AMP Discussion on FDA Final Rule: Medical Devices; Laboratory Developed Tests

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May 9, 2024

Disclaimer

- AMP is providing this webinar for educational purposes only.
- If you need guidance or assistance with compliance with the FDA medical device regulations, AMP encourages you to seek out licensed counsel and/or certified regulatory affairs professionals.

Outline

- Change to 21 CFR 809.3
- Phase-Out Timeline
- Continued Enforcement Discretion
  - Unmet Needs
  - Modifications
- EUA
- Congressional Response
- Continued Concerns

Final Regulatory Change:

Changes (in red) to 21 CFR 809.3

"In vitro diagnostic products are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. These products are devices as defined in section 201(h)(1) of the Federal Food, Drug, and Cosmetic Act (the act) and may also be biological products subject to section 351 of the Public Health Service Act, ***including when the manufacturer of these products is a laboratory***."

https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-809/subpart-A/section-809.3

https://www.govinfo.gov/content/pkg/FR-2024-05-06/pdf/2024-08935.pdf

Phase-Out Timeline:

May 6, 2024

https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests

Phase-Out Timeline:

Effective Date:
July 5, 2024

May 6, 2024

https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests

Phase-Out Timeline:

Stage 1: medical device reporting, correction and removal reporting, & complaint file

Effective Date: July 5, 2024

May 6, 2025

May 6, 2024

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Late 2025-2026

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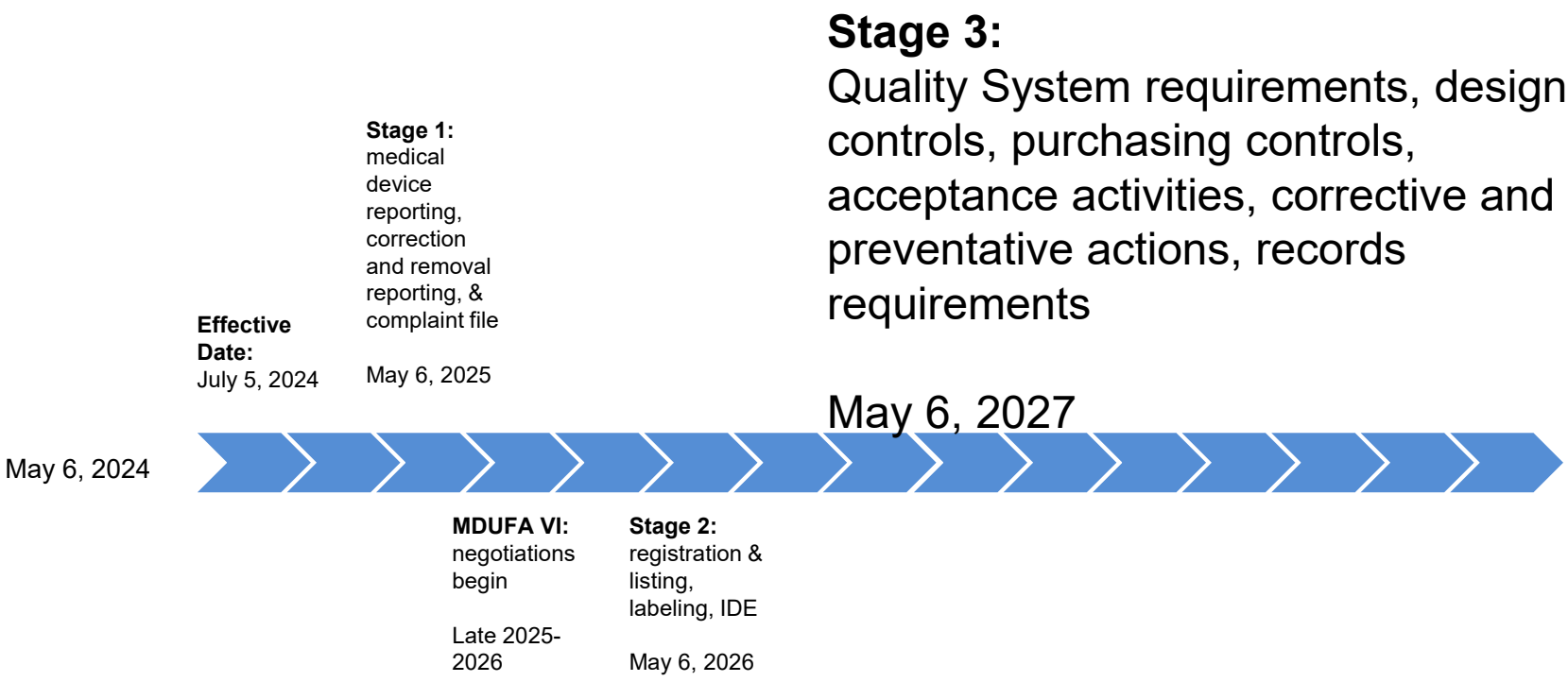
Late 2025-2026

