The Doctor Ordered an App

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As AI/ML technologies and other software continue to be employed for both clinical and patient-specific use, drug and device litigators should keep track of the FDA's evolving regulatory approach and be prepared for a corresponding increase in litigation.

Understanding AI and Machine Learning's Effect on Regulation and Litigation Risk

Two of the most exciting innovations in healthcare are Artificial Intelligence and Machine Learning ("AI/ML") in medical devices. The modern physician has access not only to the proverbial stethoscope but also cutting-edge thinking software and self-learning algorithms.

These technologies may have the potential to transform healthcare by analyzing vast amounts of real-time data and then adapting to continuously evolving circumstances. Applications include early disease detection, quicker and more accurate diagnoses, the identification of novel changes to human physiology, and the development of personalized treatments and medications. The potential promise of AI/ML in medical application may be realized by the software's ability to learn from real-world use and experience, as well as its capability to use that information to adapt and improve performance. The benefits to patients may be significant, but there are also potential risks, including increased and novel personal injury litigation risks.

The legal risks that in-house and defense counsel need to be aware of are still evolving in this complex area, as the issues are new, and few people beyond software developers themselves truly understand the applications involved. In this article, we take a step back and examine three high-level trends in AI/ML medical device applications that in-house and defense counsel in the industry should understand in order to properly evaluate potential risks. These trends are: (1) how AI/ML is being used in the next generation of medical advancements, (2) FDA's proposed regulatory framework for ensuring patient safety and device efficacy, and (3) the growing personal injury litigation trends likely to impact this new technology and the industry in general.




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Artificial Intelligence and Machine Learning May Strengthen the Doctor–Patient Relationship and Improve Health Outcomes

To better understand the risks, benefits, and challenges involved in the use of AI/ML in medical applications, it is important to understand what "artificial intelligence" is and is not and the limitations on computer "thinking." To many, the concept of AI/ML is poorly understood and is often distilled into Hollywood tropes like thinking, walking, and talking machines (Austrian accent optional).

Can machines really "think?" The answer is complicated. The idea of a "thinking machine" is widely attributed to Alan Turing, often called the "father of modern computer science." Pioneering computer scientist John McCarthy is credited with coining the term "artificial intelligence" in a 1956. Since then, the goal of many researchers has been to create a machine with "human intelligence"—a machine that is capable of independent thought and choice. But, according to McCarthy, "[AI] is not, by definition, simulation of human intelligence." This is because humans are informed as much by perception, experience, and context as by their intelligence. AI/ML currently cannot achieve those same depths and is not about to replace the family doctor. However, it has its own strengths.

The reality is more prosaic but nonetheless fascinating and potentially beneficial to doctors and patients alike. Currently, AI/ML applications are particularly strong at independently recognizing patterns in a particular data set using things like "software as a medical device" ("SaMD") algorithms and improving their own performance while they do so. In the medical device industry, this means that AI/ML software is, for now, mainly (but not exclusively) used to analyze imaging and assist in diagnosing patients by comparing images or patterns of information to databases of similar information. Given the rapid pace of development in this area, however, it is likely that current application of AI/ML technology is just a scratch on the surface.

Examples of AI/ML Medical Device Applications

AI/ML applications may be used to improve patient outcomes, achieve greater efficiency in clinics and operating rooms, and assist with critical tasks requiring observation and detection. The FDA has compiled a comprehensive, but non-exhaustive, **list of smart medical devices** that have undergone FDA review and approval. For example, computer-assisted software with a diagnostic focus has been employed to analyze breast lesions that are suspected to be cancerous. One such smart medical device developed by Koios Medical is described in its 510(k) summary on FDA's website (K190442) as a "machine learning-based support system, indicated as an adjunct to diagnostic ultrasound for breast cancer" that "classifies user-selected region(s) of interest … containing a breast lesion" into categories of cancer-likelihood. The software program, which "draws upon knowledge learned from a large database of known cases … to form a predictive model," assists physicians in detection of cancerous breast lesions by providing graphical confidence level indicators and allowing physicians to adjust, measure, and document images. Foreshadowing some of the challenges with regulating software as a medical device, Koios Medical's regulatory application cautions that users should not make patient management decisions based solely on the results of the software program's analysis. Rather, the smart medical device is intended solely as a tool to improve physicians' overall accuracy in rendering diagnoses and to reduce inter- and intra-operator variability.

