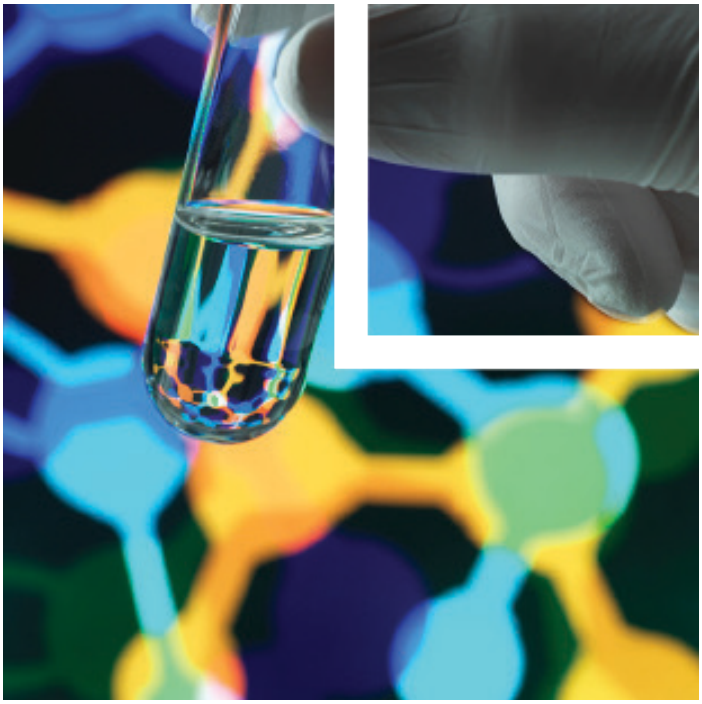
FDA Regulatory & Compliance Alert

November 2023

FDA Seeks To Step Up Regulation of Laboratory-Developed Tests



The Food and Drug Administration (FDA) has issued a proposed rule aimed at increasing the regulation of laboratory-developed tests (LDTs) as medical devices under the Federal Food, Drug, and Cosmetic Act (FDCA). The proposed rule centers on a "staged phaseout" of its long-standing "enforcement discretion" approach to LDTs, a policy under which FDA largely avoided active regulation of such products. In so doing, the agency reiterates its concerns that LDTs are becoming increasingly complex and broadly marketed, and may present additional safety and efficacy risks in the absence of active regulation.

LDTs are a type of in vitro diagnostic product (IVD) that FDA defines as intended for clinical use and "designed, manufactured and used within a single clinical laboratory" that meet certain laboratory requirements. LDTs are commonly used in the collection, preparation and examination of specimens taken from the human body, such as blood, saliva or tissue.

On Sept. 29, FDA announced the proposed rule that would (1) amend its regulations to further emphasize that IVDs, including LDTs, are regulated as "devices" under the FDCA and (2) implement a five-stage, multiyear phaseout of its passive enforcement approach to LDTs. At the end of the phaseout, LDTs would be expected to comply with the same applicable requirements as other devices, except where meeting certain requirements under the Clinical Laboratory Improvement Amendments (CLIA) can be leveraged.

Enforcement History

Historically, FDA has not actively enforced LDT requirements. The risks, however, associated with modern LDTs are increasing with their increased use by a wide consumer base and the heightened complexity of many tests.

In the 1970s and '80s, LDTs were used for the specialized needs of a local patient population in low-risk situations and in smaller numbers. But due to changing business practices and new technology, LDTs are now widely used for larger and more diverse populations and rely on high-tech instrumentation and software. The tests are also more frequently used to make critical health care decisions.

"A growing number of clinical diagnostic tests are being offered as laboratory developed tests without assurance that they work. The stakes are getting higher as these tests are increasingly being used to drive treatment decisions," said FDA Commissioner Robert M. Califf, M.D. "According to the Centers for Disease Control and Prevention, 70% of today's medical decisions depend on laboratory test results. Given the role these tests play in modern medical care, their accuracy and validity have a significant impact on public health."

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The agency expressed concern that LDTs may not provide accurate results or perform as well as tests that comply with FDA requirements. As a result, patients could be incorrectly diagnosed, initiate unnecessary treatment, delay or forgo proper treatment, or undergo inappropriate treatment for a wide range of conditions, such as cancer, heart disease, autism and Alzheimer's disease.

Phaseout Stages

The proposed rule provides a five-stage phaseout to end the general enforcement discretion approach with respect to:

Stage 1. Medical device reporting (MDR) requirements and correction and removal reporting requirements will become effective one year after FDA publishes a final phaseout policy, which FDA intends to issue in the preamble of the final rule.

- FDA believes that enforcement of the MDR requirements will enable the agency to systematically monitor significant adverse events to identify problematic IVDs offered as LDTs, such as those with poor performance or other safety issues.

Stage 2. Requirements other than MDR, correction and removal reporting, quality system regulation (QSR), and premarket review requirements will become effective two years after FDA publishes the final phaseout policy.

- These include facility registration and device listing requirements, labeling requirements and investigational use requirements.

Stage 3. QSR requirements will become effective three years after FDA publishes the final phaseout policy.

- At this point, FDA will expect compliance with the device Current Good Manufacturing Practice (CGMP) requirements of the QSR requirements under 21 CFR Part 820.

Stage 4. Premarket review requirements for high-risk IVDs will become effective three and a half years after FDA publishes a final phaseout policy, but not before Oct. 1, 2027.

- FDA proposes this time period because it believes that phasing out the general enforcement discretion approach on a timeline that is too short could cause undue disruption in the testing market.

Stage 5. Premarket review requirements for moderate-risk and low-risk IVDs that require premarket submissions will become effective four years after FDA publishes the final phaseout policy, but not before April 1, 2028.

- Premarket submissions include 510(k) submissions and de novo requests, which laboratories may submit for IVDs offered as LDTs for which there is no legally marketed device on which to base a determination of substantial equivalence.

Input Sought

FDA is seeking input on the proposed rule. Electronic or written comments may be submitted for 60 days after the proposed rule is published in the Federal Register on Oct. 3.

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7490 REV1 12-05-2023