Stage 2: registration & listing, labeling, IDE

May 6, 2026

https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests

Phase-Out Timeline:



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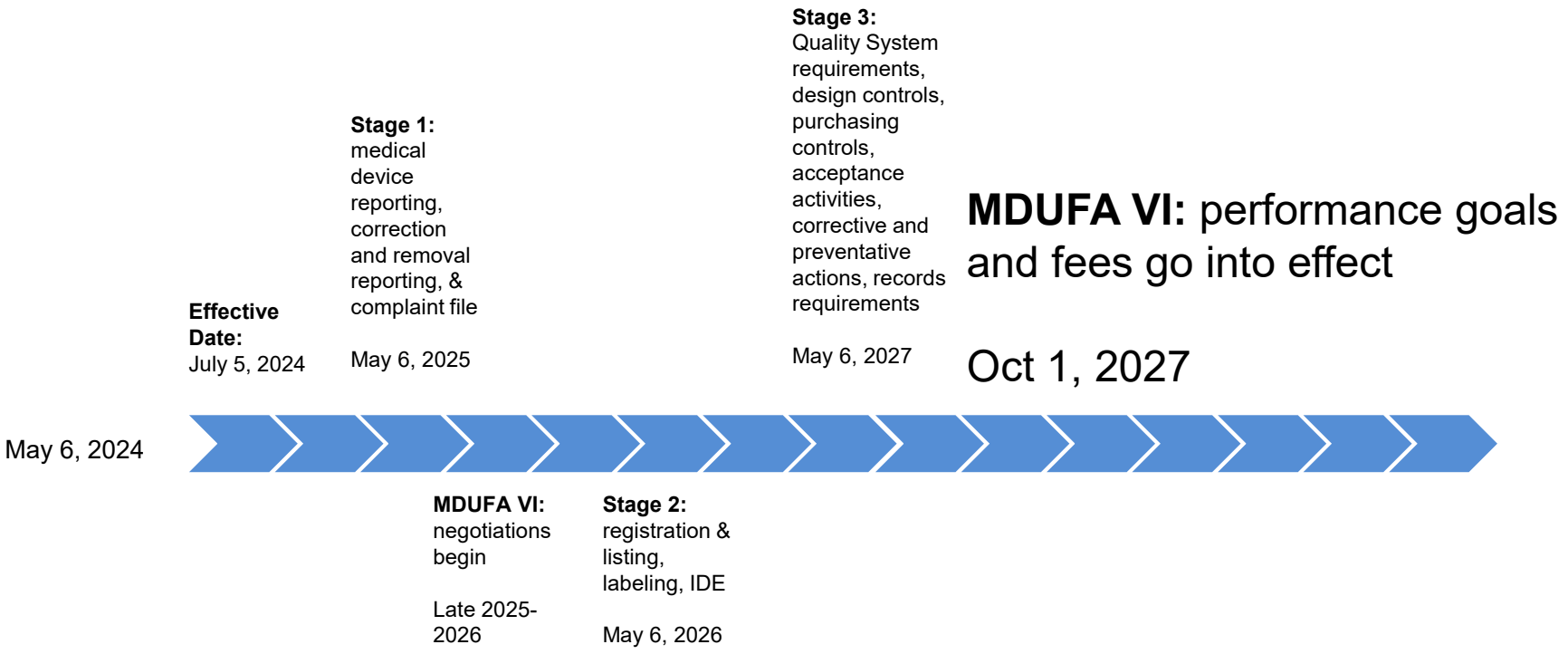

