Lab-developed test proposal reflections and predictions

written by CAP TODAY
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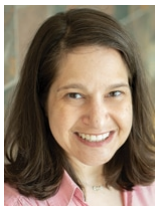
January 2024—*The Food and Drug Administration's proposed rule on laboratory-developed tests would phase out its existing enforcement discretion approach for oversight of LDTs. Instead, the FDA would classify in vitro diagnostics offered as LDTs as class I, II, or III medical devices depending on their risk to patients. Comments on the proposed rule were due Dec. 4, 2023, and when members of the Compass Group met online with* CAP TODAY *publisher Bob McGonnagle on Dec. 5, the proposal and the responses to it were top of mind.*

The Compass Group is an organization of not-for-profit IDN system lab leaders who collaborate to identify and share best practices and strategies.


Dr. Laudadio

Jennifer Laudadio, December 4 was the final day for comments on the FDA's proposed rule for laboratory-developed tests. What are your thoughts on the proposal and the responses?

Jennifer Laudadio, MD, professor and chair, Department of Pathology, University of Arkansas for Medical Sciences College of Medicine: It's definitely worrisome. As of yesterday there were more than 19,000 comments submitted on the proposed regulation. I read a comment from a nurse who wrote about a CLIA-waived point-of-care test that delivers a lot of error codes. The author equated that to a lab-developed test not working properly. I referenced that comment in my own comments and said I was disappointed that there is still a lack of understanding among health care professionals about the difference between a waived and a laboratory-developed test.

Our professional societies have submitted excellent comments, and I'm hopeful the FDA will be responsive to them.

Mike Feldman, do you have an initial reaction to what you're hearing about the response to the FDA proposal?
Michael Feldman, MD, PhD, chair, Department of Pathology and Laboratory Medicine, Indiana University School of Medicine: The 19,000 responses are a drop in the bucket compared to the FDA submissions they would be required to read and respond to if we all had to do that for each of our LDTs. The magnitude of the regulatory lift would be insurmountable for the FDA in its current size and scale. I don't see it adding value. Better off to use CLIA, and if you want to tweak CLIA to add clinical validation, so be it. We don't need 50 pages for every FDA submission that would have to go in under

their regulatory auspices.

The American Clinical Laboratory Association and the CEO of Quest are on record saying that if you implement this we're going to take you to court because we don't believe you have the legal right to do this. Is this kind of a scouting expedition by the FDA to see how bad it would be if they tried to push this through without congressional action?
Dr. Feldman (IU School of Medicine): They're responding to a couple of bad actors as opposed to evaluating the quality of what we all do and do well on a day-to-day basis. One or two bad actors threw out a garbage test during COVID and suddenly everything needs to be hyperregulated above and beyond what we already have. There's no data to support it. It's an overreach and overreaction to something that isn't a huge problem.

Linda McHale, can you comment from Atrium Health's perspective?
Linda McHale, MBA, MT(ASCP), assistant VP, core laboratory and integration, Atrium Health, Charlotte, NC: Our organization, with our core laboratory and the area we serve, has quite a few LDTs in place. They're strong tests—there was a lot of technical guidance as we put them together. Our organization has taken a strong stance and our government affairs folks drafted a letter in response.

Our biggest concern is that the FDA will implement this without a mechanism to manage the floodgates when everything starts coming in. And what's that impact to patient care?


Dr. Dysert

Pete Dysert, in our discussion last month you suggested the groups get together and let the public know what laboratories are facing. Are you encouraged to read about the number of comments the FDA has received?
Peter Dysert, MD, chief, Department of Pathology, Baylor Scott & White Health, Dallas: I am encouraged. My suggestion is that we put a front-page ad in a major periodical that summarizes, in principle, the response of the scientific laboratory community and the volume of comments it has submitted. The idea is to create a forum with visibility where the decisions, discussions, and practicalities of this rule see the light of day. Instead of trying to tackle the individual people involved in this issue, I prefer a frontal approach to the leadership of our country, because from a laboratory perspective that's how big this issue is in terms of impact. I can't think of a single, broader stroke of overhead you could throw at the laboratory industry than this proposed approach. We need to play all the cards we have now in a way that gets the public's attention as well as that of our country's leadership.

