Laboratory Developed Test (LDT) Regulation

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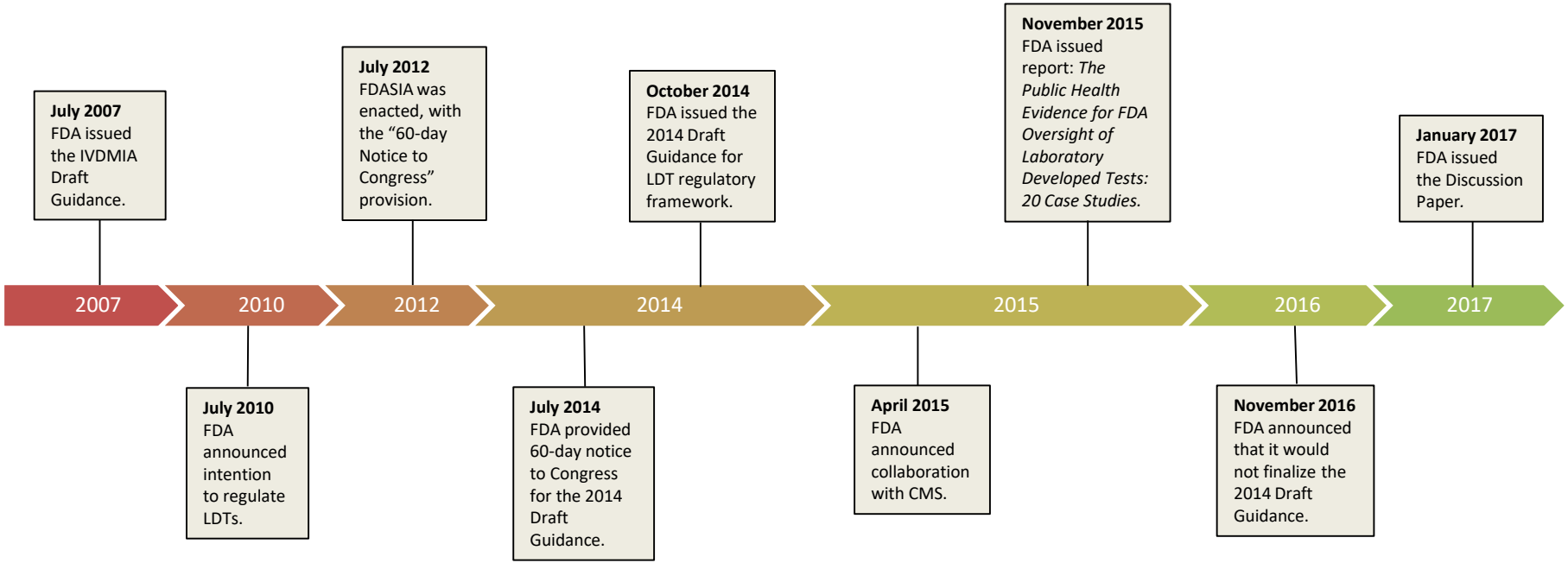
Agenda

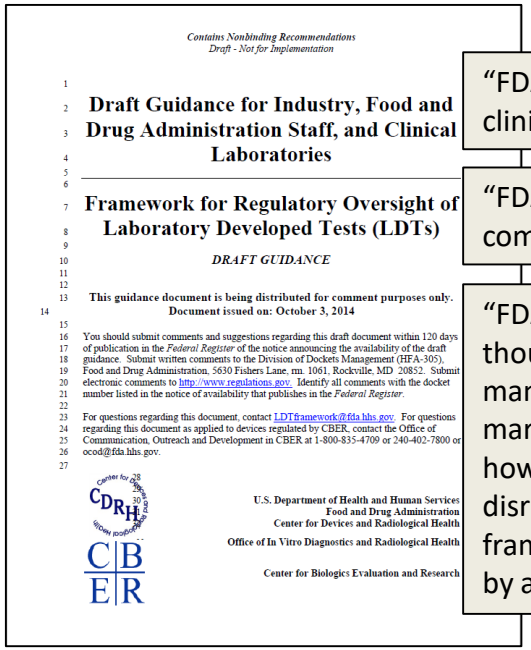
- Recent History of LDT Regulation
- 2014 Draft Guidance and Its Finalization
- 2017 Discussion Paper
- Diagnostic Accuracy and Innovation Act

Recent History of LDT Regulation



2014 Draft Guidance and Its Finalization

- In 2014, FDA released a draft guidance outlining a risk-based framework for regulating LDTs.
- Definition of "LDT":



