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Policy Summary: FDA Final Rule on Regulation of LDTs

Disclaimer: This summary is provided as an educational resource only. It is not inclusive of all applicable regulations and is not intended as a guide for complying to FDA regulations. Laboratory professionals should consult with their regulatory affairs professionals for guidance on complying with FDA requirements.

Table of Contents

I. Summary

The U.S. Food and Drug Administration (FDA) has published its final rule on Regulation of Laboratory Developed Tests (LDTs). The text of the rule was initially released on April 29, 2024 and formally published on May 6, 2024. The final rule clarifies that in vitro diagnostic products (IVDs) are devices under the Federal Food, Drug, and Cosmetic Act (FD&C Act) including when the manufacturer of the IVD is a laboratory (i.e., LDTs). The FDA intends to begin enforcing medical device regulations on LDTs using a phased approach beginning on May 6, 2025, with full enforcement of regulations by May 6, 2028.

The following document summarizes the implementation schedule, exemptions, applicable regulations, and other important information related to the rule.

II. Enforcement Discretions

The final rule includes numerous enforcement discretion policies, many of which were not included in the initial proposed rule. It is important to note that FDA could change these enforcement discretion policies at any time in the future without going through the rulemaking process. Further, the FDA notes that it retains the discretion to pursue enforcement action at any time against violative IVDs when appropriate.

See also summary table in Appendix A.

No enforcement of premarket review requirements for:

- LDTs that are approved by the New York State Department of Health's Clinical Laboratory Evaluation Program (NYS CLEP).

  This includes NYS CLEP-approved high-risk tests and moderate-risk tests that have either full approval or conditional approval. However, if conditional approval is withdrawn (e.g., because NYS CLEP approval is denied), then the test would have to go through premarket approval by FDA.

  The FDA rationalizes the premarket review exemption based on certain risk mitigations under NYS CLEP, such as evaluation of analytical and clinical validity, and the accompanying information that must be submitted. The FDA notes that there is much alignment between the FDA and NYS CLEP review processes. Further, FDA has accredited NYS CLEP as an accredited Third Party Review Organization qualified to review premarket notification (510(k)) submissions for certain IVDs.

  Note that the exemption only applies to premarket review requirements (see table in Appendix A). Other regulatory requirements will still be enforced, such as quality system (QS) requirements, registration and listing, labeling requirements, medical device report (MDR) requirements, etc. However, FDA still estimates that 12.1% of LDTs would not experience any new costs associated with this enforcement discretion policy (see pages 171-173 of the FDA's Final Regulatory Impact Analysis (FRIA)).

  Additional details are provided in section V.B.2. beginning on page 37299 of the final rule (89 FR 37299).

No enforcement of premarket review and most QS requirements (some exceptions) for:

- Validated LDTs manufactured and performed by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within that same healthcare system.

  This does not include patients that are being treated at an affiliated hospital with different corporate ownership than the laboratory. The FDA rationalizes that there is shared responsibility and potential liability for patient outcomes among physicians and laboratory professionals within the same hospital system, as well as better communication between physicians and laboratories, which helps mitigate risk.

  Unmet need means there is no available FDA-authorized IVD that meets the patient's needs. This may be because:
  (1) there is no FDA-authorized IVD for the disease or condition;
  (2) 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 (e.g., different specimen type); or
  (3) there is an FDA-authorized IVD but it is not available to the patient.

  Unmet need does not apply when there is an available FDA-authorized IVD that would sufficiently meet the needs of the patient (e.g., potential improvements in performance to an FDA-authorized IVD does not fall within this exemption). Further, if an LDT is developed to meet an unmet need but FDA subsequently approves an IVD that meets the same patient need, the laboratory would no longer be able to use their LDT under this exemption. They would either have to submit their LDT to FDA for approval or use the approved IVD.

  For these tests, the FDA generally will not enforce premarket review or QS requirements, except that records requirements under 21 CFR Part 820, Subpart M will be required. Other regulations, such as MDR, correction & removal reporting, complaint files, registration & listing, and labeling will still be enforced (see summary table in Appendix A). FDA also intends to request that laboratories offering an LDT under this exemption submit certain labeling information.

  Additional details are described in section V.B.3. beginning on page 37301 of the final rule (89 FR 37301).

- Currently marketed IVDs offered as LDTs that were first marketed prior to the date of issuance (May 6, 2024) of the final rule.

