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Shooting for the Moon: The Evolution of Key AI/ML Regulations Governing Certain Health Care Products and Services

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The U.S. Food and Drug Administration (FDA) and the U.S. Department of Health and Human Services Office of the National Coordinator for Health Information Technology (ONC), amongst other health care regulators, are developing their respective regulatory schemes to keep pace with rapid advancements in artificial intelligence and machine learning.

Artificial intelligence and machine learning (AI/ML) are poised to revolutionize health care, both with respect to their use in medical devices and in other health care-related technologies. For example, the key characteristic of AI/ML-enabled medical devices is their cornerstone feature to learn and change over time based on real-world use to improve their performance. Other technologies in health care, such as electronic medical records, are increasingly leveraging AI/ML to advance and improve the delivery of care, such as by assisting physicians in decision-making through automated means. However, while AI/ML has prompted health care innovation, its advancement has also outpaced the respective regulatory schemes of health care regulators in the United States, including those of FDA and ONC, potentially slowing its adoption and delaying full realization of the technology's substantial promise.

With the goal of fostering development of innovative technology using AI/ML for health care applications, FDA has engaged with industry and the public in recent years regarding the key components of a flexible regulatory scheme for AI/ML-enabled devices. That engagement has resulted in new guidance and other FDA pronouncements and prompted legislative action with more regulatory activity on the horizon. ONC, which has authority over certification of health information technology (Health IT) (i.e., hardware, software, integrated technologies, or packaged solutions that are designed for/support the use by health care entities or patients for creating, maintaining, accessing, or exchanging health information electronically) also recently proposed certain modifications to these certification requirements. This proposal aims to address the increase in predictive decision support interventions (DSIs) and clinical decision support (CDS) tools that rely on AI/ML, and the growing need for accountability in their operation and outcomes.

While a number of federal and state regulators continue to refine their approach to oversight in connection with the explosion in AI/ML in health care, this article focuses on recent actions of FDA and ONC specifically. In

particular, this article first discusses the current FDA regulatory scheme applicable to AI/ML-enabled medical devices in the United States, FDA's efforts to foster their development and availability, and what to expect from FDA in the near term as it continues developing its proposed contemporary regulatory framework. This article then provides an overview of ONC's proposed rule that includes certain measures designed to enhance transparency, governance, and oversight in Health IT technology that leverages AI/ML-driven predictive DSIs to aid decision-making in health care.

FDA Regulation of Medical Devices and Application to AI/ML

FDA has acknowledged that the traditional medical device regulatory framework “was not designed for adaptive AI/ML technologies, which have the potential to adapt and optimize device performance in real-time,” and that these iterative, adaptive tools “require[] a new . . . regulatory approach.”¹ FDA's traditional framework operates on the presumption that modifications to medical devices generally require evaluation for their impact on safety and efficacy and the device's intended use, and may require premarket review before such modifications may be implemented. This traditional framework would thus require premarket applications whenever such iterative changes could significantly affect device performance, safety, or effectiveness, or modify the device's intended use. Because AI/ML-driven devices may be modified after commercial launch by design, application of this regulatory framework to this new wave of devices would slow their entry to the market and restrict their full potential.

In light of the acknowledged limitations of the traditional framework for these highly iterative, autonomous, and adaptive AI/ML-enabled devices, FDA has taken, and further proposed, several actions to develop a new framework tailored to AI/ML-enabled devices and software-based devices more generally. For example, FDA initiated a digital health software pre-certification program in July 2017 as part of its Digital Health Innovation Action Plan.² The pre-certification program focused principally on the software developer or digital health technology developer, rather than primarily on the product itself (as is traditionally the case in FDA's regulation of medical devices).³ FDA has stated that the program is designed to “help inform the development of a future regulatory model”⁴ and to “provide more streamlined and efficient regulatory oversight of software-based medical devices from manufacturers who have demonstrated a robust culture of quality and organizational excellence . . . and are committed to monitoring real-world performance of their products once they reach the U.S market.”⁵ In addition, in September 2020, FDA launched the Digital Health Center for Excellence aiming to advance digital health technologies including AI/ML-based devices.⁶ Since 2017, FDA has also issued a number of guidance documents concerning software as a medical device (SaMD) and held public workshops on related issues.⁷