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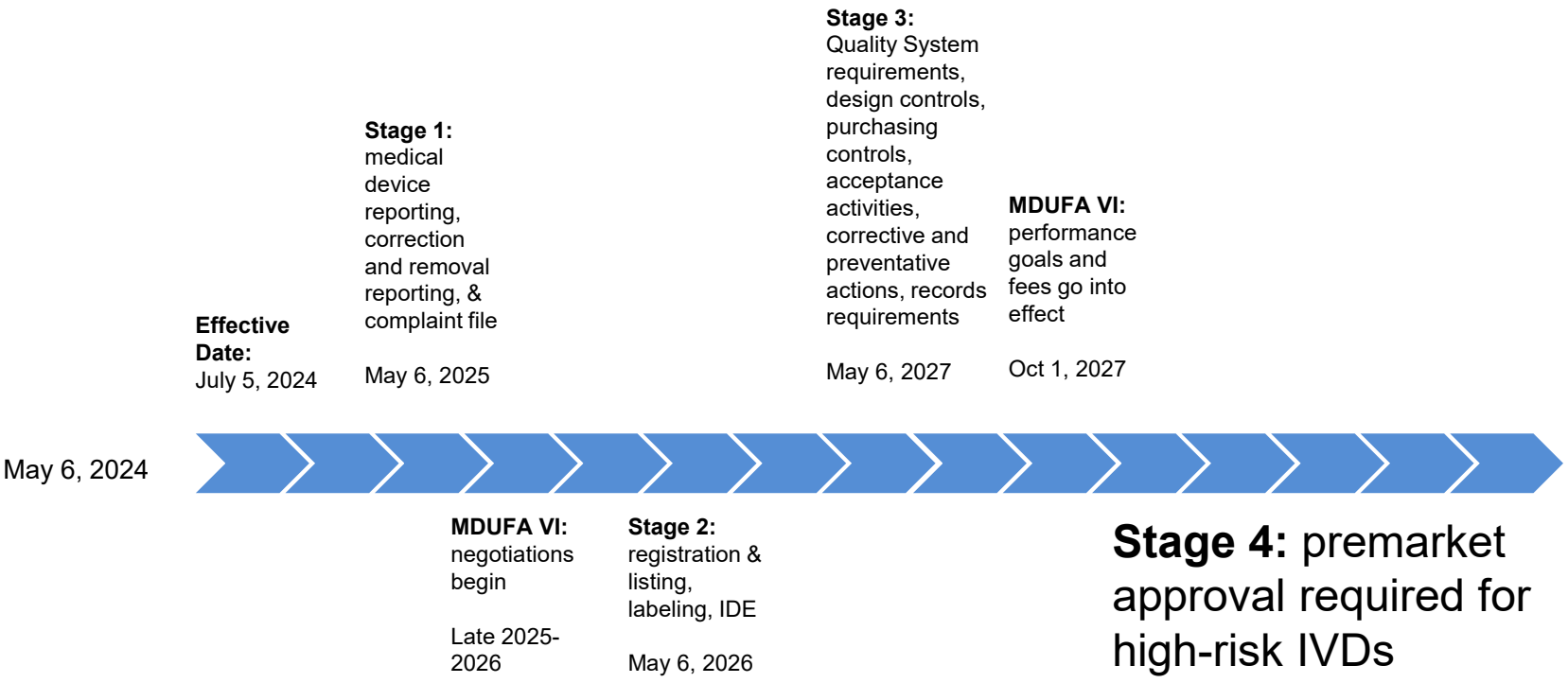

For Stage 4 and 5, if completed application submitted, IVD may remain on market while FDA completes review.