  This applies to currently marketed IVDs offered as LDTs as long as they are not modified following the issuance of the final rule, or they are only modified in certain limited ways described further in the final rule. Modifications that would trigger full compliance with premarket review and QSRs include:
  - changes to the indications for use (e.g., specimen types, intended patient population);
  - changes to the operating principal of the test (e.g., changes to critical reaction components);

- inclusion of significantly different technology in the test (e.g., addition of AI or machine learning algorithms, changing from targeted sequencing to whole genome sequencing, changing from manual to automated procedures); or
- modifications that adversely change the performance or safety specifications.

For these tests, the FDA generally will not enforce premarket review or QS requirements, except that records requirements under 21 CFR Part 820, Subpart M will be required. Other regulations, such as MDR, correction & removal reporting, complaint files, registration & listing, and labeling will still be enforced (see summary table in Appendix A). FDA also intends to request submission of the labeling for currently marketed IVDs offered as LDTs to help them identify specific tests that raise concerns.

Additional details are described in section V.B.3. beginning on page 37304 of the final rule (89 FR 37304).

- Non-molecular antisera LDTs for rare red blood cell (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 for genotyping RBC antigens. According to FDA, molecular RBC typing is a relatively new and complex technique for detection of RBC antigens (compared to serologic tests), thus they have greater concern about the risk of errors for molecular tests.

  Additional details are described in section V.B.3. beginning on page 37306 of the final rule (89 FR 37306).

FDA will generally not enforce any requirements for the following categories of tests:

- "1976-Type LDTs" which includes tests with the following characteristics: (1) use of manual techniques (without automation) performed by laboratory personnel with specialized expertise; (2) use of components legally marketed for clinical use; and (3) design, manufacture, and use within a single CLIA-certified laboratory that meets the requirements under CLIA for high complexity testing.

  FDA explains that an example of such a test might include immunohistochemistry tests that involve no automated preparation or interpretation. However, this would not include lateral flow tests as they do not generally rely on laboratory personnel expertise.

  Additional details are described in section V.B.1. beginning on page 37297 of the final rule (89 FR 37297).

- Human leukocyte antigen (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.

The FDA provided the following as part of the rationale for this exemption:

- Transplantations often require prompt medical decisions based on a patient's condition and degree of mismatch between the donor and patient.
- New alleles are continuously identified, thus modifications to HLA tests for transplantation are often made rapidly in response to urgent situations.
- These tests are often individualized within each medical facility (e.g., to reflect local HLA polymorphisms and patient demographics).

Additional details are described in section V.B.1. beginning on page 37297 of the final rule (89 FR 37297).

- Tests intended solely for forensic (law enforcement) purposes.

  Additional details are described in section V.B.1. beginning on page 37298 of the final rule (89 FR 37298).

- LDTs manufactured and performed within the Department of Defense (DoD) or Veterans Health Administration (VHA).

  FDA notes that DoD and VHA have agreed to use FDA-authorized IVDs when they are available but occasionally have unique patients needs (e.g., tests for rare chemical exposures) that require a unique LDT. Further, the DoD and VHA are taking steps in consultation with FDA to track all LDTs in their systems and to ensure the analytical and clinical validity of their LDTs, the quality manufacturing of their LDTs, and the central reporting of adverse events.

  Additional details are described in section V.B.1. beginning on page 37298 of the final rule (89 FR 37298).

Tests that are not impacted by the final rule because they are already subject to other regulations:

- 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 under 21 CFR 610.40 and 21 CFR 1271.80(c), respectively, or required for determination of blood group and Rh factors under 21 CFR 640.5.

- Tests intended for emergencies, potential emergencies, or material threats declared under section 564 of the FD&C Act.
  - In addition, FDA also released two draft guidances related to IVDs in response to an emergent situation and during a declared public health emergency. Public comments are due by July 5, 2024.

- Direct-to-consumer tests intended for consumer use without meaningful involvement by a licensed healthcare professional. The FDA was already applying medical device regulations to these tests, therefore there is no change made by this final rule.

  Additional details are described in section V.A.2. on page 37296 of the final rule (89 FR 37296).

III. Enforcement of Regulations: Implementation Schedule and Regulatory Requirements

The FDA will be using a 4-year phased approach for enforcing its medical device regulations on LDTs. The implementation schedule and relevant regulations[1] are described below. See also the summary table in Appendix A.

Additional details are described in section V.C. beginning on page 37307 of the final rule (89 FR 37307).

Stage 1: Beginning 1 year after the publication date of the final rule (**May 6, 2025**), FDA will expect compliance with MDR requirements, correction and removal reporting requirements, and QS requirements under § 820.198 (complaint files).

