U.S. FOOD & DRUG ADMINISTRATION

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Today's Topic:
FDA's Final Rule Including a Phaseout Policy Regarding Laboratory Developed Tests

May 14, 2024

FDA's Final Rule Including a Phaseout Policy Regarding Laboratory Developed Tests

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Background

The Medical Device Amendments of 1976 (the MDA) amended the Food, Drug & Cosmetic Act (FD&C) to create a comprehensive system for the regulation of devices intended for human use

In implementing the MDA, FDA has exercised enforcement discretion such that it generally has not enforced applicable requirements with respect to most LDTs, including requirements related to:

- registration and listing
- reporting adverse events to FDA
- current good manufacturing practices (CGMPs)
- premarket review

Laboratory Developed Tests (LDTs)

FDA has generally considered an LDT to be an in vitro diagnostic (IVD) that is:

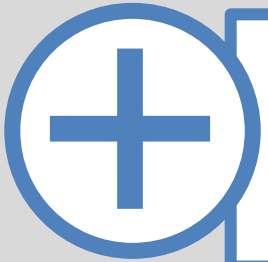
- Intended for clinical use and
- Designed, manufactured, and used within a single laboratory that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and meets the regulatory requirements under CLIA to perform high complexity testing.

Evolution of LDTs

LDTs of 1976	LDTs of Today
Mostly manufactured in small volumes by laboratories that served their local communities	Often run in high volumes for large and diverse populations
Tended to employ manual techniques (and did not use automation)	Increasingly rely on high-tech or complex instrumentation and software to generate results and clinical interpretations
Tended to be performed by laboratory personnel with specialized expertise, and to be used and interpreted by physicians or pathologists in a single institution responsible for the patient	Many LDTs are manufactured by laboratory corporations that market the IVDs nationwide, as they accept specimens from patients across the country and run their LDTs in very large volumes in a single laboratory outside the patient's healthcare setting
Manufactured using components legally marketed for clinical use	More commonly manufactured with instruments or other components not legally marketed for clinical use
Typically intended for use in diagnosing rare diseases or for other uses to meet the needs of a local patient population or were generally similar to well-characterized, standard IVDs	More often used to inform or direct critical treatment decisions, to widely screen for common diseases, to predict personal risk of developing certain diseases, and to diagnose serious medical conditions

The risks associated with most LDTs today are therefore much greater than they were at the time FDA began implementing the MDA

Substance of Rulemaking



Amends FDA's regulations to make explicit that IVDs are devices under the FD&C Act including if the manufacturer is a laboratory

Phases out FDA's general enforcement discretion approach for LDTs so IVDs manufactured by laboratories will generally fall under the same enforcement approach as other IVDs

Tests Excluded from the Scope of the Phaseout Policy

The phaseout policy does not apply to certain tests that were excluded from our general enforcement discretion approach. FDA expects the following tests will continue to comply with applicable device requirements:

Tests that are intended as blood donor screening or human cells, tissues, and cellular and tissue-based products (HCT/P) **donor screening tests** required for infectious disease testing, or required for determination of blood group and Rh factors

Tests intended for **emergencies**, potential emergencies, or material threats declared under section 564 of the FD&C Act

Direct-to-consumer tests intended for consumer use without meaningful involvement by a licensed healthcare professional

Tests manufactured and offered for use exclusively for **public health surveillance** are also not affected by the phaseout policy.

Tests Included in the Scope of the Phaseout Policy

The phaseout policy applies to “IVDs offered as LDTs”

IVDs that are manufactured and offered as LDTs by laboratories that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and that meet the regulatory requirements under CLIA to perform high complexity testing, and used within such laboratories, even if those IVDs do not fall within FDA’s traditional understanding of an LDT because they are not designed, manufactured, and used within a single laboratory.

Phaseout Policy

FDA is phasing out its general enforcement discretion approach for LDTs in stages, so that IVDs manufactured by a laboratory will generally fall under the same enforcement approach as other IVDs (i.e., FDA's expectations for compliance will generally be the same), according to the following timeline:

Beginning May 6, 2025

- Medical Device Reporting
- Correction and Removal Reporting
- Quality System Requirements re: Complaint Files

Beginning May 6, 2026

- Requirements not covered in other stages including:
- Establishment Registration & Device Listing
- Labeling Requirements
- Investigational Requirements

Beginning May 6, 2027

- Quality System Requirements*

Beginning November 6, 2027

- Premarket Review for High Risk IVDs

Beginning May 6, 2028

- Premarket Review for Moderate and Low** Risk IVDs

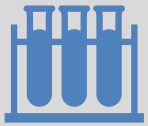
*For LDTs, FDA will expect compliance with:

- design controls under § 820.30;
- purchasing controls (including supplier controls) under § 820.50;
- acceptance activities (receiving, in-process, and finished device acceptance) under §§ 820.80 and 820.86;
- CAPA under § 820.100; and
- records requirements under part 820, subpart M

**Most Low Risk IVDs are exempt from premarket review

Enforcement Discretion Policies

FDA intends to continue the general enforcement discretion approach and generally not enforce any applicable requirements for the following tests:



"1976-Type LDTs"

Tests that have the following characteristics common among LDTs offered in 1976:

- use of manual techniques (without automation) performed by laboratory personnel with specialized expertise
- use of components legally marketed for clinical use
- design, manufacture, and use within a single CLIA-certified laboratory that meets the requirements under CLIA for high complexity testing

Certain Human Leukocyte Antigen (HLA) Tests for Transplantation

HLA tests that are designed, manufactured, and used within a single laboratory certified under CLIA that meets the requirements to perform high-complexity histocompatibility testing when used in connection with organ, stem cell, and tissue transplantation to perform HLA allele typing, for HLA antibody screening and monitoring or for conducting real and "virtual" HLA crossmatch tests.

Forensic Tests

Tests intended solely for forensic (law enforcement) purposes.

Department of Defense (DoD) and Veterans Health Affair (VHA) LDTs

LDTs manufactured and performed within the DoD or VHA. This policy applies only to LDTs used for patients that are being tested and treated within the DoD or VHA.

Enforcement Discretion Policies

FDA generally intends to exercise enforcement discretion with respect to premarket review requirements for:

LDTs approved by NYS CLEP

LDTs that are approved, conditionally approved, or within an approved exemption from full technical documentation, under New York State Department of Health's Clinical Laboratory Evaluation Program (NYS CLEP).

Certain modified versions of another manufacturer's 510(k) cleared or De Novo authorized test

This policy applies when a laboratory certified under CLIA and meeting the regulatory requirements under CLIA to perform high complexity testing modifies another manufacturer's 510(k) cleared or De Novo authorized test, following design controls and other quality system requirements for which FDA expects compliance, in a manner that could not significantly affect the safety or effectiveness of the test or and 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.

FDA expects compliance with other requirements as described in the phaseout policy:

Beginning May 6, 2025

- Medical Device Reporting
- Correction and Removal Reporting
- Quality System Requirements re: Complaint Files

Beginning May 6, 2026

Requirements not covered in other stages including:

- Establishment Registration & Device Listing
- Labeling Requirements
- Investigational Requirements

Beginning May 6, 2027

- Quality System Requirements*

*For LDTs, FDA will expect compliance with:

- design controls under § 820.30;
- purchasing controls (including supplier controls) under § 820.50;
- acceptance activities (receiving, in-process, and finished device acceptance) under §§ 820.80 and 820.86;
- CAPA under § 820.100; and
- records requirements under part 820, subpart M

Enforcement Discretion Policies

FDA generally intends to exercise enforcement discretion with respect to premarket review and most quality system requirements for:

Certain LDTs for unmet needs

These are LDTs manufactured and performed by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within the same healthcare system.

Currently Marketed IVDs offered as LDTs

These are currently marketed IVDs offered as LDTs that were first marketed prior to the date of issuance of the LDT Final Rule, as long as they are not modified after that date, or are modified but only in certain limited ways.

Certain Non-Molecular Antisera LDTs for Rare Red Blood Cell (RBC) Antigens for Transfusion Compatibility

These are non-molecular antisera LDTs for rare RBC antigens, when such tests are manufactured and performed by blood establishments, including transfusion services and immunohematology laboratories and when there is no alternative IVD available to meet the patient's need for a compatible blood transfusion. This policy does not apply to molecular tests used for genotyping RBC antigens.