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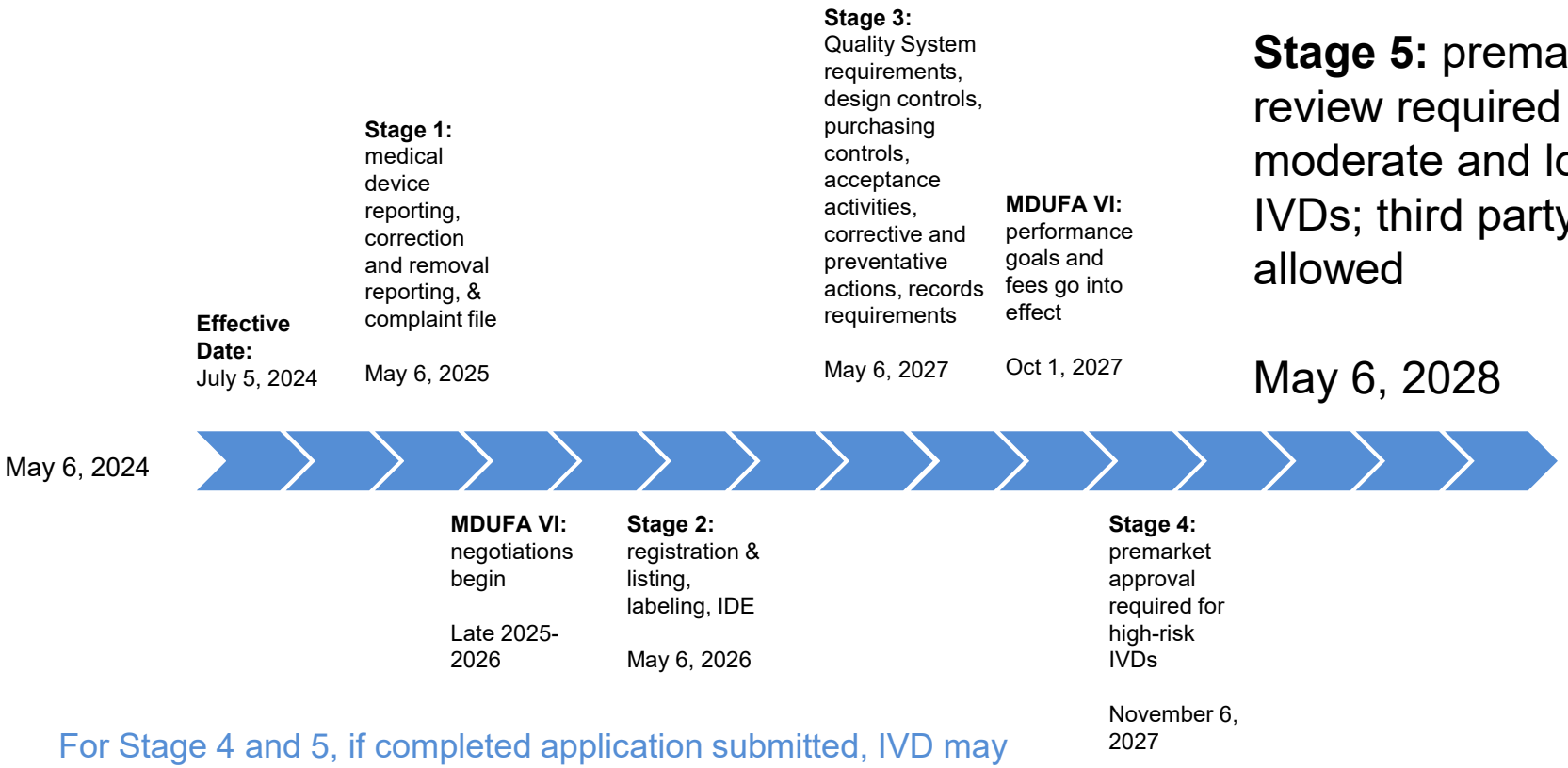

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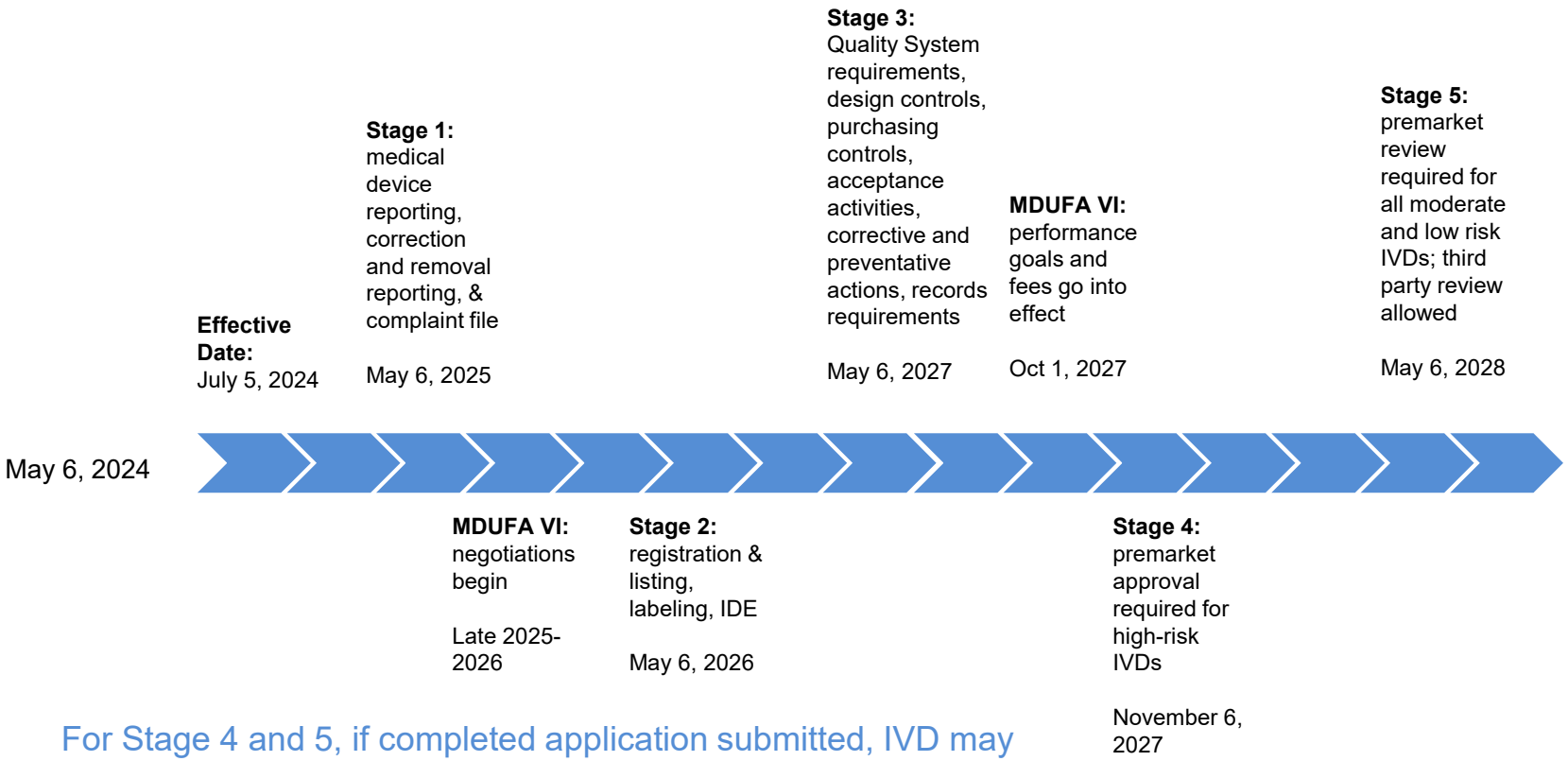

