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FDA Taking Steps to Oversee Artificial Intelligence in Labs

As artificial intelligence (AI) is increasingly used in healthcare settings, including clinical and anatomic pathology (AP) laboratories, the Food and Drug Administration (FDA) is attempting to fit AI into its regulatory framework while trying to keep pace with innovation. *Laboratory Economics Compliance & Policy Report* recently spoke with Kristen Klesh, a partner with Loeb & Loeb (Washington, D.C.) about the FDA's efforts related to medical products with AI-enabled technology.

What is the FDA's primary focus when it comes to AI in clinical and AP labs?
In labs, the FDA is mostly focused on AI in terms of machine learning, such as algorithms. One of the biggest challenges is trying to understand the AI algorithm and ensuring there is proper training to minimize bias that may be built into it. Another challenge from a regulatory perspective is developing metrics for performance estimation for reference standards – what are we cross referencing against to validate the technology to ensure it is meeting performance standards.

What has the FDA done to address AI used in diagnostics?
The FDA has cleared many medical devices that use AI, mostly in areas of radiological health. However, more recently AI has been used in diagnostic settings, such as Paige Prostate [AI software authorized by the agency in September 2021 for use in identifying potential biopsy areas of concern for prostate cancer].

The other area the FDA is working on is trying to adjust their existing regulatory framework to keep up with technology that is constantly evolving. The FDA has developed an accommodation. Instead of a manufacturer

Clinical Decision Support Software Guidance

The FDA on Sept. 28, 2022, released its guidance for clinical decision support (CDS) software in which it outlines the criteria by which the FDA will determine whether a commercial CDS software will be regulated as a medical device (similar to a laboratory testing device) or be declared a "non-device" with a lower regulatory burden.

This guidance implements statutory changes made by the 21st Century Cures Act of 2016. According to the FDA, CDC software functions are not devices if the relevant software function meets the following four criteria:

1. The software is not intended to acquire, process or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system.
2. The software is intended for the purpose of displaying, analyzing or printing medical information about a patient or other medical information.
3. The software is intended for the purpose of supporting or providing recommendations to a healthcare professional (HCP) about prevention, diagnosis or treatment of a disease or condition.
4. The software is intended for the purpose of enabling the HCP to independently review the basis for the recommendations that such software presents so that it is not the intent that the HCP rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient.

Kristen Klesh

submitting a new 510k market submission every time an algorithm changes, the FDA has said manufacturers should explain in their submission how they developed the algorithm, how it functions and what the potential is for the algorithm to change over time (see sidebar on Predetermined Change Control Plan for AI-Enabled Devices).

The 21st Century Cures Act carved out the definition of what constitutes a medical device, including so-called clinical decision support software. Generally speaking, if that analysis by the AI is focused on displaying, analyzing, or printing medical information about a patient to support or provide diagnostic recommendations to a physician, but still enables the physician to independently review the basis for the AI recommendations to make an independent diagnosis or treatment recommendations, that software may be carved out of FDA's statutory framework and is not regulated as a medical device. Of course, in such case, the physician will still need to ensure that the software is validated.

Can labs expect to see more in the way of legislative and regulatory oversight in this area?

Yes, there is an FDA work group that is continuing to track what is happening with this technology. [The Digital Health Advisory Committee was formed in October 2023 to advise the agency on issues related to digital health technologies, such as artificial intelligence and machine learning]. We can expect to see additional guidance coming out in the future.

Additionally, in October 2023 FDA issued a significant proposed rule regarding its intent to increase regulation of laboratory developed tests (LDTs), which have historically been subject to limited FDA oversight. The proposed rule would include a five-stage "phase out" of FDA's enforcement discretion policy and ultimately subject LDTs to the same FDA requirements as other medical devices.

Predetermined Change Control Plan for AI-Enabled Devices

The FDA issued draft guidance in April 2023 to further develop a regulatory approach tailored to artificial intelligence/machine learning (AI/ML)-enabled devices. This guidance would allow manufacturers to predict algorithm changes and implement future modifications without requiring additional marketing submissions.

Under a Predetermined Change Control Plan, manufacturers would be required to submit:

1. A detailed description of the specific planned device modifications.
2. The methodology to develop, validate and implement these modifications in a manner that ensures the continued safety and effectiveness of the devices.
3. An impact assessment to assess the benefits and risks of the planned modifications and risk mitigations.

The draft guidance builds on a framework initially proposed in 2021 and helps clarify the types of modifications that should be included in the Predetermined Change Control Plan. Under this framework, the FDA expects manufacturers to commit to transparency and real-world performance monitoring and to periodically update FDA on changes implemented as part of the approved pre-specifications and algorithm change protocol.

In addition, modifications should be implemented following appropriate, well-defined practices, such as the Good Machine Learning Practice guiding principles jointly developed by the FDA, Health Canada and the United Kingdom's Medicines and Healthcare Products Regulatory Agency.