FDA expects compliance with other requirements as described in the phaseout policy:

Beginning May 6, 2025

- Medical Device Reporting
- Correction and Removal Reporting
- Quality System Requirements re: Complaint Files

Beginning May 6, 2026

- Requirements not covered in other stages including:
- Establishment Registration & Device Listing
- Labeling Requirements
- Investigational Requirements

Beginning May 6, 2027

- Quality System Requirements re: Records

Conclusion

LDT Final Rule Including a Phaseout Policy

FDA believes this final rule, including the phaseout policy, will better protect the public health by helping to assure the safety and effectiveness of IVDs offered as LDTs, while also accounting for other important public health considerations such as patient access and reliance

Next Webinar

[Laboratory Developed Tests | FDA]

Date
June 5, 2024

Time
1-2PM ET

Topic
Draft Guidances on Immediate Response Tests and Consideration of Enforcement Policies for Tests in the Context of a 564 Declaration

Please submit questions in advance to:
CDRHWebinars@fda.hhs.gov

Resources

Resource	URL(s)
Final Rule Regarding LDTs	www.federalregister.gov/documents/2024/05/06/2024-08935/medical-devices-laboratory-developed-tests
Final Regulatory Impact Analysis (FRIA)	www.fda.gov/about-fda/economic-impact-analyses-fda-regulations/laboratory-developed-tests-regulatory-impact-analysis-final-rule
Laboratory Developed Tests	www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests
Complaints, Medical Device Reporting/Adverse Events, and Corrections and Removal	www.fda.gov/media/109411/download (presentation) www.fda.gov/regulatory-information/search-fda-guidance-documents/medical-device-reporting-manufacturers www.fda.gov/medical-devices/postmarket-requirements-devices/recalls-corrections-and-removals-devices
Device Registration and Listing	www.fda.gov/medical-devices/how-study-and-market-your-device/device-registration-and-listing
Device Labeling	www.fda.gov/medical-devices/overview-device-regulation/device-labeling www.fda.gov/medical-devices/device-labeling/in-vitro-diagnostic-device-labeling-requirements
Investigational Use Requirements	www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/investigational-device-exemption-ide
Quality System Requirements	www.fda.gov/medical-devices/postmarket-requirements-devices/quality-system-qs-regulationmedical-device-current-good-manufacturing-practices-cgmp
Premarket Review Requirements	www.fda.gov/medical-devices/how-study-and-market-your-device/premarket-submissions-selecting-and-preparing-correct-submission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Previously Submitted Questions

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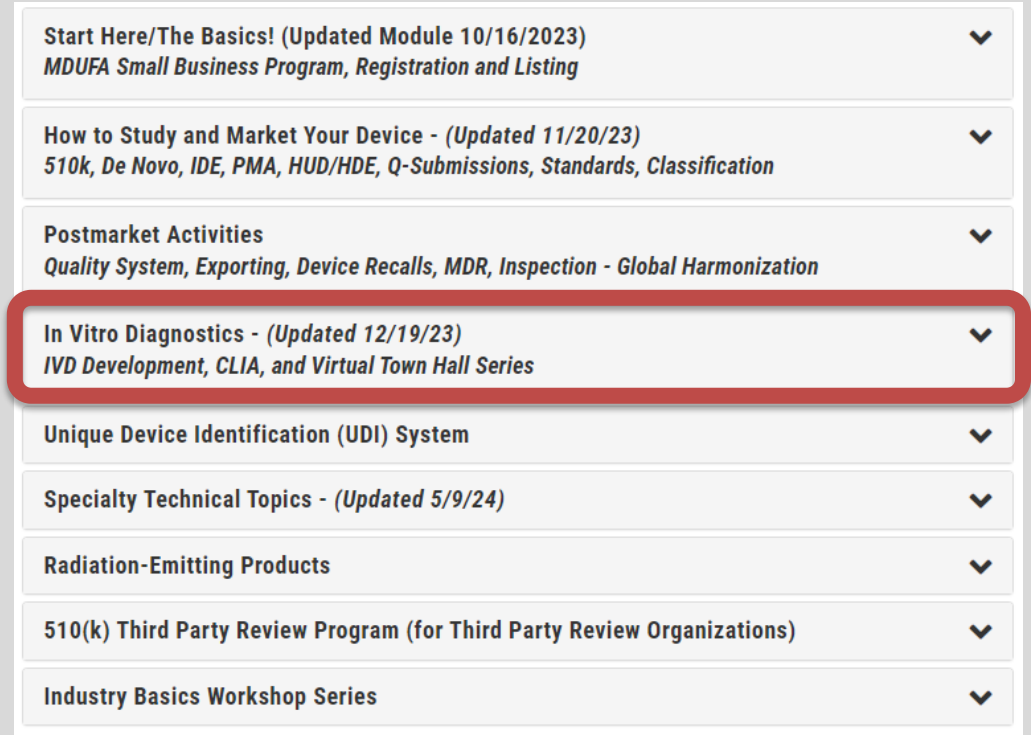
- **Additional questions about today's webinar**
  - Email: DICE@fda.hhs.gov
- **Upcoming Webinars**
  - www.fda.gov/CDRHevents

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