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Continued Enforcement Discretion

Category of Test	Stage 1: MDR, Correction & Removal Reporting, Etc.	Stage 2: Registration & Listing, Labeling	Stage 3: QSR	Stage 4 & 5: Premarket Review
1976-Type LDTs: Includes LDTs involving (1) use of **manual techniques** (**without automation)** performed by laboratory personnel with specialized expertise; (2) use of components legally marketed for clinical use.	**Exempt**	**Exempt**	**Exempt**	**Exempt**
Human Leukocyte Antigen (HLA) LDTs for transplantation	**Exempt**	**Exempt**	**Exempt**	**Exempt**
Tests intended solely for forensic purposes	**Exempt**	**Exempt**	**Exempt**	**Exempt**
VHA or DoD LDTs	**Exempt**	**Exempt**	**Exempt**	**Exempt**

Continued Enforcement Discretion

Category of Test	Stage 1: MDR, Correction & Removal Reporting, Etc.	Stage 2: Registration & Listing, Labeling	Stage 3: QSR	Stage 4 & 5: Premarket Review
LDTs Approved by the NYS CLEP: Includes LDTs that are approved, conditionally approved, or within an approved exemption from full technical documentation	Required	Required	Required	**Exempt**
LDTs for unmet needs used in an integrated healthcare system	Required	Required	**Exempt**	**Exempt**
Currently marketed LDTs (prior to May 6, 2024)	Required	Required	**Exempt**	**Exempt**
Non-molecular antisera LDTs for rare red blood cell antigens	Required	Required	**Exempt**	**Exempt**

Key Definitions in Enforcement Discretion for LDTs for Unmet Need:

Unmet Need:

- **No available FDA-authorized IVD** that meets the patient's needs
- **There is no FDA-authorized IVD** for the disease or condition
- There is an FDA-authorized **IVD** for the disease or condition, but it is **not indicated for use on the patient**, or a unique attribute needs to be added to the LDT to meet the patient's needs; or
- There is an FDA-authorized IVD but it is **not available to the patient.**
- **Does not include potential improvements in performance or lower cost** in comparison to an FDA-authorized IVD that meets the patient's needs

Integrated Health System:

- Affiliated hospital must have **same corporate ownership**
- LDTs must be **ordered by a healthcare practitioner on the staff or with credentials and privileges** at a facility owned and operated by the same healthcare system employing the laboratory director and performing the LDT

Additional guidance will be issued

Modifications:

Currently Marketed LDTs:

- FDA will use **reporting requirements to monitor for concerns** and take enforcement action if needed.
- Modified => comply with QSR and premarket review requirements:
  - **change in indications for use**
  - **altered operating principle** (e.g., changes in the critical reason components)
  - includes significantly **different technology**
  - **adversely changes the performance or safety** specifications
- New LDTs must comply with medical device regulations in accordance with phaseout policy.