The flipside is we can point to current industry processes for credentialing tests as being the bad actors too. You can't just point a finger at us. You have to ask the fundamental question about whether the processes in place serve the patient's best interest. I believe they do. But until you understand the complexity of what we're trying to do and the variables involved, I'll argue the people who are locally accountable are the best people to do that. I don't see the benefit from the FDA's position.

Odenbrett

Rochelle Odenbrett, Sanford represents the interests of rural and home health care. What are your thoughts about the LDT proposal?
Rochelle Odenbrett, MT(ASCP), MBA, senior executive director of laboratories, Sanford Health, Sioux Falls, SD: We submitted a six-page letter and focused much of it on rural health and the health disparities we see across the country in rural health care. The impact on our patients and the costs it would add to the system are significant.

I am concerned individuals in our government do not understand this. The response we received from our legislators to the American Society for Clinical Laboratory Science form letter we sent was concerning. They responded with a form letter about PAMA and SALSA. They did not understand this is a different topic. I worked with our government affairs team to draft a response and shared my concern that I don't think our legislators understand. Our government affairs team said it would reach out to the offices of our legislators to ensure they understand the difference between this effort and the PAMA and SALSA legislation. There is a lot of confusion around what this means.


Dr.
Henricks

Wally Henricks, what is the Cleveland Clinic thinking about this?
Walter Henricks, MD, vice chair, Pathology and Laboratory Medicine Institute, and laboratory director, Cleveland Clinic: We submitted a letter separately; we did not sign on to another organization's letter. Here are the bullet points of what we emphasized, framing it as points for the FDA to consider.

The underserved patient population, be it rural or urban, are often the ones who benefit from these LDTs—patients with rare diseases and rare specimens for which an LDT might be the only test available or for which there's no incentive for other laboratories to develop a test.

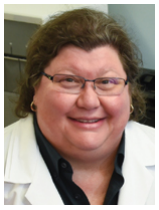
We anticipate greater availability of companion diagnostics. Some are already in use, especially in immunohistochemistry. If there's proficiency testing available for such a test, we asked that there be an opportunity to down-classify the risk so there's no hindrance to using that test as a companion diagnostic.

An exemption for academic medical centers was previously proposed and we agreed with that, but the exception should be that an LDT could be exempt if the ordering physician is employed by the laboratory's health care system or has active clinical privileges in the hospital owned by the health care system.

Finally, we requested an extension of implementation.

We also included that our laboratory has 700 unique, orderable LDTs.

Would you care to take a spin at the crystal ball?
Dr. Henricks (Cleveland Clinic): With all the comments and concerns, I believe the FDA will take these seriously, and what was put out originally might change substantially. Maybe that's more of a hope than a reality.


Dr. Wolk

Donna Wolk, you have a lot of expertise in this area with your mastery of infectious disease testing. What is top of mind for you as we contemplate the FDA proposal?
Donna M. Wolk, MHA, PhD, D(ABMM), division chief, molecular and microbial diagnostics and development, Geisinger Medical Laboratories, Danville, Pa.: I'm speaking to relay the actions of the Department of Laboratory Medicine at Geisinger. We wrote a strongly worded letter that our legal department approved. We pointed out many negative impacts that would occur if the FDA's intentions were realized. One example was the critical impact on pediatric testing. Laboratory-developed tests and modified LDTs are often required for pediatric testing for infectious diseases because many manufacturers do not include children in the FDA clearance of the product. The FDA's plans would bottleneck or eliminate many critical pediatric tests. Other critiques of the FDA's plans included pediatric and adult genetic testing and toxicology. The letter highlighted the fact that every one of our departments supports at least one modified FDA-cleared test or LDT, so the impact to our diagnostic menu would be crippling.

One of my own observations is related to the academic medical center rules. It seems to me the FDA thinks academic laboratories have more skills and student labor to respond to pandemics and EUA testing, as with COVID. But it's not a reasonable assumption that other large or interdisciplinary nonprofit laboratories do not have the same resources and skills. I don't think the FDA needs to categorize laboratories in the way they have when the CMS already classifies laboratories within the CLIA regulations. I find that troublesome because some university systems did no better than other laboratories in the EUA COVID-19 experience.

I received several troubling calls from the FDA, asking questions such as, "What happens in operations in a hospital laboratory?" Those questions would never come from the CMS or the CDC Division of Laboratory Sciences. Both have a grasp on hospital medical laboratories; the FDA does not. The FDA works with bioindustry organizations and does not have an acceptable understanding of hospital-based laboratories.