FDA's Progress on AI/ML-Based SaMD Action Plan

In April 2019, FDA released a discussion paper titled *Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)* (Discussion Paper). In the Discussion Paper, FDA requested stakeholder feedback on a potential new regulatory framework for premarket review of modifications to AI/ML-based SaMD.⁸ The Discussion Paper recognized that “additional statutory authority” may be required to fully implement a new regulatory framework for these devices.⁹ Most notably, consistent with the approach envisioned in the digital health software pre-certification program, the Discussion Paper announced the possibility of a “total product lifecycle” approach for AI/ML-based devices, which would be designed to allow FDA to assess the “culture of quality and organizational excellence of a particular company [to obtain] . . . reasonable assurance of the high quality of their software development, testing, and performance monitoring of their products.”¹⁰ The framework would allow evolution of the software in a real-world setting within the scope of a “predetermined change control plan” without requiring new premarket review for each change.¹¹ As FDA described, the predetermined change control plan would include the types of anticipated modifications (the SaMD Pre-Specifications) and the associated methodology (the Algorithm Change Protocol) being used to implement those changes in a controlled manner that manages risks to patients.¹²

After receiving stakeholder feedback on the Discussion Paper, in January 2021, FDA published an AI/ML-based SaMD “Action Plan” on FDA’s development of a proposed regulatory framework for AI/ML-based medical devices.¹³ The Action Plan described the steps FDA intends to take to “advance the concepts from the AI/ML discussion paper toward a practical oversight of AI/ML-based SaMD and of the field in general.”¹⁴ According to the Action Plan, FDA planned to focus on further developing a regulatory framework for AI/ML-based medical devices in the following ways:

1. Draft Guidance on a Predetermined Change Control Plan for AI/ML-Based SaMD

FDA noted its plan to issue draft guidance detailing what should be included in a predetermined change control plan. Subsequently, on December 29, 2022, the Food and Drug Omnibus Reform Act of 2022 (FDORA) was enacted as part of the Consolidated Appropriations Act, 2023. FDORA amended the Federal Food, Drug, and Cosmetic Act to add a new Section 515C, which authorizes FDA to approve a predetermined change control application as part of a premarket application or supplement “if the device remains safe and effective without any change” and, in the case of a predetermined change control application submitted as part of a premarket notification, “the device would remain substantially equivalent to the predicate.”¹⁵ Section 515C further provides that a new premarket application or supplement that would otherwise be required for a modification to a device is not required if such changes are consistent with an authorized predetermined change control plan.¹⁶

On April 3, 2023, FDA issued a draft guidance document, *Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions*.¹⁷ The draft guidance sets forth FDA’s recommendations concerning the content of predetermined changed control plans, based on the statutory amendment and feedback from stakeholders, including through comments to the Action Plan.¹⁸ Specifically, FDA recommends that a predetermined change control plan include a description of modifications, describing the modifications that will be made to the ML-enabled device software function; a modification protocol, describing verification and validation activities to support the modifications; and an impact assessment identifying the benefits and risks introduced by the planned modifications and how the verification and validation activities in the modification protocol will continue to assure the safety and effectiveness of the device.¹⁹

2. Harmonized Good Machine Learning Practice (GMLP) Standards

The Action Plan discusses FDA’s commitment to develop a set of harmonized GMLP standards for best practices in the quality systems of AI/ML-based device developers. On October 27, 2021, FDA published a set of ten guiding principles to inform the development of GMLP standards.²⁰ These principles were co-developed and jointly issued by FDA, Health Canada, and the UK Medicines and Healthcare Products Regulatory Agency (MHRA) to lay the groundwork for developing GMLP standards to address the unique nature of AI/ML-enabled devices and to “help promote safe, effective, and high-quality medical devices that use [AI/ML].”²¹ To date, FDA has not published such GMLP standards.