Currently Marketed IVDs:

- High complexity laboratories certified under CLIA may modify 510(k) cleared or De Novo authorized tests:
  - In a manner that **does not significantly affect the safety or effectiveness of the test**;
  - **Does not constitute a major change or modification in intended use**; and
  - Where the modified test is performed only in the laboratory making the modification
- Note: these are the same changes for which FDA expects premarket submission from the original manufacturer
- Modifications without review to PMA approved or BLA licensed tests are prohibited

Emergency Use Authority Draft Guidance

No Declaration Under Section 564

- Enforcement discretion for tests intended to help ensure the government's coordinated and effective public health response
- Allows the use of "immediate response tests"
- Limited to certain tests and labs: **US government labs, state or local public health labs, and other labs with agreements with the US government**

Declaration Under Section 465

- **FDA will consider issuing enforcement discretion policy** to expand the availably of test during a public health emergency based on:
  - The need for accelerated availability of tests
  - Known or potential risks of such tests
  - Availability of appropriate alternative tests that are authorized or approved
  - Availability of sufficient mitigations to address risks of false results

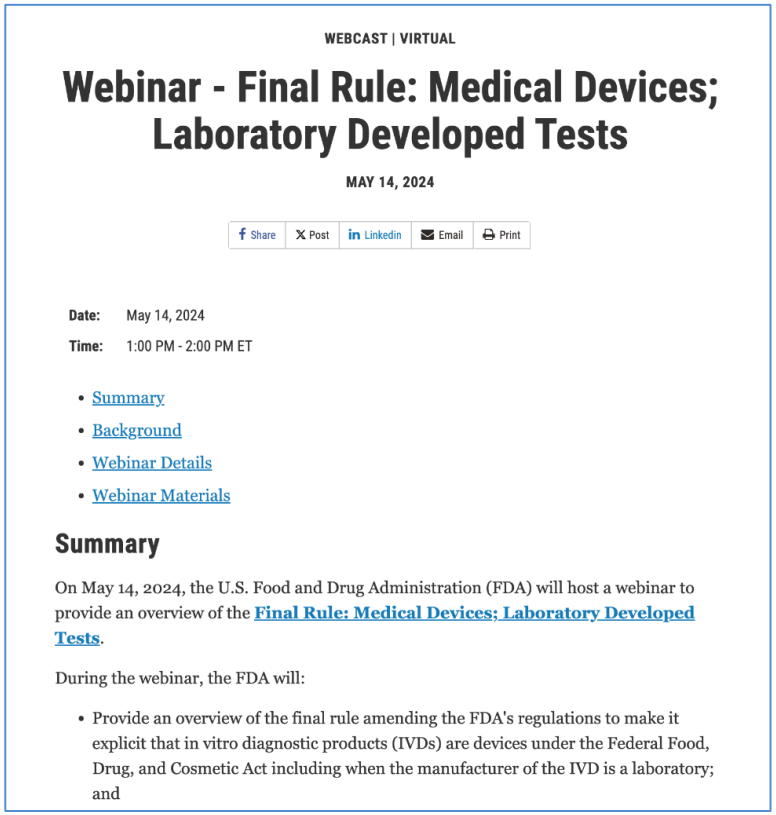
Draft guidance documents available for comment until July 5, 2024

Other Points for Consideration

- What does this mean for **new LDTs**?
  - Rule is ambiguous, but assumption is that **new LDTs introduced after the effective date will need to comply with the phased-in requirements in effect at that time**
- Will FDA leverage collection devices to require premarket review?
  - Footnote #21 says "IVDs offered as LDTs" does not include IVDs manufactured or used outside of a laboratory, including collection devices
- How will FDA use its discretion?
  - Rule states that FDA will use reporting requirements to monitor for concerns and take enforcement action if needed
- **Will the implementation of the rule be delayed**?
  - **Possible litigation could upend the process**
  - The financial impact on both labs and FDA could be so great that the agency delays enforcement of requirements
  - NYS CLEP program becomes overwhelmed
- Do the rule's areas of continued enforcement discretion create market incentives/advantages?

FDA Educational Webinars

- **May 14th**: overview of final rule and phaseout policy
- **June 2024**: draft guidances for enforcement policy related to public health emergencies
- **July 2024**: IVD classification
- **August 2024**: MDRs, QS Complaint Requirements, Recalls



WEBCAST | VIRTUAL

Webinar - Final Rule: Medical Devices; Laboratory Developed Tests

MAY 14, 2024

Share | Post | Linkedin | Email | Print

Date: May 14, 2024

Time: 1:00 PM - 2:00 PM ET

- Summary
- Background
- Webinar Details
- Webinar Materials

Summary

On May 14, 2024, the U.S. Food and Drug Administration (FDA) will host a webinar to provide an overview of the **Final Rule: Medical Devices; Laboratory Developed Tests**.

