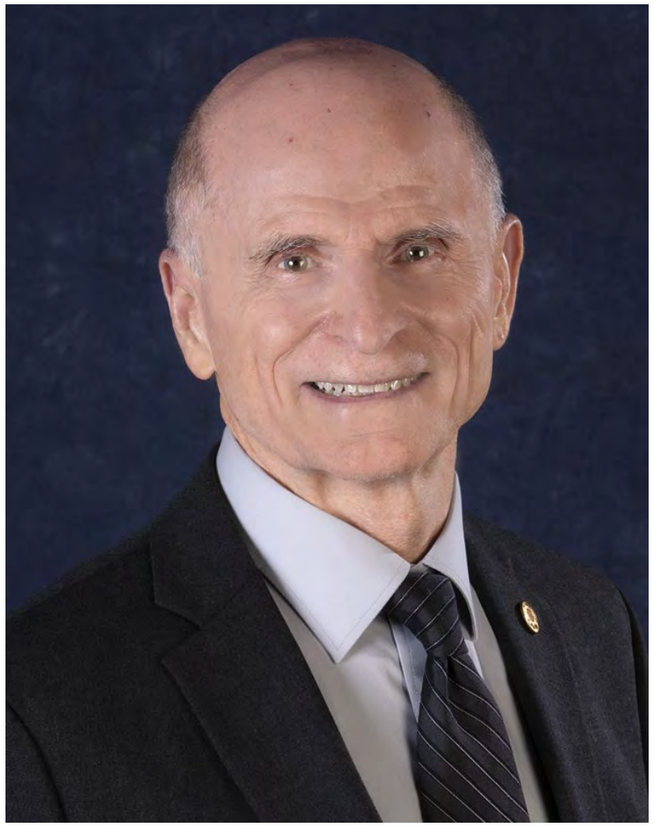
COLLEGE of AMERICAN PATHOLOGISTS

Preparing for Implementation of FDA's Laboratory-Developed Test Final Rule

May 2024

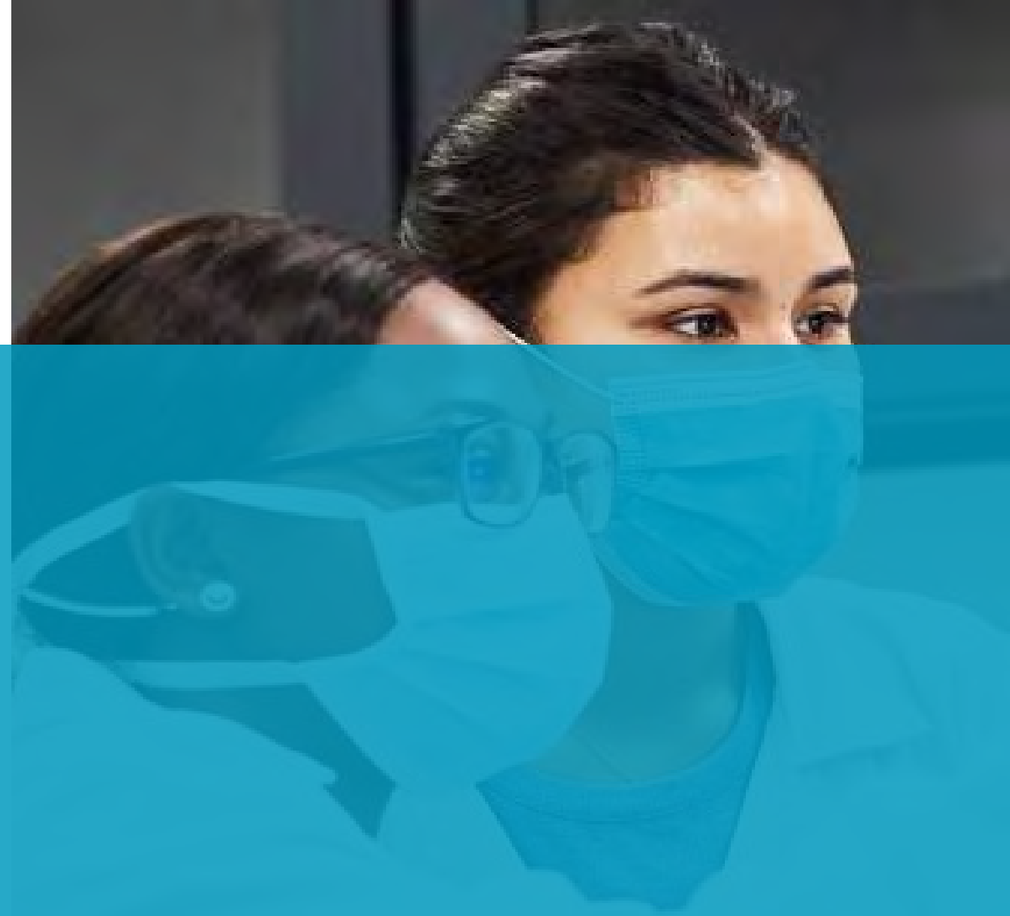
Welcome

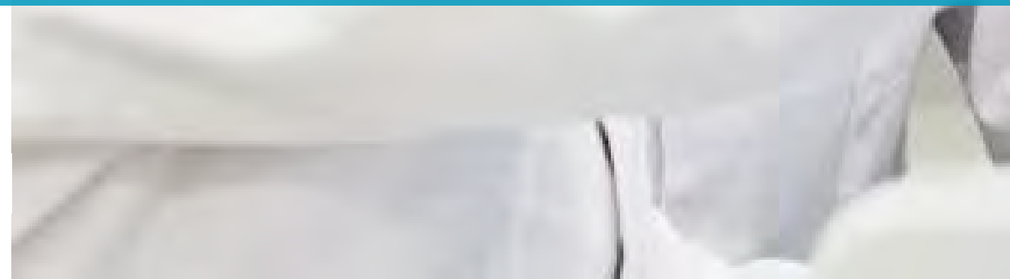
Donald S. Karcher, MD, FCAP
President



Agenda

- Welcome and introductions
- Overview of FDA LDT regulation
- FDA response post rulemaking
- Where Congress is on this issue
- Q&A





Bobbi Pritt, MD, FCAP
Chair, Council on Scientific Affairs

Joe Saad, MD, FCAP
Chair, Council on Government and Professional Affairs

FDA Oversight of LDTs

- **Proposed oversight of LDTs by FDA has been an issue for more than 10 years.**
- **When a legislative solution (VALID Act) didn’t pass in 2022, FDA said they would regulate LDTs under their existing statutory authority.**
- **FDA released proposed oversight rule in October 2023 and final rule on April 29.**

CAP Opposed the FDA Rule

- CAP vigorously opposed the FDA rule and sought changes.
- Actions included detailed written comments, Congressional testimony, and meetings with FDA, members of Congress, and the White House.
- In final rule, FDA made several changes, including some CAP advocated for.

FDA Final Rule

FDA Oversight of LDTs

- **As noted, FDA made several changes, including some CAP advocated for, but the CAP is still concerned about the burden on laboratories and pathologists.**
- **Basic provisions:**
  - **Employs a three-tiered, risk-based structure.**
  - **Phases out general enforcement discretion in 5 stages by May 2028.**

FDA Oversight of LDTs

Key changes advocated for by CAP:

- LDTs developed prior to the regulation's issuance will remain under enforcement discretion.
- Enforcement discretion will apply to LDTs developed and performed by a laboratory integrated within a health system to meet an unmet clinical need.
  - Patients must be receiving care within the same system.
  - No equivalent FDA-authorized test is available.

Stage 1

- **May 6, 2025**
- Compliance with medical device reporting, correction and removal reporting, and quality system requirements for complaints.

Stage 2

- **May 6, 2026**
- Compliance with registration and listing, labeling, and investigational use requirements.

Stage 3

- **May 6, 2027**
- Compliance with all quality system requirements.

Stage 4

- **November 6, 2027**
- Pre-market review for high-risk LDTs.

Stage 5

- **May 6, 2028**
- Pre-market review for moderate- and low-risk LDTs.