3. Public Workshops and Meetings to Discuss User Transparency and Enhancement of Trust in AI/ML-Based Devices

In its Action Plan, FDA anticipated holding a public workshop to discuss the role of transparency for users (i.e., patients and health care providers) of AI/ML-enabled medical devices.²² In October 2020, FDA first held a Patient Engagement Advisory Committee meeting devoted to AI/ML-based devices to gain insight from patients into what factors impact their trust in these technologies.²³ Thereafter, in October 2021, FDA held a virtual public workshop titled *Transparency of Artificial Intelligence/Machine Learning-Enabled Medical Devices*, which discussed the role of transparency in enhancing safe and effective use of AI/ML-enabled medical devices and using labeling and other methods to educate users about AI/ML functionalities.²⁴ FDA intends to use insights from these

workshops to help develop labeling requirements for AI/ML-enabled devices to enhance transparency and user trust.²⁵

4. Regulatory Science Efforts to Develop Methods for Evaluating and Improving AI/ML Algorithms

FDA's Action Plan discussed the need for improved methods to evaluate and address algorithmic bias and promote algorithm robustness, given the opacity of the functioning of many AI/ML algorithms.²⁶ Specifically, FDA stated it would further regulatory science initiatives that aim to evaluate and develop methods to prevent algorithms from mirroring and exacerbating biases already present in health care delivery, including with respect to race, ethnicity, and socio-economic status.²⁷ FDA collaborates with leading research universities through the Centers of Excellence in Regulatory Science and Innovation program to address these concerns.²⁸ FDA's Center for Devices and Radiological Health (CDRH) also conducts research in AI/ML-based technology through its Office of Science and Engineering Laboratories to support the agency's regulatory efforts.²⁹

5. Programs to Generate Real-World Evidence for AI/ML-Based SaMD

Finally, the Action Plan addressed mechanisms that support real-world performance monitoring. FDA explained that real-world data collection and monitoring may be leveraged “to mitigate the risk involved with AI/ML-based SaMD modifications, in support of the benefit-risk profile in the assessment of a particular marketing submission.”³⁰ As part of the Action Plan, FDA identified a number of potential means to achieve real-world performance monitoring, including annual reporting or through its Case for Quality pilot program, while noting that reporting type and frequency may be tailored based on the risk of the device, number and types of modifications, and maturity of the relevant algorithm.³¹

Through FDA's Action Plan and recent congressional action, the FDA regulatory framework for AI/ML has evolved rapidly, in an effort to catch up to the wave of innovation. But these regulatory actions are only the beginning of a new world for AI/ML-based medical devices. Stakeholders must keep abreast of the near-term, anticipated FDA actions touching on the regulation of AI/ML-based devices as the regulatory framework for these devices continues to crystallize.

ONC Proposed Rulemaking on Algorithmic Transparency

On April 18, 2023, ONC issued a proposed rule, the “Health Data, Technology, and Interoperability: Certification Program Updates, Algorithm Transparency, and Information Sharing Proposed Rule” (Proposed Rule). The Proposed Rule includes certain new requirements for the certification of Health IT technology or “Health IT Modules” that enable or interface with predictive models and algorithms to support health care decision-making.³² The new “decision support interventions” (DSI) criterion would replace the existing “clinical decision support” (CDS) criterion, and is intended to reflect the continued evolution of the functionalities, data elements, and software applications used to support clinical decision-making, including the use of AI/ML-driven predictive models.³³ Technology certified to the current CDS criterion would need to be updated to the new DSI criterion by December 31, 2024.³⁴ The Proposed Rule defines “predictive DSIs” as a technology that is “intended to support decision-making based on algorithms or models that derive relationships from training or example data and then are used to produce an output or outputs related to, but not limited to, prediction, classification, recommendation, evaluation, or analysis.”³⁵