During the webinar, the FDA will:

- Provide an overview of the final rule amending the FDA's regulations to make it explicit that in vitro diagnostic products (IVDs) are devices under the Federal Food, Drug, and Cosmetic Act including when the manufacturer of the IVD is a laboratory; and

https://www.fda.gov/medical-devices/medical-devices-news-and-events/webinar-final-rule-medical-devices-laboratory-developed-tests-05142024

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Congressional Response

"The **FDA does not have the authority** to unilaterally increase its regulatory jurisdiction. This rule will undermine access to essential laboratory tests, increase healthcare costs, and ultimately harm patients."

-- Ranking Member Cassidy

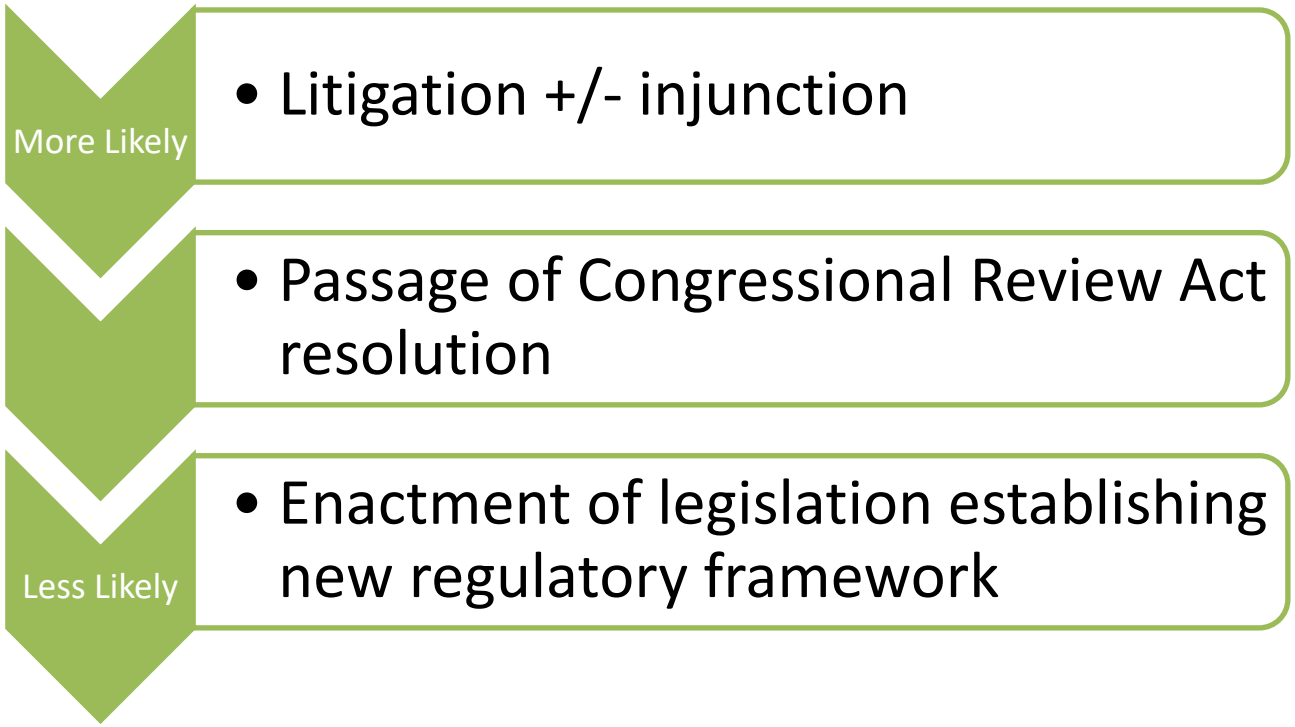
"The Biden Administration's final rule is the latest example of executive branch overreach that will have devastating impacts on patients and families across the country… The **FDA should abandon the rule, as it lacks clear statutory authority to implement it**."