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In Japan, a similar cancer-detection software is noteworthy (even somewhat famous) for its beginnings in bakery checkout lines. An AI system originally developed to quickly tell baked goods and pastries apart to help employees ring up customers' orders at Japanese bakeries also excels at identifying cancer cells, which just so happen to be of similar shapes to baked goods. With input from a doctor who realized the tool might be used to detect microscopic cancer cells, the system, known as "BakeryScan," was adapted to help identify cancers.

Physicians have also used smart, software-only medical devices to do things like identify anatomical structures considered to be "organs at risk," a process that is required to develop individualized treatment plans for patients facing head, neck, and thoracic body cancers. This software potentially allows physicians to use automated analysis of medical images to improve the accuracy and consistency of "organs at risk" contouring, personalize cancer treatment decisions, and reduce the overall amount of time required to develop such treatment plans.

The development of smart medical devices is not limited to physician users and diagnostic purposes. Devices utilizing AI/ML technologies have also been used for disease monitoring in patients and to provide patients with automated and programmable delivery of drugs. For example, over the last few years, Chinese tech giant Tencent has developed a product that uses AI to monitor for and diagnose Parkinson's disease. Tencent's product is novel, because it uses a camera to capture video of the way patients move their hands to determine the severity of Parkinson's symptoms. Also, it claims to allow patients to carry out this assessment using a mobile app. Empatica, an Italian company, has similarly employed smart technology to passively and remotely monitor patients suffering from epilepsy. The company developed the Embrace biosensor smart watch to automatically sense Electrodermal Activity and motion data that detect patterns associated with seizures in epilepsy patients. As indicated in its 510(k) summary on FDA's website (K181861), when a seizure event is detected, the smart device "sends a command to a paired wireless device that is programmed to initiate an alert to a designated caregiver." Such devices are not, of course, without potential risk, and it is doubtful they are intended to replace regular clinical exams and check-ins with physicians.

Other smart medical devices are being developed to automate certain forms of patient care. Closed-loop insulin delivery systems, otherwise known as an "artificial pancreas," are used to automatically administer insulin to diabetes patients using real-time continuous glucose monitor data. The closed-loop system transmits real-time data from a patient's continuous glucose monitor directly to the patient's pump, which then uses an algorithm to interpret rising and falling glucose levels and adjust the patient's insulin amount accordingly and automatically. Though this closed-loop device, like most medical devices, is certainly not without risks and must undergo thorough safety and efficacy review, the functionality of smart medical devices like this one to continuously monitor patient physiology and automate the required adjustments to treatment may help eliminate the human factor concerning potential dosage errors.

AI and ML Are Here to Stay as Part of the Booming Internet of Medical Things

AI/ML applications in medicine are no longer rare. In fact, they are growing steadily and may become even more prevalent over the coming decade. They are just a subset of smart medical devices and the Internet of Medical Things (IoMT), the expansion of which has been swift and broad. The increasing emphasis on technological and digital innovation represents a shift to what has been described as the "fourth industrial revolution," and this rapid change includes the healthcare sector. Indeed, in 2020, the global IoT, of which the IoMT is a substantial and growing sector, was sized at $71.84 billion, with an estimated compound annual growth rate of over 25.9 percent between 2021 and 2028. Current market research also indicates that the smart medical devices market, specifically, exceeded $25.3 billion in 2020. This market for smart medical devices is expected to grow 11.2 percent between 2021 and 2027, driven largely by the rising demand for wireless, smartphone-compatible medical devices and an increasing societal awareness of health and fitness. And the COVID-19 pandemic has only intensified calls for strengthening domestic and global expenditure on healthcare that is technologically innovative, adaptive, and accessible. But this growth also

raises key questions regarding regulatory and litigation risks: How, if at all, will the current regulatory framework apply to devices that are purely software, and how will such innovation impact a smart medical device developer's litigation risk?

Artificial Intelligence and Machine Learning Are on FDA's Radar

FDA's Software as a Medical Device Action Plan

One of the biggest issues facing the industry is how the FDA will regulate AI/ML medical devices to ensure safety and efficacy, particularly where the algorithm is not "fixed" but evolves or changes as the software "learns." In its January 2021 "Artificial Intelligence and Machine Learning (AI/ML) Software as a Medical Device Action Plan" (the "Action Plan"), the FDA acknowledged that it has received a continuously high volume of marketing submissions and pre-submissions for "products leveraging artificial intelligence/machine learning technologies." Such submissions show no signs of slowing down. Rather, the agency notes in its Action Plan that it expects the already-high volume of submissions to increase over time. To ensure that patient safety and device efficacy remains the vanguard, the Action Plan outline five actions the FDA intends to take concerning the development of devices that consist solely of software (Software as Medical Device or SaMD) and/or AI/ML software used in medical devices. The Action Plan is a direct response to feedback elicited in response to an FDA discussion paper proposing a regulatory framework for AI/ML and seeking comment from industry stakeholders in order to further develop the following five action items:

