FDA grapples with 'living' medical devices

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Imagine a not-too-distant future when medical devices powered by artificial intelligence continuously adapt to new symptoms presented by patients and learn how to make accurate diagnoses much like a well-trained physician would.

The Food and Drug Administration is preparing for such a future and weighing how to assess and certify such medical devices, seeing them more like living things that can't be regulated in the same manner as old-fashioned equipment.

The agency is pivoting to new ways of assessing devices driven by machine learning and artificial intelligence because traditional approaches don't apply to the new machines, Bakul Patel, director of the FDA's digital health division, said in an interview.

As technology evolves, "artificial intelligence and machine-learning based devices can be created quickly, and iterations of the product" can be rapidly fielded, Patel said. "It's a living thing to some degree, so having a concept of authorizing it (to) go to market and waiting for things to happen and then doing a review seems to be outdated."

In early April the agency released a white paper outlining a total product lifecycle approach that will focus on processes, quality control, testing and the organizational culture of the maker of such medical devices rather than the typical static assessment of a piece of equipment. The agency is seeking comments and feedback on the proposals.

Such an approach "would provide reasonable assurance of safety and effectiveness throughout the lifecycle of the organization and products so that patients, caregivers, health care professionals, and other users have assurance of the safety and quality of those products," the FDA said in the white paper.

The agency's proposal calls for assessing the device maker's overall culture, starting with an assessment of its machine-learning practices, which include the kinds of data chosen to train and fine-tune algorithms, how the manufacturer intends to turn the training model into a production one, the process used to monitor and evaluate performance of the model once it's deployed, and how the company will take the real-world data to retrain its model.

The FDA's oversight of the medical device approval process has been found wanting in other areas. After a yearlong investigation, the International Consortium of Investigative Journalists last year found that the agency approved implant devices too quickly and failed to stop devices inserted into patients, such as breast implants, mesh and surgical staplers, from being sold and used despite receiving many complaints from patients and doctors.

The investigation cited the FDA's fast-track approval process for devices, known as the 510(K), as one reason the faulty devices were being sold. The FDA's new approach to artificial intelligence-driven devices extends the agency's fast-track process.

The agency is testing the new process, intended to apply to emerging devices that have the capability to evolve, learn and modify their software algorithms to yield better results, said Zach Rothstein, associate vice president for technology and regulatory affairs at AdvaMed, a trade group that advocates for the use of technology in health care. The group is preparing comments on the FDA's proposal, he said.

"Right now under FDA statute and rules, there isn't a mechanism for the agency to let that happen," Rothstein said. "All products that use machine learning and neural networks are locked, in the sense they're not evolving anymore, and the FDA is attempting to come up with a pathway to allow products to learn in a post-market environment."

A so-called locked algorithm used in an artificial intelligence device means that any changes to the algorithm based on new information gathered from real-life use would "likely require FDA premarket review for changes beyond the original market authorization," the agency said in its proposal.

One such locked artificial intelligence-based device the FDA approved last year is called the IDx-DR, which autonomously analyzes images of a patient's retina for signs of diabetic retinopathy—a disease that causes swelling in parts of the retina of diabetic patients and leads to vision loss.

Unlike other artificial intelligence-based devices that require a physician to confirm a machine's diagnosis, the IDx-DR's decision is made autonomously without human oversight, said Michael Abramoff, the founder and CEO of IDx Technologies, based in Coralville, Iowa.

The device is typically installed in primary care practices and can be operated by anyone with a high school diploma, Abramoff said. Using a fundus camera—a low power microscope attached to a camera—the device takes pictures of a patient's retina and sends them to a secure server where the algorithm resides and returns an assessment in less than a minute, according to the company.

Instead of trying to average out multiple doctors' assessments of a given image, the algorithm assesses likely outcome for a patient, Abramoff said. "We look at images of retina, and given that image, assess what's going to happen to the patient if you don't treat, rather than look at

whether doctors agree with each other," Abramoff said.

The algorithm employs a series of deep-learning detectors to look for lesions that indicate diabetic retinopathy and recommends referral to an eye care physician if it detects more than mild diabetic retinopathy.

The device was approved by the FDA after it went through a clinical trial involving 900 patients with diabetes at 10 different primary care sites, according to the agency.

The FDA's proposal to find new ways to assess continuously adapting artificial intelligence-based devices is an extension of a process that began nearly five years ago when the agency issued its first guidance on mobile medical applications.

Since then the agency has steadily moved toward assessing the overall quality of a software maker instead of trying to certify each iteration of software.

The FDA already has in place a precertification pilot program that began in 2017 for makers of software that function as medical devices. Software makers who are approved under this process could potentially launch new products without the FDA's premarket review or win approval with a few simple steps.

The FDA's Patel said the approach is similar to the Transportation Security Administration's PreCheck program that allows cleared passengers to go through security without taking off their shoes or removing laptops from bags.

Once the agency is satisfied that a company's culture and organization structure is geared toward patient safety, the software maker is granted the precertification, Patel said.

Nine companies are participating in the pilot program, including Apple, Fitbit, Samsung and Johnson & Johnson.

In September 2018, Apple Watch's Series 4 devices, for example, were cleared by the FDA for two new applications that allow the device to perform an electrocardiogram of a user's heart as well as detect and alert a user to irregular heartbeats.