Record Keeping and Adverse Event Reporting:

Medical Device Reporting, Corrections & Removals, and Quality System Complaint Requirements

LDT Industry Education

October 28, 2024

REAGAN-UDALL FOUNDATION FOR THE FDA

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Welcome

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Agenda

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- **Background**
  Alberto Gutierrez, PhD
- **Medical Device Reporting, Corrections and Removals, and Quality System Complaint Requirements**
  Donna Hartzfeld, PhD
  Bobbi Druyor-Sanchez, MS
- **Case Studies**
  Julie Ballard
- **Question and Answer**

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Background

Alberto Gutierrez, PhD
Partner, NDA Partners

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background

- FDA jurisdiction over Laboratory Developed Tests (LDTs)
- On May 6, 2024, FDA published a final rule
  - Set in regulation FDA jurisdiction
  - Set a timetable for laboratories to comply with FDA regulations
- This is the first in a series of webinars to help laboratories understand their responsibilities
- These seminars are based on information the FDA has provided to the public in their webpage: https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests

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summary phaseout requirements

Requirement	Pre-1976 LDTs	HLA for Trans.	Forensic	DoD and VHA	Rare RBC Antigen	Currently Marketed	Unmet Needs	NYS CLEP	Significant Modifi-cations	New LDT
Phase 1 MDR, Correction and Removing Reporting, Complaints	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes*
Phase 2 Registration & Listing, Labeling	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes*
Phase 3 QSR: Design Controls	No	No	No	No	No	No	No	Yes	Yes	Yes*
Phase 3 QSR: Purchasing Controls	No	No	No	No	No	No	No	Yes	Yes	Yes*
Phase 3 QSR: Acceptance Activities	No	No	No	No	No	No	No	Yes	Yes	Yes*
Phase 3 QSR: CAPA	No	No	No	No	No	No	No	Yes	Yes	Yes*
Phase 3 QSR: Records	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes*
Phase 4 Premarket Review: PMA	No	No	No	No	No	No	No	No	Yes	Yes*
Phase 5 Premarket Review: 510(k) and De Novo	No	No	No	No	No	No	No	No	Yes	Yes*

* Depends on when the LDT is marketed and when the PMA/510(k)/De Novo applications are submitted

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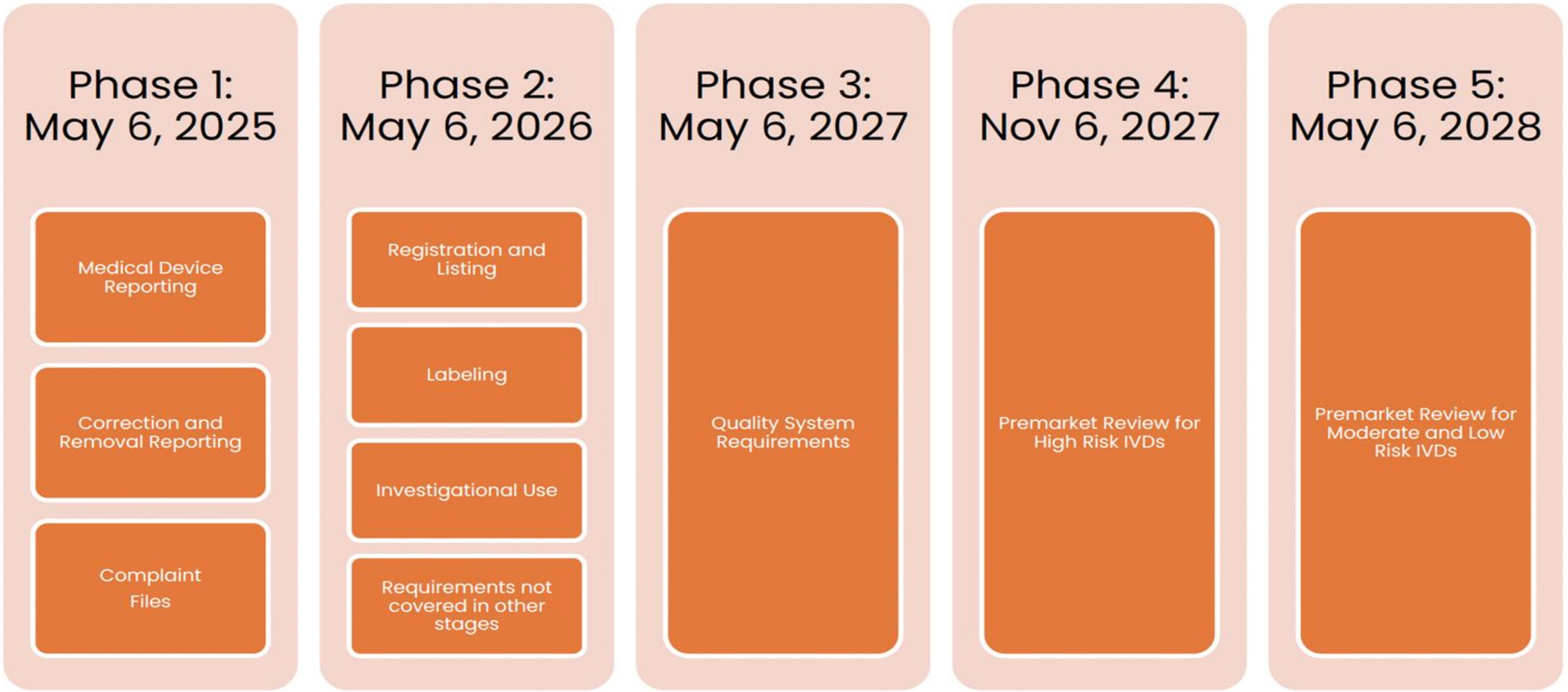
timing of phase out policy