In the preamble to the Proposed Rule, ONC notes that predictive DSIs, also commonly referred to as “augmented intelligence” or “automated decision-making,” are increasingly embedded into Health IT systems, within a medical device, or as a standalone medical device.³⁶ While ONC recognizes the potential value for the use of predictive models in health care, it also expresses concern for “model risk” (i.e., “the potential that use of a model

negatively influences an entity”), and the potential for resulting “patient harm, bias, widening health disparities, discrimination, inefficient resource allocation decisions, or ill-informed clinical decision-making.”³⁷ ONC has coined the term “FAVES” to illustrate that predictive DSIs can promote “positive outcomes and avoid harm” when DSIs are “fair, appropriate, valid, effective, and safe.”³⁸ ONC emphasizes the importance of transparency as a prerequisite for trustworthy AI, and notes that the proposed predictive DSI criterion is intended to provide potential users with sufficient information about how a predictive DSI was “designed, developed, trained, and evaluated to determine whether it is trustworthy.”³⁹ As such, users can make informed decisions about whether the predictive DSI is a high-quality model that adheres to FAVES principles.⁴⁰

Health IT Modules that enable or interface with predictive DSIs certified to Section 170.315(b)(11) would need to meet certain requirements, including:

- (i) employ or engage in intervention risk management practices (including risk analysis, risk mitigation and governance), and make summary information about these practices publicly available;⁴¹
- (ii) enable users to review information about source attributes (including race, sexual orientation, gender identity, ethnicity and social determinants of health) relevant to health equity;⁴² and
- (iii) enable users to provide feedback regarding the intervention.⁴³

ONC intends for such requirements to “improve transparency, promote trustworthiness, and incentivize the development and wider use of fair, appropriate, valid, effective, and safe predictive DSIs to aid decision-making.”⁴⁴ Further, by expanding the list of source attributes that will be provided to users, ONC reinforced its goal of health equity by design, a concept that ONC states is a prerequisite to trust in the greater adoption of AI/ML-supported decision-making in health care, and an important development in the health information regulatory landscape that is increasingly focused on identifying and preventing algorithmic bias.⁴⁵

ONC sought public comment on the Proposed Rule by June 20, 2023, on issues such as health equity, information privacy and security, and data stewardship. As AI/ML technologies become increasingly prevalent in Health IT, regulators such as ONC are challenged with balancing the desire to utilize innovative methods to advance wellness and patient care, with the public’s need for transparency and trust in the evolving technologies driving that innovation.

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¹ FDA, *Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD): Discussion Paper and Request for Feedback* (Apr. 2019), at 3, <https://www.fda.gov/media/122535/download> (FDA Discussion Paper).

² FDA, *Digital Health Innovation Action Plan* (2017), at 5-6, <https://www.fda.gov/media/106331/download>.

³ FDA, *Digital Health Software Precertification (Pre-Cert) Pilot Program*, <https://www.fda.gov/medical-devices/digital-health-center-excellence/digital-health-software-precertification-pre-cert-program> (last updated May 6, 2021).

⁴ Bakul Patel, FDA, *Tailoring FDA's Regulatory Framework to Encourage Responsible Innovation in AI/ML* (Feb. 25, 2020), at 12, <https://www.fda.gov/media/135703/download>.

⁵ FDA, *Developing a Software Precertification Program: A Working Model v1.0* (Jan. 2019), at 6, <https://www.fda.gov/media/119722/download>.

⁶ FDA, *FDA Launches the Digital Health Center of Excellence* (Sept. 22, 2020), <https://www.fda.gov/news-events/press-announcements/fda-launches-digital-health-center-excellence>.

⁷ See, e.g., FDA, *Guidance for Industry and Food and Drug Administration Staff: Software as a Medical Device (SaMD): Clinical Evaluation* (Dec. 8, 2017), <https://www.fda.gov/media/100714/download>; FDA, *Guidance for Industry and Food and Drug Administration Staff: Deciding When to Submit a 510(k) for a Software Change to an Existing Device* (Oct. 25, 2017), <https://www.fda.gov/media/99785/download>; FDA, *Public Workshop – Evolving Role of Artificial Intelligence in Radiological Imaging* (Feb. 25-26, 2020), <https://www.fda.gov/medical->

[devices/workshops-conferences-medical-devices/public-workshop-evolving-role-artificial-intelligence-radiological-imaging-02252020-02262020](#).