Contains Nonbinding Recommendations
Draft - Not for Implementation

Draft Guidance for Industry, Food and Drug Administration Staff, and Clinical Laboratories

Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
Document issued on: October 3, 2014

You should submit comments and suggestions regarding this draft document within 120 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, contact LDTframework@fda.hhs.gov. For questions regarding this document as applied to devices regulated by CBER, contact the Office of Communication, Outreach and Development in CBER at 1-800-835-4709 or 240-402-7800 or ocod@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of In Vitro Diagnostics and Radiological Health

Center for Biologics Evaluation and Research

> "FDA defines the term *laboratory developed test* (*LDT*) as an IVD that is intended for clinical use and designed, manufactured and used within a single laboratory."

> "FDA does not consider devices to be LDTs if they are designed or manufactured completely, or partly, outside of the laboratory that offers and uses them."

> "FDA recognizes that some laboratories may currently be offering devices as LDTs, even though they do not meet FDA's definition of an LDT (e.g., they are not designed, manufactured, and used within a single laboratory). Laboratory tests that are being marketed as LDTs but are in fact not LDTs are out of compliance with the FD&C Act6; however, in the interest of ensuring continuity in the testing market and avoiding disruption of access to these tests, FDA intends to apply the same risk-based framework, described in Section D of this document, to any IVD that is offered as an LDT by a CLIA-certified laboratory."

2014 Draft Guidance and Its Finalization (Cont'd)

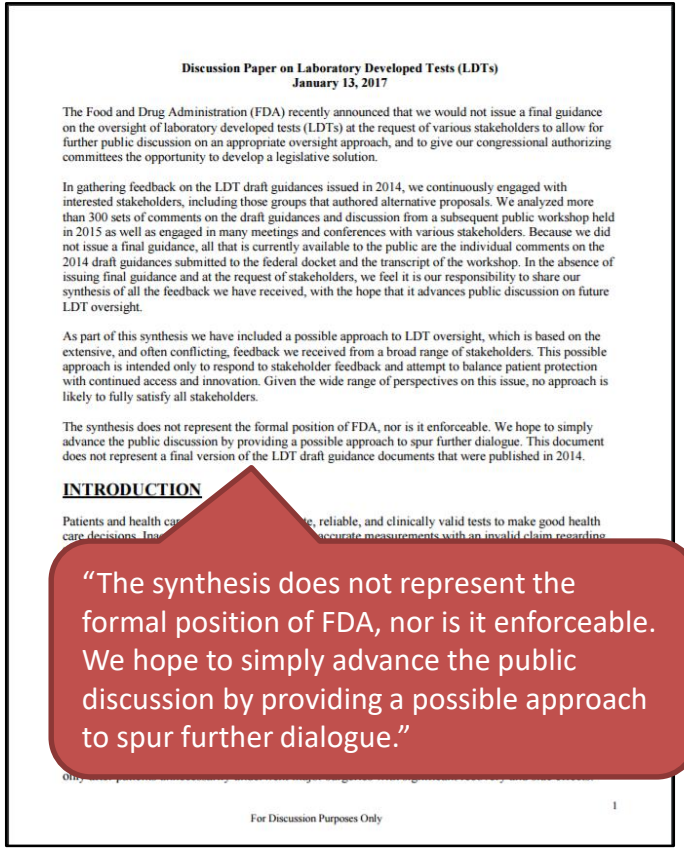
- Feedback: Industry players have criticized the framework as being overly burdensome, expensive, and slow. Further, the laboratory and pathologists communities insist that LDTs should only be regulated by the Centers for Medicare & Medicaid Services (CMS) under the Clinical Laboratory Improvement Amendments (CLIA).
- In Nov. 2016, amid post-election uncertainty, FDA decided to delay finalizing the 2014 draft guidance.

"The FDA believes that patients and health care providers need accurate, reliable, and clinically valid tests to make good health care decisions inaccurate or false test results can harm individual patients. We have been working to develop a new oversight policy for laboratory developed tests, one that balances patient protection with continued access and innovation, and realize just how important it is that we continue to work with stakeholders, our new Administration, and Congress to get our approach right. We plan to outline our view of an appropriate risk-based approach in the near future. It is our hope that such an approach will help guide continued discussions."