Relevant regulations:

- MDR:
  - Regulations at 21 CFR Part 803
  - Additional information from FDA here
- Corrections & Removals
  - Regulations at 21 CFR Part 806
  - Additional information from FDA here
- Complaint Handling
  - Regulations at 21 CFR § 820.198
  - Additional information from FDA here

Stage 2: Beginning 2 years after the publication date of the final rule (**May 6, 2026**), FDA will expect compliance with requirements not covered during other stages of the phaseout policy, including registration and listing requirements, labeling requirements, and investigational use requirements.

Relevant regulations:

- Registration & listing
  - Regulations at 21 CFR Part 807
  - Additional information from FDA here
- Labeling
  - Regulations at 21 CFR Part 801 and 21 CFR Part 809
  - Additional information from FDA here
- Investigational device exemptions
  - Regulations at 21 CFR Part 812
  - Additional information from FDA here

Stage 3: Beginning 3 years after the publication date of the final rule (**May 6, 2027**), FDA will expect compliance with quality systems (QS) requirements under 21 CFR Part 820 (other than complaint files requirements under 21 CFR 820.198 which are already covered in stage 1). FDA also expects laboratories to retain manufacturing records they may already have or may create for certain IVDs prior to stage 3 of the phaseout policy.

[1] The regulations listed in this section may not be a complete list of applicable regulations. For example, this section does not include regulatory references for IVDs that are regulated as biologics (see more information here).

Relevant regulations:

- QS regulations:
  - General provisions – Regulations at 21 CFR Part 820, Subpart A
  - QSRs – Regulations at 21 CFR Part 820, Subpart B
  - Design controls – Regulations at 21 CFR Part 820, Subpart C
  - Document controls – Regulations at 21 CFR Part 820, Subpart D
  - Purchasing controls – Regulations at 21 CFR Part 820, Subpart E
  - Identification and traceability – Regulations at 21 CFR Part 820, Subpart F
  - Product and process controls – Regulations at 21 CFR Part 820, Subpart G
  - Acceptance activities – Regulations at 21 CFR Part 820, Subpart H
  - Nonconforming product – Regulations at 21 CFR Part 820, Subpart I
  - Corrective and preventive action (CAPA) – Regulations at 21 CFR Part 820, Subpart J
  - Labeling and packaging control – Regulations at 21 CFR Part 820, Subpart K
  - Handling, storage, distribution, and installation – Regulations at 21 CFR Part 820, Subpart L
  - Records – Regulations at 21 CFR Part 820, Subpart M
  - Servicing – Regulations at 21 CFR Part 820, Subpart N
  - Statistical Techniques – Regulations at 21 CFR Part 820, Subpart O
- Additional information from FDA here

Stage 4: Beginning 3.5 years after the publication date of the final rule (**November 6, 2027**), FDA will expect compliance with premarket review requirements for high-risk IVDs offered as LDTs, unless a premarket submission has been received by the beginning of this stage in which case FDA intends to continue to exercise enforcement discretion for the pendency of its review. FDA goes on to explain that this timeline allows for alignment with the next round of user fee negotiations (see section on Applicable Regulatory Fees, below).

Relevant regulations:[2]

- PMA:
  - Regulations at 21 CFR Part 814
  - Additional information from FDA here

Stage 5: Beginning 4 years after the publication date of the final rule (**May 6, 2028**), FDA will expect compliance with premarket review requirements for moderate-risk and low-risk IVDs offered as LDTs (that require premarket submissions), unless a premarket submission has been received by the beginning of this stage in which case FDA intends to continue to exercise enforcement discretion for the pendency of its review.

Relevant regulations:[2]

- 510(k):
  - Regulations at 21 CFR Part 807, Subpart E
  - Additional information from FDA here
- *De novo*:
  - Regulations at 21 CFR Part 860, Subpart D
  - Additional information from FDA here
- Third party review program for 510(k) applications:
  - Additional information from FDA here

[2] See information from FDA about selecting and preparing the correct submission here.

Note that FDA does not intend to apply premarket review requirements for changes to another manufacturer's legally marketed test when the following criteria are met:

- the laboratory is certified by CLIA to perform high complexity testing;
- the original test is legally marketed following 510(k) clearance or *de novo* authorization;[3]
- the laboratory complies with design controls and other QSRs;
- the modification does not significantly affect the safety or effectiveness of the test;
- the modification does not constitute a major change to the intended use (see also 21 CFR 807.81(a)(3) and guidance titled "Deciding When to Submit a 510(k) for a Change to an Existing Device"); and
- the modified test is only used in the laboratory that made the modification.