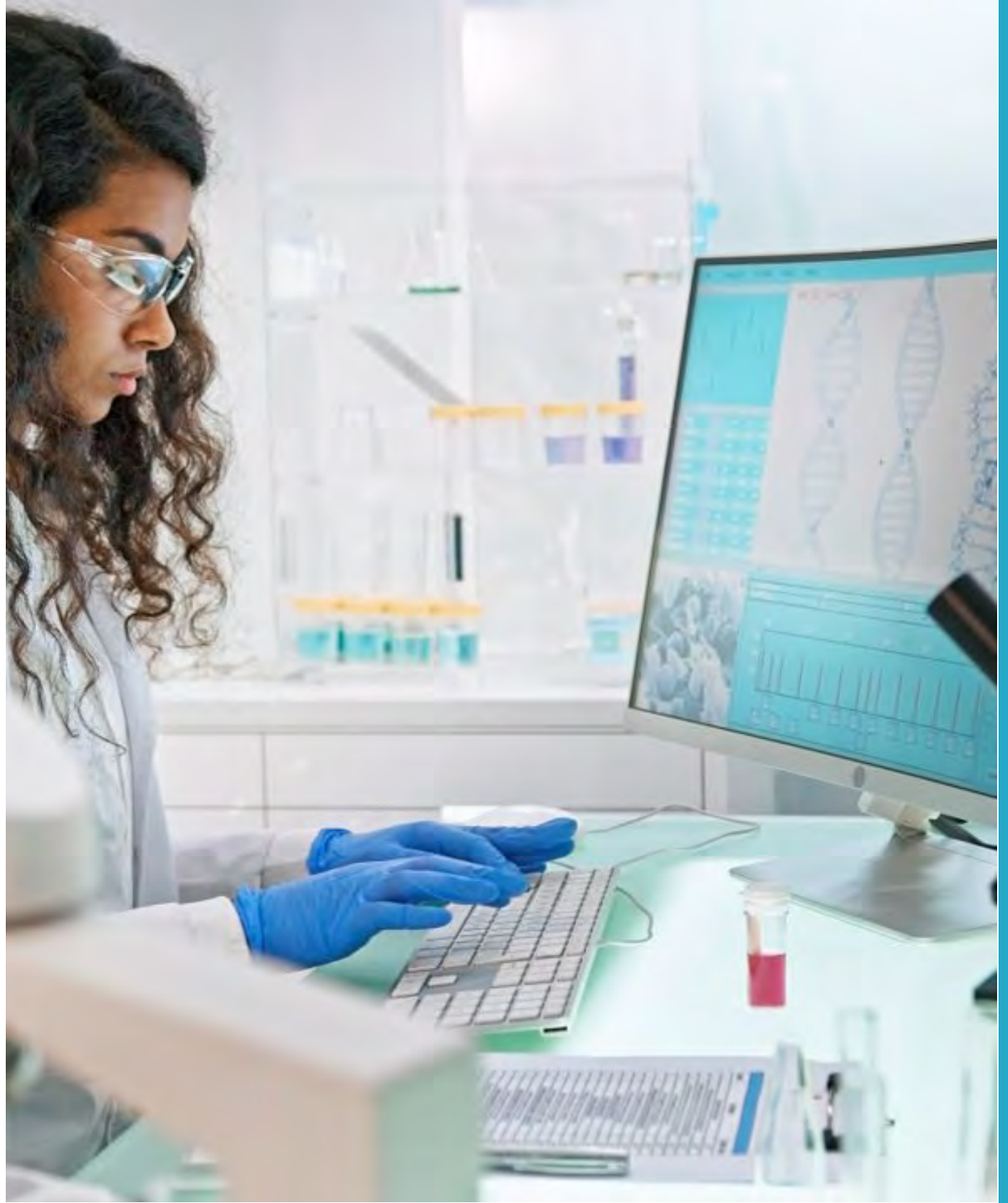
Tests Not Subject to Phaseout Policy

Tests Never Subject to Enforcement Discretion:

- Tests for blood donor screening or human cells, tissues, cellular and tissue-based products (HCT/P) donor screening
- Tests for public health emergencies
- Direct-to-consumer tests

Other Tests Not Subject To Phaseout

- Tests used for public health surveillance



FDA Enforcement Discretion Policies

FDA enforcement discretion will continue to apply to:

- "1976-Type LDTs" that have these characteristics:
  - Use manual techniques (no automation used)
  - Components legally marketed for clinical use
  - Used within a single CLIA-certified, high-complexity laboratory
- Certain human leukocyte antigen (HLA) tests for transplantation
- Forensic tests
- LDTs used by the Department of Defense and Veterans Health Administration

FDA Enforcement Discretion Policies

FDA enforcement discretion will apply (with respect to premarket requirements in stages 4 and 5):

- **Currently marketed LDTs**
  - **Marketed prior to issuance date of LDT rule (May 6, 2024)**
  - **Not modified or modified in limited ways**
- **LDTs for unmet clinical needs in local health system**
- **LDTs approved by NYS Clinical Laboratory Evaluation Program (CLEP)**
- **Non-molecular antisera LDTs for rare RBC antigens for transfusions**
- **Modified versions of a 510(k) cleared or De Novo authorized test with only minor changes**

NOTE: These LDTs must still meet requirements in stages 1, 2, and 3.

