Christine P. Bump
Penn Avenue Law & Policy

Quadax
Revenue Cycle Optimizers

Q&A

FDA's Final LDT Rule: Setting Priorities and Next Steps In Your Lab

Note: The webinar Q&A has been edited for clarity

Q. ***What defines "on market" for the LDT? Does limited commercial availability "count"? For example, if select institutions could purchase the test before May 6, is this considered on market and therefore exempt from premarket review and most QS requirements.***

A: Yes. Hopefully FDA will clarify any specific requirements they have for being "on the market" under the final rule. But, "on the market" generally means that your test was offered to and available to patients. So, if on May 6, you had a test that was available for any patients or institutions to order, you were on the market and are "currently marketed" under the final rule.

Q. ***Many health systems and academic medical centers compete for lab business through outreach programs. It seems they are exempt from the FDA approval process if they use their tests only for their own doctors and patients, but would they also be exempt from testing they perform in those competitive outreach programs?***

A: FDA clearly stated in the final rule that this exercise of enforcement discretion was for LDTs manufactured and performed by a laboratory integrated within a healthcare system to meet an unmet need of patients *receiving care* within the same healthcare system. This is not a blanket or broad exemption for academic medical centers generally or tests for rare diseases. FDA believes that the integration of the laboratory and the ordering/treating physicians in the same healthcare system (under the same corporate ownership) provides some level of built-in risk mitigation.

Again, the criterion for the healthcare system to qualify for this exercise of enforcement discretion is that the patients are *receiving care* within the same system as the laboratory. The criteria do not include any details or requirements about how the patients become patients at the healthcare system, and FDA cannot regulate the practice of medicine. It should not matter how a patient became a patient of the healthcare system as long as the patient is being treated within the healthcare system when the test to address an unmet need is ordered. That said, FDA could look into outreach programs to determine whether the outreach provides a reason for the agency to stop exercising enforcement discretion. The details of the outreach program should be analyzed by counsel.

Q. ***How do you define a "modification to an approved LDT"? For example, if we use bulk chemicals in our test and switch vendors, will that require a new submission? Or if we can find a more efficient column for a liquid chromatography test, will that require a new submission or relabeling?***

A: Most likely not. Under the final rule and existing device regulations, the types of modifications that prompt the need for a new clearance, authorization, or approval are those that change the intended use of the product and that raise new issues of safety and/or effectiveness.

Generally, switching vendors for bulk chemicals should not raise new issues of safety or effectiveness, so long as the new vendor's bulk chemicals are substantially similar and do not change the performance of the test or the test's safety specifications. Changing to a more efficient column for a liquid chromatography test is also not likely to change the test's performance or safety specifications or introduce new issues of safety or effectiveness.

The burden is on the laboratory to make and confirm these determinations. Under FDA's regulations, the device manufacturer (laboratory) must assess whether these changes raised new issues of safety or effectiveness or changed the intended use. Then, the laboratory has to document this conclusion and the basis for the conclusion. If the conclusion is that intended use, safety, and effectiveness did not change, a new submission to FDA is not required. However, when your laboratory is inspected by FDA, these change records are subject to inspection. If FDA's investigator disagrees with your conclusion that the changes were not significant enough to require a new submission, the agency may request additional information or a new submission.

Q. ***Does the FDA have a guidance for test results that are based on algorithms which use various biomarker results?***

A: FDA has several guidance documents regarding biomarkers and clinical decision support tools. For specific issues, you have to read the existing guidance documents to see if they apply to your test or situation. For tests that have gone through FDA clearance, authorization, or approval, there are publicly available summaries that provide high-level information about the data that were required to support the tests.

Any tests that go through the De Novo authorization process have associated special controls. If there is a De Novo authorization for a test with an algorithm that also uses biomarker results, the special controls provide more detail about what data are required for that type of test. Information about already cleared, authorized, or approved tests is very test specific. You must determine whether they apply to your test.

FDA may be issuing more guidance to clarify questions the agency receives. FDA announced it will conform with Good Guidance Practices (GGPs), and release draft guidance documents with the opportunity for stakeholders to comment. Comments can inform the final guidance.

Q. ***Regarding what firms should do now, can you map your suggested preparation steps to a ballpark timeline? We'd like to begin stretching out our readiness plan and want to know how much time we should give ourselves and when to kick things off.***

A: It depends on the size of your lab and the number of tests that you offer. But by the end of July, going into August, you should be very familiar with whether your tests fall under any of the enforcement discretion categories and exactly what requirements will apply to your tests. The fall of 2024 should be spent learning and understanding the requirements under Stage 1 and what systems your lab will need to put in place to comply with the requirements for medical device reporting (which are for adverse events), corrections and removals, and complaint files under FDA's regulations. By the end of 2024, I would recommend that you have new employees, consultants, and/or lawyers ready to put those systems in place for you. Then, you can begin implementation at the start of 2025, and be ready for May 2025.

Q. ***Do you have any guidance if dry laboratory/informatics labs using a distributive testing model that is CAP/CLIA will fall under the LDT rule or will FDA view as a software as a medical device?***

A: This depends on the specific intended use of your testing model, the functionality of the software, and the type of technology used. To determine whether this product would be considered software as a medical device requires a specific analysis of the product and how existing requirements apply. I am happy to talk further with the laboratory that asked this question.