See additional information in section V.C.4. on page 37310 (89 FR 37310) and section V.C.5. on page 37311 of the final rule (89 FR 37311).

Additional regulatory references for Stages 4 and 5: Medical devices, including IVDs, fall into one of three categories, or classes, based on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

- **Test classification:**
  - Regulations at 21 CFR Part 860 (definitions in 21 CFR 860.3)
    - Class I (general controls) – Means the device (test) is subject only to the general controls authorized by or under sections 501 (adulteration), 502 (misbranding), 510 (registration), 516 (banned devices), 518 (notification and other remedies), 519 (records and reports), and 520 (general provisions) of the FD&C Act.
    - Class II (special controls) – Means general controls alone are insufficient to provide reasonable assurance of the safety and effectiveness of the device (test) and there is sufficient information to establish special controls, including the promulgation of performance standards, post market surveillance, patient registries, development and dissemination of guidelines, recommendations, and other appropriate actions deemed necessary.
    - Class III (premarket approval) – Means insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device (test), or that application of Class II special controls described in addition to general controls would provide such assurance, and if, in addition, the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.
  - FDA's database on medical device classification is available here.
  - Additional information from FDA here and in section III.A. beginning on page 37289 of the final rule (89 FR 878289).
  - See also recent FDA notice on down classification of certain high risk IVDs here.

[3] This exception does not apply to tests that are PMA-approved or BLA-licensed because they are higher risk. However, it will apply to tests that are reclassified from class III to class II as described in the FDA's announcement on January 31, 2024.

IV. Applicable Regulatory Fees[4]

Registration Fees:

- Annual registration fee: $7,653

User Fees:

Application Type	Standard Fee	Small Business Fee[5]
510(k)♯	$21,760	$5,440
513(g)	$6,528	$3,264
PMA, PDP, PMR, BLA	$483,560	$120,890
De Novo Classification Request	$145,068	$36,267
Panel-track Supplement	$386,848	$96,712
180-Day Supplement	$72,534	$18,134
Real-Time Supplement	$33,849	$8,462
BLA Efficacy Supplement	$483,560	$120,890
30-Day Notice	$7,737	$3,869
Annual Fee for Periodic Reporting on a Class III device (PMAs, PDPs, and PMRs)	$16,925	$4,231

See additional information on user fees here.

[4] Note that the fees above are based on the Fiscal Year 2024 User Fees. User fees are negotiated every 5 years as part of the Medical Device User Fee Agreements (MDUFA) which must be approved by Congress.

[5] Small business is defined as a business, including its affiliates, whose gross receipts and sales are less than $100 million for the most recent tax year. Must have an approved Small Business Determination (SBD) from FDA. Additional waivers are available for small businesses with gross receipts or sales of $30 million or less.

Appendix A: Summary of Enforcement Dates and Applicable Regulations

The table below summarizes the medical device regulation compliance dates for LDTs. For additional details about exemption categories, see text above.

	Stage 1 MDR, correction & removal reporting, complaint files	**Stage 2** Registration/listing, labeling, investigational use, other requirements not covered in other stages	**Stage 3** QS Requirements	**Stage 4** Premarket review for high-risk LDTs	**Stage 5** Premarket review for moderate-risk & low-risk LDTs
1976-Type LDTs	Exempt	Exempt	Exempt	Exempt	Exempt
HLA LDTs for allele typing associated with transplantations	Exempt	Exempt	Exempt	Exempt	Exempt
Forensic tests	Exempt	Exempt	Exempt	Exempt	Exempt
DoD/VHA	Exempt	Exempt	Exempt	Exempt	Exempt
NYS CLEP	May 6, 2025	May 6, 2026	May 6, 2027	Exempt	Exempt
Unmet need of patients receiving care within the same healthcare system	May 6, 2025	May 6, 2026	Most exempt	Exempt	Exempt
LDTs offered prior to 5/6/2024 & unmodified	May 6, 2025	May 6, 2026	Most exempt	Exempt	Exempt
Non-molecular antisera LDTs for rare RBC antigens	May 6, 2025	May 6, 2026	Most exempt	Exempt	Exempt
All other LDTs	May 6, 2025	May 6, 2026	May 6, 2027	November 6, 2027	May 6, 2028

Note: The exemptions summarized above are based on the final rule published on May 6, 2024. These exemptions could change in the future at FDA's discretion.