1. A Tailored Regulatory Framework for AI/ML-based SaMD.
2. Good Machine Learning Practice (GMLP).
3. Patient-Centered Approach Incorporating Transparency to Users.
4. Regulatory Science Methods Related to Algorithm Bias and Robustness.
5. Real World Performance (RWP).

While these action items are focused specifically on emerging issues and technology in the smart medical device world, if we take a step back, we can see that they closely track the life cycle of traditional medical device innovation and implementation—from development and manufacturing (or upgrading, as is relevant here) through end-user and patient counseling and finally through post-market surveillance and evaluation. In-house and defense counsel should understand the safety and efficacy of the devices as set out by the manufacturers and controlled by regulators in order to evaluate risk and liability.

A major driver of FDA's proposed regulatory framework is the development and inclusion of a "Pre-determined Change Control Plan" (PCCP) by a manufacturer in the premarket submission. At its core, a PCCP essentially outlines how the manufacturer expects and intends the algorithm or smart medical device to act, function, and evolve when in use over time. The anticipation for functional change or adaptation in a device through the PCCP takes us far out of the traditional device regulatory framework and opens the potential for iterative change without the need for a new or supplemental regulatory submission. Contrast that with FDA's **current guidance** on potential 510(k) submissions for software changes in smart medical device, and it creates the potential for both great benefits (lowering cost and timing barriers for proposed changes) and challenges for manufacturers (increased uncertainty and less control over the SaMD device, which increases potential liability risk).

Even in AI/ML enabled devices, the PCCP will not completely eliminate the potential need for additional regulatory clearance. The FDA still anticipates the potential for additional supplemental regulatory submissions if, among other things, a manufacturer seeks to change the algorithm or code underlying the PCCP, or if new/additional intended uses for the device are sought. However, notwithstanding any timing issues with new regulatory submissions, that virtually all smart medical devices can effectively be "upgraded" or altered "with the stroke of a keyboard" highlights both the unique ability of smart medical devices to potentially address patient issues through real-time monitoring of data and the potential regulatory risk accompanying such swift and possibly automatic upgrades.

How Does a Predetermined Change Control Plan Work?

The main inputs of the PCCP that drive device modification and operation are called (1) SaMD Pre-Specifications ("SPS") and (2) Algorithm Change Protocols ("ACP"). In plain language, the SPS controls the type of modifications anticipated by the AI/ML enabled device, and the ACP is the methodology used to implement those changes. Key to proper ACP development is the ability to implement any changes in a controlled manner that allows for the management of risk to patients.

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One potential useful aspect of the SPS/ACP interplay will be the ability to build a measure of safety control into a SaMD device, *i.e.*, the ability to incorporate triggers in the algorithm that can help detect potential adverse events in "real time" and provide this information for purposes of specific or general population patient safety. We already see many of these types of features incorporated into smart devices, such as heart monitors and blood-oxygen level detectors built into the Apple Watch. While these consumer devices are not intended by manufacturers to provide medical care, and thus so far are not generally regulated by the FDA, they may be instructive of how smart medical devices will progress in the future to provide real world performance metrics to ensure patient safety and device efficacy. And, indeed, smart

medical devices, such as the Empatica biosensor smart watch discussed above, are already being employed to detect early warning signs of adverse medical conditions and alert patients, medical providers, and even first responders of the potential need of emergent care and treatment.

As of now, the FDA is working to draft guidance on what should be included in an SPS and ACP to support and ensure smart medical devices are safe and effective. Through the PCCP, the agency expects to increase transparency and real-time monitoring of, among other things, device performance, so as to allow both the manufacturer and the FDA to evaluate the device from development through post-market surveillance. The hope is that this will allow the FDA to maintain reasonable assurances of device safety and efficacy, while also allowing the iterative, and perhaps exponential, growth and improvement of the device through AI/ML.