– Chair McMorris Rodgers

"Rational oversight of in-vitro diagnostics, including laboratory-developed tests, is vital for innovation in diagnostics and public health. **We are disappointed that the FDA has moved ahead with a burdensome rule based on an inflexible statute that was never designed to regulate in vitro diagnostics.**"

– Reps. DeGette and Bucshon, sponsors of VALID Act

Anticipated Action to Stop Implementation



Reasons Why AMP is Still Concerned

Reason #1: Molecular Pathologists are Healthcare Professionals, NOT Manufacturers

- Extensive post-graduate education
- Clinical training
  - Accreditation Council for Graduate Medical Education
- Board-certification examinations
  - American Board of Pathology
  - American Board of Medical Genetics and Genomics under the umbrella of the Accreditation Council for Graduate Medical Education, or other recognized professional boards.
- ***"laboratory developed testing procedure"***
  - LDPs ≠ boxed and shipped test kits

Reason #2: FDA Review is Costly, Burdensome, and Resource-Intensive

	Cost Per LDT	
	Stanford University Study	FDA Analysis
PMA	**$75 million**	**$4.3 million**
510(k) Method Comparison	**$24 million**	**$247,000**
510(k) Moderately Complex Clinical Study		**$498,000**
510(k) de novo		**$527,000**

Reason #3: Compliance with Rule with QSR and Premarket Review Not Feasible for Many Laboratories

- 92% of the assumed 1,193 laboratories impacted by the final rule are small businesses
  - Their average annual receipts = ~$4 million
  - 807 of these laboratories have revenue of less than $4 million
  - **Thus, these entities could not afford even a single PMA submission at $4M/submission**

Reason #4: FDA Does Not Have the Appropriate Resources to Handle the Added Workload

- One report indicates that 5,110 genetic tests are entering the market per year
- However, FDA has only authorized 144 human genetic tests to date

FDA still underestimates the number of new tests that will require review, still their estimated increase in FDA workload is:

>141% PMAs
>405% de novo 510(k)s

Reason #5: LDPs Already Regulated by CLIA

- Laboratory must be accredited (42 CFR 493.61)
- Must establish performance specifications (42 CFR 493.1253)
- Subject to quality system requirements (42 CFR 493 Subpart K)
- Must be performed under supervision of a board-certified pathologist (42 CFR § 493.1443(b)(3))
- Subject to proficiency testing (42 CFR 493 Subpart I)
- Laboratory subject to inspections (42 CFR 493 Subpart Q)
- Must correct and report laboratory errors (42 CFR 493.2; 42 CFR 493.1233; 42 CFR 493.1291(k))
- ***CLIA requirements are the floor***

Reason #6: The Rule Will Harm Innovation and Patient Care

- Numerous gaps not addressed by "exemptions":
  - Currently marketed tests:
    - Will more significant modifications be allowed?
  - Unmet needs
    - Many laboratories are not a part of integrated health care systems including public health laboratories and regional laboratories
    - FDA-authorized test = "Met need"
- Many details have not been provided
- Enforcement Discretion is POLICY
  - can change at any time
  - continued enforcement discretion not guaranteed

AMP Advocacy Website:

Tell Congress It's Time to Modernize CLIA

Over three decades old, the CLIA regulations need to be modernized to better reflect advancements in molecular testing. This effort would also lead to a flexible system of oversight that fosters innovation and ensures patients have continued access to precise, accurate, and the most up-to-date tests. Over 50 stakeholders have urged Congress to modernize CLIA and **AMP has supported this cause with our 2023 CLIA Modernization Proposal**. You can read more about how AMP's proposed legislation and endorse it here:

Legislative Proposal to Modernize CLIA

Frequently Asked Questions on Legislative Proposal

Section by Section Summary of Legislative Proposal

Endorse CLIA Legislative Proposal

https://www.amp.org/advocacy/laboratory-developed-testing-procedures-ldps11/

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AMP Advocacy: Support CLIA Modernization

Modern Field of Laboratory Medicine	• **Expands CLIA** to reflect the modern field of laboratory medicine requiring **new federal standards** for molecular and genomic testing, laboratory analytics, and bioinformatics-focused laboratory procedures/examinations.

Test Quality & Transparency	• Clarifies **that CLIA should develop minimum levels of standards for analytical and clinical validity.**
	  • Laboratories are required to share summary information on validation data with inspectors.
	  • Laboratories are also required to share summary validation information with the public.

Proficiency Testing	• **Expands proficiency testing requirements** so there are continual assurances that laboratories are providing high-quality care. When a proficiency testing program is not available, it requires laboratories to perform certain alternative assessments deemed acceptable by the CMS.
Third Parties	• Continues the successful role of **third-party accreditation organizations**.
Updated regulations	• **Requires CMS to update regulations**, including as it relates to “black box” tests and laboratory errors.

Questions