An intelligent approach for regulating medical device AI

5 April 2019

Hogan Lovells has been at the forefront of advising our clients on the clearance or approval of an increasing number of software as a medical device (SaMD) products and other medical devices that incorporate artificial intelligence or machine learning (AI/ML) algorithms.

From analysis of medical imaging such as echocardiograms, computed tomography (CT), endoscopy, and skin photographs, to tissue histology and physiological data such as electrocardiograms (ECG), these technologies have demonstrated enormous potential for health care by helping screen for diseases, classify malignancies, and provide personalized treatment recommendations, often sooner than is possible via standard technologies. At the same time, these products raise unique regulatory questions due to their iterative and potentially self-updating nature, which is incongruent with the U.S. Food and Drug Administration's (FDA or the agency) historical approach of seeking validation of a frozen device design prior to submission to FDA. The use of machine learning offers the opportunity for continual optimization of an algorithm as new training data becomes available; however, this potential has been in tension with FDA's standard policies on when to submit new marketing applications to the agency.

On Tuesday, 2 April 2019 FDA took the first step toward developing a new regulatory framework for medical devices incorporating adaptive AI/ML algorithms by releasing a discussion paper seeking input on an initial proposed framework to inform future draft guidance. In a corresponding press announcement, FDA Commissioner Scott Gottlieb indicated that FDA aims to apply its current authorities in new ways to keep pace with the innovation reflected in the continually evolving nature of these devices, while still ensuring that their safety and effectiveness are maintained.

To date, FDA has cleared or approved only "locked" algorithms which are trained and then verified and validated upon each update. Manual modifications to such devices are appropriately assessed using FDA's existing guidance, "Deciding When to Submit a 510(k) for a Software Change to an Existing Device." The agency has not yet authorized fully "adaptive" or "continuously learning" algorithms, which use new data obtained during clinical use for further algorithm optimization. Even before the discussion paper, FDA had begun investigating methods for addressing this phenomenon by asking sponsors to include in their marketing applications protocols for postmarket changes to the algorithm. The proposed framework is more tailored to adaptive AI/ML algorithms than the existing regulatory paradigm, accounting for algorithm modifications based on real-world learning. Ultimately, the goal is to design a total product life

cycle (TPLC) regulatory approach that would allow patients to benefit fully from AI/ML technologies, while controlling for the risks introduced by real-world modifications without the need for additional agency review or clearance in all situations.

The proposed regulatory framework is based on the risk categorization principles of the International Medical Device Regulators Forum (IMDRF)[1] for SaMD, as well as FDA's benefit-risk framework and related medical device guidelines and review practices. The main idea is that, in the premarket setting, FDA would review the initial algorithm along with information to demonstrate that the manufacturer will be vigilant in maintaining its safety and effectiveness throughout continuous evolution. Manufacturers would submit a predetermined change control plan explaining the anticipated modifications (SaMD pre-specifications (SPS)) and the associated methodology (Algorithm Change Protocol (APC)) to implement those changes in a controlled way that manages patient risk. Algorithm modifications within the scope of the approved SPS and ACP could then be documented by the manufacturer – essentially as a Letter to File – rather than requiring a new premarket submission. Modifications exceeding that scope, would still require a new premarket submission if they resulted in a change to the intended use, algorithm inputs, or significant changes to performance that require revalidation. FDA would also expect transparency and real-world performance monitoring of AI/ML-based SaMD as part of this TPLC framework, similar to (and potentially working well in concert with) FDA's new Precertification (Pre-Cert) program for SaMD.[2] In addition, FDA introduces the concept of Good Machine Learning Practices (GMLP) that should be followed in developing such devices.

It remains to be seen what elements of the proposed framework – which FDA emphasizes is not a final proposal – will be included in a future guidance. A new regulatory approach for these devices is unlikely to be implemented quickly, and FDA has acknowledged that additional statutory authority may be required. Nevertheless, the proposed framework represents a first step in formalizing this approach, which the agency has already demonstrated willingness to apply for in-development products given the recent De Novo requests granted for Viz.AI and IDx. At a minimum, this development signals the agency's openness to itself adapting based on evolving real-world considerations.

Comments on the discussion paper may be submitted through http://www.regulations.gov to Docket #FDA-2019-N-1185-0001, by 3 June 2019. Contact us to discuss this evolving framework and navigating the FDA regulatory process for your novel devices.

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[1] The IMDRF approach for evaluating modifications to SaMD is further discussed in our prior alert from October 2016 (after the draft guidance on this topic was issued by FDA). *See here.*

[2] *See* U.S. Food and Drug Administration, *Developing a Software Precertification Program: A Working Model – v1.0* (January 2019). *Available here.*

Contacts

John J. Smith, M.D., J.D.
Partner, Washington, D.C.
T +1 202 637 3638
john.smith@hoganlovells.com

Yarmela Pavlovic
Partner, San Francisco
T +1 415 374 2336
yarmela.pavlovic@hoganlovells.com

Kristin Zielinski Duggan
Counsel, Washington, D.C.
T +1 202 637 8894
kristin.duggan@hoganlovells.com

Danielle C. Humphrey
Counsel, Washington, D.C.
T +1 202 637 8853
danielle.humphrey@hoganlovells.com

Lina R. Kontos
Counsel, Washington, D.C.
T +1 202 637 5713
lina.kontos@hoganlovells.com

Suzanne Levy Friedman
Senior Associate, Washington, D.C.
T +1 202 637 5532
suzanne.friedman@hoganlovells.com

www.hoganlovells.com