— An FDA Spokesperson

2017 Discussion Paper

- On Jan. 13, 2017, FDA took an unusual move to publish a discussion paper, which proposes a new regulatory framework for LDTs.
- Issuing the discussion paper allows FDA to publicize, gauge and build support for its proposals on a controversial topic while avoiding the 60-day notice requirement.
  - Section 1143 of the Food and Drug Administration Safety and Innovation Act (FDASIA) prohibits FDA from issuing any draft or final guidance on the regulation of LDTs without providing at least 60 days prior notice to the Energy and Commerce Committee of the House of Representatives and the Senate Health, Education, Labor, and Pensions (HELP) Committee.
- The discussion paper defines "traditional LDTs" as "tests that use components that are legally marketed for clinical use – e.g., general purpose reagents, immunohistochemical stains, and other components marketed in compliance with applicable FDA regulatory requirements, e.g., properly labeled for in vitro diagnostic use (21 CFR 809.10(a)(4)) and manufactured in compliance with quality system requirements (21 CFR Part 820) – and whose output is the result of manual interpretation by a qualified laboratory professional, without the use of automated instrumentation or software for intermediate or final interpretation."



Discussion Paper on Laboratory Developed Tests (LDTs)
January 13, 2017

The Food and Drug Administration (FDA) recently announced that we would not issue a final guidance on the oversight of laboratory developed tests (LDTs) at the request of various stakeholders to allow for further public discussion on an appropriate oversight approach, and to give our congressional authorizing committees the opportunity to develop a legislative solution.

In gathering feedback on the LDT draft guidances issued in 2014, we continuously engaged with interested stakeholders, including those groups that authored alternative proposals. We analyzed more than 300 sets of comments on the draft guidances and discussion from a subsequent public workshop held in 2015 as well as engaged in many meetings and conferences with various stakeholders. Because we did not issue a final guidance, all that is currently available to the public are the individual comments on the 2014 draft guidances submitted to the federal docket and the transcript of the workshop. In the absence of issuing final guidance and at the request of stakeholders, we feel it is our responsibility to share our synthesis of all the feedback we have received, with the hope that it advances public discussion on future LDT oversight.

As part of this synthesis we have included a possible approach to LDT oversight, which is based on the extensive, and often conflicting, feedback we received from a broad range of stakeholders. This possible approach is intended only to respond to stakeholder feedback and attempt to balance patient protection with continued access and innovation. Given the wide range of perspectives on this issue, no approach is likely to fully satisfy all stakeholders.

The synthesis does not represent the formal position of FDA, nor is it enforceable. We hope to simply advance the public discussion by providing a possible approach to spur further dialogue. This document does not represent a final version of the LDT draft guidance documents that were published in 2014.

INTRODUCTION

Patients and health ca… …e, reliable, and clinically valid tests to make good health care decisions. Ina… …accurate measurements with an invalid claim regarding

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For Discussion Purposes Only

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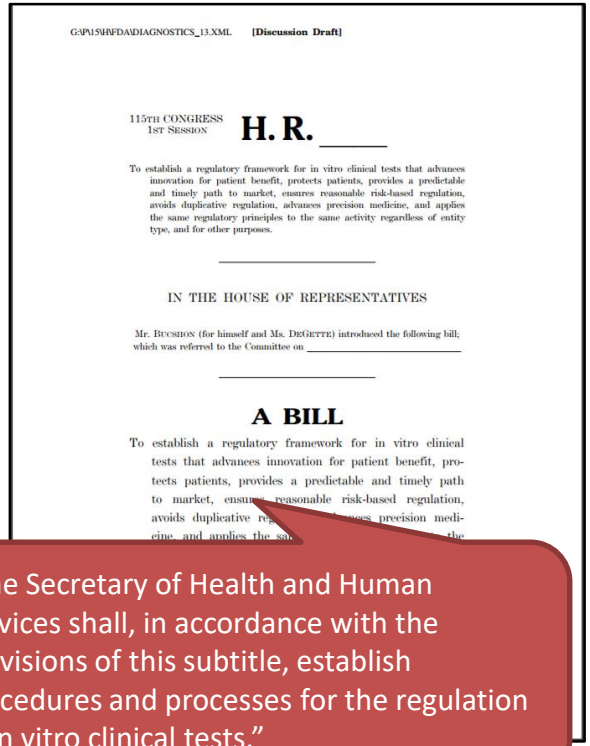
2017 Discussion Paper (Cont'd)