The acute care hospitals will be harmed by the FDA proposal. For-profit reference laboratories will have an advantage over acute care, which will be harmful to patients since turnaround time will be delayed. We can't survive another pandemic or other emergencies without the ability to have the local laboratories perform LDTs and EUAs in a timely manner onsite. Infectious disease diagnostics and

health care is local. We can't wait three to 20 days for a for-profit laboratory to send results back to hospitals.


Dr.
McHardy

Ian McHardy at Scripps, what is your view of the FDA proposal?
Ian McHardy, PhD, D(ABMM), director, microbiology, molecular, and immunology laboratory, Scripps Health, San Diego: Shangxin Yang and colleagues at UCLA put out an interesting story in the December 2023 issue of *Journal of Clinical Virology* that was very revealing about the challenges that may exist once the FDA's proposed regulation is implemented. Essentially, the authors describe their attempt to implement an EUA for mpox, the challenges presented by the FDA, and the impact this all had on patient care. It's an important read for anyone who may still be on the fence about the proposed regulations.

Dwayne Breining, your thoughts?
Dwayne Breining, MD, executive director, Northwell Health Laboratories, New York: I liked the AMP's approach; we signed on to it in some form and encouraged everyone at Northwell to contribute to the responses. We encouraged them to emphasize that there aren't many places that do the more esoteric, lower-volume tests. In an industry where there's ever-shrinking margins, people are going to decide it's not worth the effort to do the test. That's a huge risk. Let's hope they get the message, take a step back, and consult with people who have expertise and rethink the whole thing.

Any preparations being made?
Dr. Wolk (Geisinger): We collaborate with Clinical Laboratory 2.0 [an initiative that leverages longitudinal lab data to produce actionable insight]. We've created data sets to prove the worth of the laboratory based on body site and infection type. We use them for our business plans because we need to document the downstream positive impact of an LDT or new technology. They were a proactive investment and hopefully we continue to gain more examples that could be used to document the cost benefit, mortality benefit, length of stay, and overall impact of LDTs. We have LDT verification templates that comply with CLIA and are constantly monitored for accuracy and positive impact. We can document the cost benefit of any test, including LDTs.

Clinical laboratories are responsible for and compliant with CLIA LDT verification. Have you seen anything in the news about harm coming from a compliant, established laboratory-developed test? It's not a thing. The FDA is trying to fix something that isn't broken. Every test has some variability, FDA cleared or not. Clinical laboratories understand how to monitor and mitigate that variability. They should not be burdened with extra costs and paperwork.

Greg Sossaman, your reaction to what's been said?
Gregory Sossaman, MD, system chairman and service line leader, pathology and laboratory medicine, Ochsner Health, New Orleans: Donna is spot-on about the CDC Division of Laboratory Sciences and the CMS being in tune with what goes on in a clinical laboratory. I don't think the FDA has any idea, except

for the designated representative from the FDA on the Clinical Laboratory Improvement Advisory Committee. Maybe CLIAC is a good way to inform those institutional individuals what clinical labs do and how the proposed rulemaking would affect them.

There's so little information about what will happen in the future that it's almost impossible to prepare. Most of us don't have mechanisms to know how our LDT will be classified. So how would I respond and put in a fee to have it classified with the FDA as a certain type of complexity test?

I love Pete Dysert's idea about putting together the information about the responses from our colleagues to show what really is the feeling in the lab community about the FDA proposal.


Schofield

Stan Schofield, it's early but what do you see happening with this?
Stan Schofield, VP and managing principal of the Compass Group (formerly of NorDx/MaineHealth): I am encouraged by the scope and scale of the responses. I think the FDA is going to be shocked by the initial comments and is going to grind through this. We're going to be faced with big changes in the LDT world over the next year before it's formalized. Then we'll have two or three years to start implementing.

With 19,000 comments, they can't ignore it. The quality of the commentary is powerful. But Washington does what Washington wants to do, and quite often they ignore or disregard. They'll come up with one or two weak cases that aren't representative of the effort and the value of the laboratory industry and base everything on that. I thought they were going down the road of slam-dunking on us, but the situation is a little different on the court as we come to the basket on the opposite side. It won't be as easy as they thought it was going to be.

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