FDA Response Post Final Rulemaking

FDA Webinar on May 14

Question addressed by FDA:

- **Regarding FDA policy on LDTs for unmet needs, is a health system's LDT for an unmet need impacted by FDA authorization of an IVD for that unmet need?**
  - **The health system's LDT would no longer fall within the unmet need enforcement discretion policy.**
  - **However, if the FDA-authorized IVD is unavailable to the patient in the health system, then the LDT for the unmet need can be offered.**

FDA Webinar on May 14

Question addressed by FDA:

- **For LDTs in use prior to the rule's issuance date, are they required to comply with stages 1 and 2 of the final rule? Will there be additional guidance outlining these processes?**
  - **Additional guidance from FDA will be forthcoming.**
  - **FDA will expect compliance with, for example, medical device reporting in phase one; and registration and device listing, labeling, and investigational requirements in phase two.**

FDA Webinar on May 14

- FDA was also asked about “1976-type LDTs” and whether immunohistochemistry or flow cytometry would qualify for enforcement discretion?
- FDA responded that the “1976-type LDTs” must:
  - use manual techniques (without automation) performed by laboratory personnel with specialized expertise
  - use components legally marketed for clinical use
  - be designed, manufactured, and used within a single CLIA-certified laboratory that meets the requirements under CLIA for high complexity testing.

FDA LDT Website

Category of IVD	*Stage 1* Adverse Event Reporting (21 CFR pt. 803) Reporting of Corrections and Removals (21 CFR pt. 806) Complaint Files (21 CFR 820.198)	*Stage 2* Requirements Not Covered In Other Stages, Including: Establishment Registration & Device Listing (21 CFR pts. 607, 807 subpts. A-D) Labeling (21 CFR pts. 801, 809) Investigational Use Requirements (21 CFR pt. 812)	*Stage 3* Quality System Requirements Other than Complaint Files (21 CFR pt. 820 other than 21 CFR 820.198) (For LDTs,[1] FDA generally will not expect compliance with quality system requirements other than design controls, purchasing controls, acceptance activities, CAPA, and records requirements)	*Stages 4 & 5* Premarket Review (21 CFR pt. 807, subpt. E; 21 CFR pt. 860, subpt. D; 21 CFR 814; 21 CFR pt. 601)
Donor screening tests for infectious diseases and certain blood typing tests **Section V.A.2.a of preamble**	compliance currently expected	compliance currently expected	compliance currently expected	compliance currently expected
Direct-to-Consumer (DTC) tests **Section V.A.2.c of preamble**	compliance currently expected	compliance currently expected	compliance currently expected	compliance currently expected
Public Health Surveillance tests **Section V.A.2 of preamble**	compliance generally not expected	compliance generally not expected	compliance generally not expected	compliance generally not expected
1976 type LDTs **Section V.B.1 of preamble**	compliance generally not expected	compliance generally not expected	compliance generally not expected	compliance generally not expected
HLA tests for transplantation **Section V.B.1 of preamble**	compliance generally not expected	compliance generally not expected	compliance generally not expected	compliance generally not expected
Forensic tests **Section V.B.1 of preamble**	compliance generally not expected	compliance generally not expected	compliance generally not expected	compliance generally not expected

Upcoming FDA Webinars

- June 5: Enforcement policies
- Month of July: IVD classification (tentative)
- Month of August: Medical device reporting, quality system, complaint requirements, and recalls (tentative)

Outlook on Congressional Response

Congress Responds to FDA Final Rule

- The FDA's final rule was met with disappointment from Congress.
- Many say FDA doesn’t have the authority to regulate LDTs.
- Others say FDA should abandon the rule.
- Some continue to say Congress should act and resume work on the VALID Act.

The Congressional Review Act (CRA)

- CRA allows Congress to void rules by federal agencies.
- During the Trump administration,16 administrative rules were repealed.
  - Before 2017, the only successful use of the CRA was in 2001.
- Lawmakers opposed to the FDA rule introduced CRA resolutions in the House and Senate on May 17.
  - Passage of the resolutions is unlikely.

The VALID Act

- **The Verifying Accurate Leading-edge IVCT Development (VALID) Act:**
  - **Establishes guardrails on FDA oversight authority and lowers burden on laboratories with exemptions and new pathways to down-classify test requirements.**
- **Bill has been reintroduced in the House, but not in the Senate.**
- **Currently, the bill continues to be discussed in Congress.**

Questions/Answers

Resources

- Webinar recording and slides will be posted on CAP.org
- More webinar programs will be scheduled ahead of each stage
- Updates will appear in our *Advocacy Update* weekly newsletter
- Educational and other compliance materials from the CAP will be forthcoming

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