⁸ FDA Discussion Paper, *supra* note 1, at 1.

⁹ *Id.* at 4.

¹⁰ *Id.* at 7.

¹¹ *Id.* at 10.

¹² *Id.*

¹³ FDA, *Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan* (Jan. 2021), <https://www.fda.gov/media/145022/download> (FDA Action Plan).

¹⁴ *Id.* at 2.

¹⁵ 21 U.S.C. § 360e-4.

¹⁶ *See id.*

¹⁷ FDA, *Draft Guidance for Industry and Food and Drug Administration Staff: Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Modifications* (Apr. 3, 2023), <https://www.fda.gov/media/166704/download>.

¹⁸ *See id.* at 5.

¹⁹ *See id.* at 11.

²⁰ FDA, *Good Machine Learning Practice for Medical Device Development: Guiding Principles* (Oct. 2021), <https://www.fda.gov/media/153486/download>.

²¹ FDA, *Good Machine Learning Practice for Medical Device Development: Guiding Principles*, <https://www.fda.gov/medical-devices/software-medical-device-samd/good-machine-learning-practice-medical-device-development-guiding-principles> (last updated Oct. 27, 2021).

²² FDA Action Plan, *supra* note 13, at 4.

²³ FDA, *Executive Summary for the Patient Engagement Advisory Committee Meeting, Artificial Intelligence and Machine Learning (ML) in Medical Devices* (Oct. 22, 2020), <https://www.fda.gov/media/151482/download>.

²⁴ FDA, *Virtual Public Workshop – Transparency of Artificial Intelligence/Machine Learning-Enabled Medical Devices* (Oct. 14, 2021), <https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/virtual-public-workshop-transparency-artificial-intelligencemachine-learning-enabled-medical-devices>.

²⁵ FDA Action Plan, *supra* note 13, at 14.

[26](#) *Id.* at 5.

[27](#) *Id.*

[28](#) *Id.* at 6; FDA, *Centers of Excellence in Regulatory Science and Innovation (CERSIs)*, <https://www.fda.gov/science-research/advancing-regulatory-science/centers-excellence-regulatory-science-and-innovation-cersis> (last updated Oct. 19, 2021).

[29](#) FDA, *Artificial Intelligence and Machine Learning Program: Research on AI/ML-Based Medical Devices*, <https://www.fda.gov/medical-devices/medical-device-regulatory-science-research-programs-conducted-osel/artificial-intelligence-and-machine-learning-program-research-aiml-based-medical-devices> (last updated Mar. 24, 2021).

[30](#) FDA Action Plan, *supra* note 13, at 6.

[31](#) *See, e.g.*, FDA, *Framework for FDA’s Real-World Evidence Program* (Dec. 2018), <https://www.fda.gov/media/120060/download>.

[32](#) ONC, *Health Data, Technology, and Interoperability: Certification Program Updates, Algorithm Transparency, and Information Sharing*, 88 Fed. Reg. 23746 (Apr. 18, 2023).

[33](#) *Id.* at 23774.

[34](#) *Id.* at 23808 (proposed 45 C.F.R. § 170.315(b)(11) to replace existing 45 C.F.R. § 170.315(a)(9)).

[35](#) *Id.* at 23785.

[36](#) *Id.* at 23776.

[37](#) *Id.* at 23777 n.103.

[38](#) *Id.* at 23779.

[39](#) *Id.* at 23780.

[40](#) *Id.* at 23780.

[41](#) *Id.* at 23782.

[42](#) *Id.* at 23781.

[43](#) *Id.* at 23783-4.

[44](#) *Id.* at 23749.

[45](#) *See, e.g., id.* at 23748-9.