- The discussion paper describes a risk-based approach that differs significantly from FDA's initial proposal in the 2014 draft guidance and reflects a "lighter touch" for most LDTs. Key provisions in FDA's proposal include:
  - **Prospective oversight** – The proposed framework focuses on new and significantly modified high and moderate-risk products and exempts "grandfathered" products from most FDA regulatory controls.
  - **Grandfathered products** – Products already on the market would not have to comply with FDA regulatory requirements, including premarket review, Quality System Regulation (QSR) or registration and listing requirements. "Grandfathered" products would, however, be subject to serious adverse event and malfunction reporting.
  - **Traditional, low-risk and other LDTs** – Certain new or significantly modified LDTs — including low-risk LDTs and LDTs for rare diseases — also would not be subject to regulatory requirements other than serious adverse event and malfunction reporting.
  - **Premarket evidence** – FDA would review clinical and analytical data in premarket submissions and expand its third-party premarket review program.
  - **LDT modifications** – FDA would have limited pre-market review of changes to cleared LDTs.
  - **Quality System requirements** – FDA would leverage CLIA certification requirements and only focus on three Quality System requirements: (1) design controls (21 C.F.R. § 820.30); (2) acceptance activities (21 C.F.R. § 820.80); and (3) procedures for corrective and preventive actions (CAPAs) (21 C.F.R. § 820.100).
  - **Conventional IVD kits** – The paper does not apply to conventional IVD kits, which would require premarket review.

Diagnostic Accuracy and Innovation Act

- On Mar. 20, 2017, Representatives Larry Bucshon, M.D. (R-IN) and Diana DeGette (D-CO) released a discussion draft of the Diagnostic Accuracy and Innovation Act (DAIA), which is fashioned closely after a framework developed by the Diagnostic Test Working Group in 2015.
- The DAIA would:
  - Create a new regulatory category for in vitro clinical tests (IVCTs). IVCTs would be distinct from medical devices as defined in the Food, Drug, and Cosmetic Act, though both LDTs and test kits could be IVCTs.
  - Spread oversight responsibilities for IVCTs across FDA, CMS, and the states. FDA would oversee test development and validation, CMS would remain in charge of traditional lab activities necessary to perform testing, and states would maintain oversight of interpreting test results by healthcare professionals.
  - Require premarket FDA approval for high-risk tests and create a new center under FDA to regulate IVCTs.
  - Set up a detailed transition phase to allow industry and the regulatory authorities adequate time to implement the new construct.



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115TH CONGRESS
1ST SESSION

H. R. _____

To establish a regulatory framework for in vitro clinical tests that advances innovation for patient benefit, protects patients, provides a predictable and timely path to market, ensures reasonable risk-based regulation, avoids duplicative regulation, advances precision medicine, and applies the same regulatory principles to the same activity regardless of entity type, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

Mr. BUCSHON (for himself and Ms. DEGETTE) introduced the following bill; which was referred to the Committee on _____

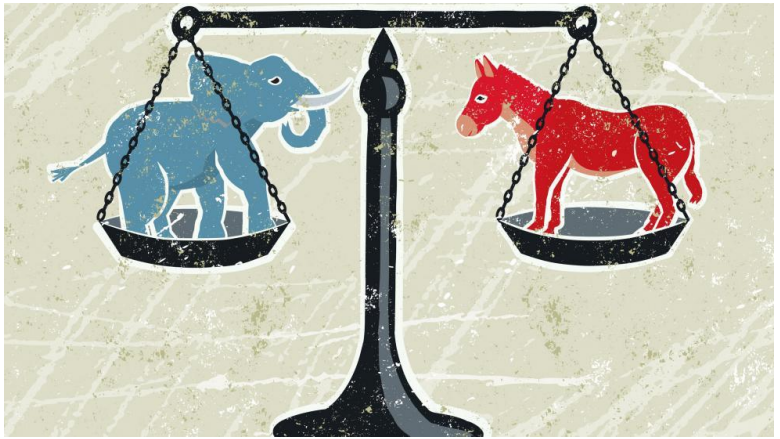
A BILL

To establish a regulatory framework for in vitro clinical tests that advances innovation for patient benefit, protects patients, provides a predictable and timely path to market, ensures reasonable risk-based regulation, avoids duplicative regulation, advances precision medicine, and applies the same

"The Secretary of Health and Human Services shall, in accordance with the provisions of this subtitle, establish procedures and processes for the regulation of in vitro clinical tests."

Diagnostic Accuracy and Innovation Act (Cont'd)

- Though the DAIA appears to have bipartisan support, it is unclear how far this bill will go in the current Republican-controlled Congress and with a White House that has signaled a commitment to slashing government regulation.
  - Many in the laboratory and pathologists communities want to keep LDT oversight out of the FDA's hands and make any changes to regulation by amending CLIA.
  - The CLIA-only approach appears to have support from a number of Republican Senators, though CMS leadership has testified that the centers do not have the resources to expand oversight over LDTs.



Questions?

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