDA to develop as many detailed examples as possible to support the development of GMLP. FDA's examples have been very helpful to the digital health community in past guidance documents.

Finally, we urge FDA to consider adding more common pitfalls of AI/ML design and development to its GMLP framework by reaching out to industry experts. For example, developers should ensure AI/ML is tied to clinical outcomes research and ensure that the AI/ML is not confounded by data unrelated to these outcomes.

How do manufacturers and software developers incorporate GMLP in their organization?

Innovative manufacturers and developers absolutely following good ML practices (GMLP) throughout the lifecycle of a medical devices, while also ensuring alignment with FDA requirements for validation, verification, etc. Past FDA requirements, CHI believes that GMLP includes taking a lifecycle approach to addressing key issues including bias, utilization of an active and continuous feedback loop, and other quality assurance metrics.

What additional level of detail would you add for the described components of an ACP?

CHI urges FDA's algorithm change protocol (ACP) to focus on assessing risk consistent with the FDA's approach to SaMD with additional categories for autonomy level and locked vs. continuous learning considered as part of the ACP. We urge the FDA's ACP to incorporate concepts including:

- Ensuring algorithms, datasets, and decisions are auditable and clinically validated and explainable;
- Tying AI/ML to clinical outcomes research;
- Utilization of rigorous procedures and documentation of methods and results;
- Identification, disclosure, and mitigation of bias while encouraging access to databases and promoting inclusion and diversity, towards ensuring that data bias does not cause harm to patients or consumers;
- Providing truthful and easy to understand representations regarding intended use and risks that would be reasonably understood by those intended, as well as expected, to use the AI solution; and
- Timely reporting of adverse events.

Further, CHI believes that the FDA's providing of as many detailed examples/use cases as possible will have high value to digital health stakeholders impacted by the FDA's approach to AI SaMD. We strongly encourage the FDA to develop these detailed examples/use cases to illustrate components of an ACP.

In what ways can a manufacturer demonstrate transparency about AI/ML-SaMD algorithm updates, performance improvements, or labeling changes, to name a few?

CHI supports the following as ways a manufacturer demonstrate transparency about AI-SaMD algorithm updates, performance improvements, or labeling changes:

- Ensuring algorithms, datasets, and decisions are auditable and clinically validated and explainable;
- Tying AI/ML to clinical outcomes research;
- Utilization of rigorous procedures and documentation of methods and results;
- Identification, disclosure, and mitigation of bias while encouraging access to databases and promoting inclusion and diversity, towards ensuring that data bias does not cause harm to patients or consumers;
- Providing truthful and easy to understand representations regarding intended use and risks that would be reasonably understood by those intended, as well as expected, to use the AI solution; and
- Timely reporting of adverse events.

What role can real-world evidence play in supporting transparency for AI/ML-SaMD?

CHI supports the FDA's AI SaMD framework including the concept of thoughtful design, including a requirement for the design of AI systems in health care to be informed by real-world workflow, human-centered design and usability principles, and end-user needs. Also, AI systems should help patients, providers, and other care team members overcome the current fragmentation and dysfunctions of the healthcare system. AI systems solutions should facilitate a transition to changes in care delivery that advance the quadruple aim. The design, development, and success of AI in healthcare should leverage collaboration and dialogue between caregivers, AI technology developers, and other healthcare stakeholders to have all perspectives reflected in AI solutions.

What additional mechanisms might be needed for real-world performance monitoring of AI-SaMD?

CHI supports the FDA's AI SaMD framework including the concept of thoughtful design, including a requirement for the design of AI systems in health care to be informed by real-world workflow, human-centered design and usability principles, and end-user needs. AI/ML real-world performance monitoring should be tied to patient outcomes. Also, AI systems should help patients, providers, and other care team members overcome the current fragmentation and dysfunctions of the healthcare system. AI systems solutions should facilitate a transition to changes in care delivery that advance the quadruple aim. The design, development, and success of AI in healthcare should leverage collaboration and dialogue between caregivers, AI technology developers, and other healthcare stakeholders to have all perspectives reflected in AI solutions.

Further, we encourage FDA to provide as many detailed examples as possible of real-world evidence that may be used.

V. Conclusion

CHI appreciates the opportunity to submit its comments to the FDA and urges its thoughtful consideration of the above input. We look forward to further work with the FDA and other stakeholders towards responsibly realizing a connected and AI SaMD-enabled continuum of care.

Sincerely,

Brian Scarpelli
Senior Global Policy Counsel

Kate Hirzel
Policy Associate

Connected Health Initiative
1401 K St NW (Ste 501)
Washington, DC 20005