AI/MI Developers in the Medical Device Industry Face Potential Personal Injury Litigation Risk

Personal injury litigation risk lies downstream from the AI/ML medical device market and regulatory pathway. Potential allegations of software failures, inaccuracies, risk of hacking, and challenges must be weighed against the potential benefits of the devices. Risks may encompass nearly any function performed by the software, including regulating dosages, controlling the operation of devices, or performing imaging analysis. For instance, much has been made of the potential impact of so-called black-box medicine in the medical malpractice context. *See, e.g.,* Zach Harned, Matthew P. Lungren & Pranav Rajpurkar, Comment, *Machine Vision, Medical AI, and Malpractice*, Harv. J.L. & Tech. Dig. (2019). Where a physician uses imaging software or another algorithm-based software tool to diagnose or treat a patient, without fully understanding how the algorithm works, that may affect the physician's duty of care. Specifically, the physician may be held liable for alleged problems in an AI/ML device or program. The flipside, however, is that plaintiffs might seek to also blame the developer of the software algorithm, and potentially force co-defendants to allocate liability between themselves where the alleged issue lies in the software.

This is a new area of law, but so far it is clear that there is no one-size-fits-all approach to AI/ML medical device liability in personal injury actions. Indeed, AI/ML medical devices may not fit neatly into the familiar product liability framework. Liability theories may instead fall into several buckets. Manufacturers and their counsel should be familiar with each approach that plaintiffs' counsel might pursue. These theories will intersect with the particular factual context of AI/ML medical devices in unique ways during nearly all phases of litigation, particularly given the new, constantly evolving nature of the industry.

While plaintiffs may be able to pursue negligence and breach of warranty claims depending on the context and factual circumstances, they may not be able to consistently rely on strict product liability theories in the context of medical devices that consist solely of software—*i.e.*, SaMDs. It is still an open question how far courts will go in extending strict liability to pure software. There is no consensus that it qualifies as product—courts have trended in nearly the opposite direction, in fact. In the recent *Rodgers v. Christie* decision, for instance, the Third Circuit considered that exact question, albeit not in the context of medical devices. 795 F. App'x 878 (3d Cir. 2020) (not selected for publication). The software at issue in *Rodgers* was pretrial release risk assessment software for use in the criminal justice system. Plaintiff alleged the software was defective under the New Jersey Products Liability Act (NJPLA) because it contributed to the release of a man days before he later murdered plaintiff's son. The Third Circuit upheld dismissal at the pleading stage, reasoning that software was not "tangible personal property" or "distributed commercially for use or consumption" under the relevant definition in the Third Restatement of Torts. The court held that the software therefore did not qualify as a product under the NJPLA. For that reason, among others, the court explained that plaintiff's complaint could not survive a Rule 12 challenge. It is not certain that the Third Circuit's approach will transfer seamlessly to the SaMD context, and in-house and defense counsel should continue monitoring this area closely.

Plaintiffs may also pursue strict liability claims regarding mixed smart medical devices, *i.e.*, those that contain both tangible hardware and intangible software components—a family that includes devices that utilize AI/ML. These complaints are increasingly common, with some recent high-profile actions involving automotive software. But plaintiffs still face hurdles. Mere hand-waving gestures toward generic software defects should not survive the pleading stage, and while it may be true perhaps that software may seem complicated or novel, that should not excuse insufficient specificity. For instance, in a recent decision in the Eastern District of Louisiana, plaintiffs alleged, among other things, that "defective software design" caused two defibrillators to malfunction under various theories, including strict liability under the Louisiana Products Liability Act (LPLA). *Celino v. Biotronik, Inc.*, No. 20-2298, 2021 WL 1699847 (Apr. 29, 2021). However, the allegations were too conclusory, failed to meet the elements of a design claim under the LPLA, and "fail[ed] to point to an alternative design." The district court ultimately dismissed with leave to amend.

Finally, in-house and defense counsel should also be aware that plaintiffs may possibly seek class action treatment, on purported theories that individualized determinations of alleged software failure are not necessary in every case once it has been established that the AI/ML application is causally related to the alleged injury and the same software is at issue. Plaintiffs have pursued design defect theories on a class action basis in the context of other software-integrated products, but it is not clear that plaintiffs will be able to obtain class treatment in AI/ML medical device cases, particularly given the heavily individualized nature of medical causation.

As This Field Continues to Grow and Change, Keep the Key Points in Mind

The development of AI/ML applications in the medical device industry shows no signs of slowing down. As AI/ML technologies and other software continue to be employed for both clinical and patient-specific use, drug and device litigators should keep track of the FDA's evolving regulatory approach and be prepared for a corresponding increase in litigation.