Q. ***Most specialized LDT's are not developed by health system labs, but by specialized labs or academic centers. What is the philosophy of integrated health system then?***

A: During the four years that the VALID Act was pending, stakeholders and lobbyists advocated for academic medical centers to be exempt from the requirements laid out in that Act. But, the last version of the VALID Act in 2022 did not include an exemption for academic medical centers. FDA was very involved with the VALID Act and had a large role in developing the IVCT framework. The agency asserted under the final rule that there is no simple definition for an academic medical center, and if it cannot be defined then it cannot be exempt. FDA's primary concern is controlling or mitigating the risks they believe LDTs present. In the final rule, FDA explains that the integration of health system, with the laboratories and the physicians all under the same corporate ownership, mitigates risk. That is their explanation. Again, this is a targeted, narrow exception.

Q. ***Where does routine LCMS urine toxicology for quantification of "typical" drugs, illicit, benzos, etc. fall into this rubric?***

A: You first have to identify, based on the intended use of your test and the population being tested, whether the test is subject to FDA's device regulations. Many toxicology tests are Class II devices subject to premarket notification. However, if the test is used for law enforcement purposes, it is exempt from FDA's device regulations and the final rule. If it is used for employment or insurance testing, it is already exempt from premarket review requirements under FDA's device regulations.

Once you determine how your test fits under the current device system, determine how it fits under the final LDT rule. If it was marketed as an LDT before May 6, 2024, the test does not have to comply with the quality system requirements (except for complaint files). If it has no automated processes, it may be completely exempt as a 1976-type LDT. You have to assess which requirements apply to each test.

Q. ***Are physician-owned labs exempt according to the new rule by FDA?***

A: There is no general exemption or exercise of enforcement discretion for physician-owned laboratories under the final rule. If tests are developed and performed at physician-owned laboratories, they will only be exempt from one or more requirements under the phaseout policy if they satisfy the specific exemption criteria, which apply to all laboratories. For example, if a test meets the criteria for a 1976-type LDT, it would be exempt. If it qualifies under the final rule as a currently marketed LDT, it would be exempt from premarket review and QS requirements. A physician-owned laboratory has to perform the same assessments as other laboratories to determine how the final rule will apply.

Q. ***You said results will be part of the FDA label. Will our order forms (test requisition forms) be part of the FDA label? Marketing material?***

A: FDA stated that it will be issuing guidance regarding labeling for LDTs. Such guidance should clarify for laboratories what constitutes a label and labeling, and the requirements for labels and labeling. The agency's existing regulations for IVDs include specific label and labeling requirements for the immediate container and the outer packaging.

IVDs (which now include LDTs) are devices under the Federal Food, Drug, and Cosmetic Act. This Act defines "label" as written, printed, or graphic matter upon the immediate container of the device. But, "labeling" includes all written, printed, or graphic matter "accompanying" the device. FDA has long interpreted "accompanying" to extend beyond the physical device and beyond "physical association" with the device. Pamphlets, brochures, and presentation posters are labeling, and most advertising is also labeling. For IVDs, FDA has specifically considered laboratory report forms, presentation posters, and claims made on a website to be labeling. I advise my clients to consider any statement about their

tests, including the requisition forms, report forms, pamphlets, brochures, posters, and anything else that they would consider to be "marketing," "advertising," or "promotion" to be labeling.

Q. ***Is there any consideration to review Class 3 tests to be downgraded to Class 2? Hear this may occur in July, have you heard any additional details on this topic?***

A: FDA announced on January 31, 2024, that it intends to initiate a reclassification process to down-classify "most" Class III IVDs into Class II. The agency specifically stated that the "majority" of these tests are infectious disease and companion diagnostic IVDs. FDA did not include a timeline for this process in the announcement. I have not seen an update or any additional information from the agency about when the reclassification process will begin.

Q. ***Does a currently modified FDA-authorized test count as a "currently marketed IVDs offered as LDTs"?***

A: Under the final rule, FDA explains that a currently marketed LDT is one that, as of May 6, 2024, was manufactured and offered as an LDT by a laboratory certified under CLIA to perform high-complexity testing. So, if a high-complexity laboratory was offering a modified version of an FDA-authorized test *as an LDT* before the publication date of the final rule, there is a strong argument that the test should be considered a "currently marketed" LDT and be exempt from premarket review and compliance with the QS requirements. However, because FDA created a different enforcement discretion category for modified versions of 510(k)-cleared or De Novo-authorized tests, the agency may take the position that such tests are only exempt from premarket review requirements.

Additionally, the laboratory must be mindful to not make any additional modifications that would affect the test's status under either category of enforcement discretion. This is something I am happy to discuss further with the laboratory that asked this question.

Q. ***Can you define the modification "alteration of the operating principle"?***

A: In the final rule, FDA provides an example for an alteration of the operating principle: "changes in clinical reaction components."

Q. ***How does this LDT rule apply, if it does, any guidance on clinical decision support tools which fall under digital pathology category?***

A: Many clinical decision support tools are regulated by FDA as devices. However, the Cures Act exempted several types of CDS software from being classified as devices. The LDT rule would apply to a CDS tool, including for digital pathology, that (a) is considered a device under the Cures Act, as clarified in FDA guidance, and (b) that was or is developed and marketed as an LDT. I am happy to discuss this further with the laboratory that asked this question.