Appendix B: Regulatory References

Medical Device Regulations, general – 21 CFR Chapter I, Subchapter H

510(k) – 21 CFR Part 807, Subpart E
Classification of Devices (Tests) – 21 CFR Part 860
Corrections & Removals – 21 CFR Part 806
de novo – 21 CFR Part 860, Subpart D
Humanitarian Device Exemption – 21 CFR Part 814, Subpart H
Investigational Device Exemptions – 21 CFR Part 812
Labeling – 21 CFR Part 801 and 21 CFR Part 809
Medical Device Report – 21 CFR Part 803
PMA – 21 CFR Part 814
QS Requirements:

- General provisions – 21 CFR Part 820, Subpart A
- QSRs – 21 CFR Part 820, Subpart B
- Design controls – 21 CFR Part 820, Subpart C
- Document controls – 21 CFR Part 820, Subpart D
- Purchasing controls – 21 CFR Part 820, Subpart E
- Identification and traceability – 21 CFR Part 820, Subpart F
- Product and process controls – 21 CFR Part 820, Subpart G
- Acceptance activities – 21 CFR Part 820, Subpart H
- Nonconforming product – 21 CFR Part 820, Subpart I
- Corrective and preventive action (CAPA) – 21 CFR Part 820, Subpart J
- Labeling and packaging control – 21 CFR Part 820, Subpart K
- Handling, storage, distribution, and installation – 21 CFR Part 820, Subpart L
- Records – 21 CFR Part 820, Subpart M
    - Complaint Handling – 21 CFR § 820.198
- Servicing – 21 CFR Part 820, Subpart N
- Statistical Techniques – 21 CFR Part 820, Subpart O

Registration & Listing – 21 CFR Part 807

The FDA has developed guidance documents on many of these topics to provide additional details on how to comply with regulations. You can search for guidance documents on a given topic here.

Appendix C: Definitions

510(k) – premarket notification
BLA – biologics license application
CFR – Code of Federal Regulations
de novo – *de novo* classification request
DoD – Department of Defense
FDA – U.S. Food and Drug Administration
FD&C Act – Federal Food, Drug, and Cosmetic Act
FR – Federal Register
FRIA – Final Regulatory Impact Analysis
HDE – humanitarian device exemption
HLA – human leukocyte antigen
IVD – in vitro diagnostic (under this rule, includes LDTs)
IND – investigational new drug application
LDT – laboratory developed test
MDR – medical device report
MDUFA – medical device user fee amendments
NYS CLEP – New York State Department of Health's Clinical Laboratory Evaluation Program
PMA – premarket approval application
QS – quality system
QSR – quality system regulations
RBC – red blood cell
VHA – Veterans Health Administration

Appendix D: Helpful Resources

ACMG Webinar, May 21, 2024, "Update on the Regulation of LDTs: FDA, VALID Act, CLIA Modernization, and More" – https://www.acmgeducation.net/Public/Catalog/Details.aspx?id=Ba95YJMEriB16WM5NnUJVQ==&returnurl=/Users/UserOnlineCourse.aspx?LearningActivityID=Ba95YJMEriB16WM5NnUJVQ%253d%253d

FDA Webinar on Final Rule, May 14, 2024 – https://www.fda.gov/medical-devices/medical-devices-news-and-events/webinar-final-rule-medical-devices-laboratory-developed-tests-05142024?utm_medium=email&utm_source=govdelivery

FDA Final Rule on Regulation of LDTs – https://www.federalregister.gov/documents/2024/05/06/2024-08935/medical-devices-laboratory-developed-tests

FDA Final Regulatory Impact Analysis (FRIA) – https://www.fda.gov/media/178133/download

FDA Frequently Asked Questions on LDTs – https://www.fda.gov/medical-devices/laboratory-developed-tests/laboratory-developed-tests-frequently-asked-questions

FDA General Website on LDTs – https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests

Medical Device User Fees, General – https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/medical-device-user-fees

2024 User Fee Structure – https://www.fda.gov/industry/fda-user-fee-programs/medical-device-user-fee-amendments-mdufa

FDA Guidance Document Search – https://www.fda.gov/regulatory-information/search-fda-guidance-documents

Medical Device Classification Database – https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/classification.cfm

510(k) Premarket Notification Database – https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm

de novo Classification Database – https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/denovo.cfm

PMA Database – https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm

Manufacturer and User Facility Device Experience (MAUDE) Database – https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/TextSearch.cfm

Establishment Registration & Device Listing Database – https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRL/rl.cfm