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Summary of FDA's 2023 Proposed Rule on Regulation of Laboratory-Developed Tests

Background:
On September 29, 2023, the U.S. Food and Drug Administration (FDA) released a proposed rule (available here) outlining their intentions to regulate laboratory-developed tests (LDTs) as medical devices under the Federal Food, Drug and Cosmetic (FD&C) Act. The associated public comment period closes on December 4, 2023 at 5:00pm ET. FDA is legally required to review all public comments and summarize their responses to them when finalizing a rule. Thus, we encourage individuals and organizations to submit their own comments through Federal Docket number FDA-2023-N-2177.

FDA's Authority to Regulate LDTs:
For years there has been much debate over whether the FDA has the legal authority to regulate LDTs under existing law. The FDA has long argued that they have the authority to regulate LDTs as devices under the 1976 Medical Device Amendments and that they have been using enforcement discretion for these tests to date. Many disagree and have argued that new legislation would be needed to give FDA authority, citing that LDTs are clinical procedures that do not meet the definition of a device and thus cannot be regulated as such.

FDA's Rationale for Regulating LDTs:
When announcing their proposed rule, FDA stated that "*the agency has become increasingly concerned that some LDTs may not provide accurate test results or perform as well as FDA-authorized tests and others complying with FDA requirements*". They go on to explain that they are "*concerned patients could initiate unnecessary treatment, or delay or forego proper treatment altogether, based on inaccurate test results, which could result in harm, including worsening illness or death*". Throughout the proposed rule, FDA references reports of tests yielding an inaccurate result or in which an inappropriate medical decision was made without diagnostic or confirmatory testing. FDA also acknowledges in their own rule that much of this information is anecdotal, stating that "*this information, though anecdotal, points to potential problems among IVDs offered as LDTs, the scope and scale of which FDA cannot fully assess or address without phasing out the general enforcement discretion approach for applicable requirements (such as adverse event reporting)*".

The FDA also references their 2015 report of 20 case studies "*involving inaccurate, unsafe, ineffective, or poor quality LDTs that caused or may have caused patient harm*". In 2015, the Association for Molecular Pathology (AMP) reviewed each case and concluded that only a few of the 20 tests identified by the FDA could cause patient harms that FDA oversight might have prevented (detailed response available here).

Costs and Benefits:
The Proposed Rule is accompanied by FDA's economic analysis to "*quantify benefits to patients from averted health losses due to problematic IVDs offered as LDTs*". Although the FDA acknowledges that there are limitations to the analysis, they drew the following conclusions:

- The FDA estimates that the annualized benefits over 20 years would range from $2.67 billion to $86.01 billion at a 7 percent discount rate, with a primary estimate of $31.41 billion, and from $1.81 billion to $61.41 billion at a 3 percent discount rate, with a primary estimate of $22.33 billion.
- The FDA estimates that the annualized costs would range from $2.52 billion to $19.45 billion at a 7 percent discount rate, with a primary estimate of $5.87 billion, and from $2.39 billion to $18.55 billion at a 3 percent discount rate, with a primary estimate of $5.60 billion.

The full economic analysis is available here.

Summary of the Proposed Rule:

The proposed rule would modify the regulatory definition for in vitro diagnostic products (IVDs) to say that IVDs are considered devices under the FD&C Act "*including when the manufacturer of these products is a laboratory*". In fact, this is the only proposed change to codified regulation.

The proposed rule also lays out FDA's plan to phase out their current enforcement discretion for LDTs over a four-year period.

- Phase 1: One year after finalization of the Rule, the FDA would end enforcement discretion for medical device reporting (MDR) and removal reporting requirements.
- Phase 2: Two years after finalization of the Rule, the FDA would end enforcement discretion for all requirements other than quality systems and premarket review. This includes requirements for registration and listing, labeling, and investigational use.
- Phase 3: Three years after finalization of the Rule, the FDA would end enforcement discretion for quality system regulations (QSRs).
- Phase 4: Three and a half years after finalization of the Rule (but not before October 1, 2027), the FDA would end enforcement discretion for premarket review of high-risk IVDs. This would include LDTs classified as class III devices.
- Phase 5: Four years after finalization of the Rule (but not before April 1, 2028), the FDA would end enforcement discretion for premarket review of low- and moderate-risk LDTs. This would include LDTs classified as class II devices and possibly some classified as class I that require 510(k) applications or de novo applications.

The proposed rule does not include any exemptions for academic medical centers or grandfathering of LDTs currently used in clinical testing. However, FDA requests information from stakeholders on the following items:

- the public health rationale for generally exercising enforcement discretion with respect to premarket review and some or all quality system requirements, for LDTs that are being offered as of the date of issuance of this proposed rule and are not changed with respect to indications for use or performance after that date;
- the public health rationale to have a longer phaseout period for IVDs offered as LDTs by laboratories with annual receipts below a certain threshold (e.g., $150,000);
- the specific characteristics of and activities within programs, such as the New York State Department of Health Clinical Laboratory Evaluation Program, that justify a general enforcement discretion approach; and

- the characteristics of an academic medical center (ACM) laboratory and whether there should be different policies for ACMs.

Takeaways and Looking Ahead:

- Legal Authority:
  - Many stakeholders, including some who want to see FDA regulation of LDTs, do not believe that FDA has the legal authority under current law to regulate LDTs as medical devices. Thus, finalization of this rule could spur litigation. This could lead to a significant delay in implementation of the rule.
- U.S. Congress:
  - Controversy over the FDA proposed rule puts pressure on Congress to pass legislation that clarifies FDA's authority to regulate LDTs. Congress failed to pass the Verifying Accurate Leading-edge IVCT Development (VALID) Act last year, but the legislation has been reintroduced in the current Congress (House only). We are likely to see renewed advocacy efforts to encourage Congress to address the issue, whether that be through the VALID Act or some other legislative approach.
- FDA Capacity:
  - If the Rule is finalized and allowed to be implemented, the FDA may find it challenging to keep up with the volume of submissions. It has been estimated that there are anywhere between 70,000-100,000 LDTs currently offered for clinical testing. If we go with FDA's estimation that 50% of LDTs will require some form of premarket review, that means 35,000-50,000 product applications for FDA to review in addition to any new LDTs developed. During the COVID-19 pandemic, FDA struggled to keep up with emergency use authorization (EUA) submissions for SARS-CoV-2 tests and ultimately limited their review to only certain types of tests. The volume of EUA submissions was a fraction of the number of premarket and 510(k) applications that would be expected under this proposed rule which further points to concerns about FDA's capacity to implement this rule.

Acronyms:

ACM – academic medical center
CFR – Code of Federal Regulations
EUA – emergency use authorization
FD&C Act – Federal Food, Drug and Cosmetics Act
FDA – U.S. Food and Drug Administration
IVD – in vitro diagnostic
LDT – laboratory-developed test (also referred to as a laboratory-developed testing procedure, LDP)
MDR – medical device reporting
QSR – quality system regulations
VALID Act – Verifying Accurate Leading-edge IVCT Development Act

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Helpful links:

FDA 2023 Proposed Rule on Regulation of LDTs – https://www.federalregister.gov/documents/2023/10/03/2023-21662/medical-devices-laboratory-developed-tests

FDA Economic Analysis on Impact of the Proposed Rule – https://www.fda.gov/media/172557/download?attachment

Docket for submitting Public Comments (closes 12/04/2023) – https://www.regulations.gov/document/FDA-2023-N-2177-0001

ACMG Webpage on Regulation of LDTs – https://www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/Laboratory_Developed_Tests_LDTs_.aspx