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planned webinars

1. Record Keeping and Adverse Event Reporting
2. Labeling and Registration and Listing
3. Building and Using Quality Systems
4. Demonstrating Clinical and Analytical Validity

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Medical Device Reporting, Corrections and Removals, and Quality System Complaint Requirements

Donna Hartzfeld, PhD, Expert Consultant, NDA Partners

Bobbi Druyor-Sanchez, MS, Partner, NDA Partners

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record keeping and adverse event reporting:

medical device reporting, corrections, and quality system compliant requirements

Alberto Gutierrez, Bobbi Druyor-Sanchez, Julie Ballard, and Donna Hartzfeld

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complaints file requirements

- 21 CFR pt. 820.198
- Definition of a complaint:
  - Any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.
    - For an LDT this would be a report/complaint of an erroneous result.

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complaints investigation records

- Test identification
- Date complaint was received
- Name, address, and phone number of the complainant
- The nature and detail of the complaint
- The dates and results of the investigation
- Corrective actions taken
- Any reply to complainant

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21 CFR part 803

MDR Requirements

What is an MDR Reportable Event?

- An erroneous test result that may have caused or contributed to a death or serious injury, or
- A test malfunction that would likely cause or contribute to a death or serious injury if the malfunction were to recur.

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MDR Definitions

What is a Serious Injury?

- Life threatening; or
- Results in permanent impairment or damage to a body function or structure; or
- Requires medical or surgical intervention to preclude permanent impairment or damage to a body function or structure.

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MDR Definitions

What is a Malfunction?

- The failure of a device to meet its performance specifications or otherwise perform as intended.

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mandatory reporting timeframes

- Death and Serious Injuries
  - To FDA, within 30 calendar days of becoming aware of an event
- Malfunctions
  - To FDA, within 30 calendar days of becoming aware of an event
- For recurring events, the laboratory can request reporting via summary reports, and if eligible such reports can be filed quarterly.
  - An example of this could be reporting of failed runs that were caught by a control failures

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how to submit an MDR

- A step-by-step description of what you need to do can be found in the following FDA presentation on LDTs: https://www.fda.gov/media/181138/download?attachment
- FDA maintains a website with detail instructions at https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems

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Correction and Removal Definitions

What is a Correction?

- A correction means repair, modification, adjustment, relabeling, destruction, or inspection (including patient monitoring) of a product without its physical removal to some other location.

What is a Removal?

- A removal means the physical removal of a device from its point of use to some other location for repair, modification, adjustment, relabeling, destruction, or inspection.

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corrections and removals reporting

- 21 CFR pt. 806
- Identify the problem
  - Complaints, internal quality checks, other
- Investigate the problem
  - What is the cause?
  - What is the scope?
- Determine actions and next step
  - Fix the problem
  - Is the correction or removal reportable to the FDA?

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what is a recall?

- Recalls are actions taken by a laboratory regarding its LDT to remove the test or correct the test that:
  - FDA considers in violation of the laws it administers; and
  - Against which FDA would initiate legal action.

- Laboratories execute a recall to protect the public health for products that present a risk of injury or gross deception or are otherwise defective.
  - Recall guidance 21 CFR 7 provides guidance so that companies may conduct an effective recall.
  - In rare instances, where the laboratory or manufacturer fails to voluntarily recall a device that is a risk to health, FDA may issue a recall to the company under 21 CFR 810.

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FDA recall classifications

Class 1

- Reasonable probability that the use of test will cause serious adverse health consequences or death.

Class 2

- The use of the test may cause temporary or medical reversible adverse health consequences or where the probability of serious adverse health consequences is remote.

Class 3

- The use of the test is not likely to cause adverse health consequences.

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notification to FDA

- Class 1 and 2 recalls must be reported to the FDA
- Reporting must occur within 10 days
- Submit recall to relevant recall division
  - ORADevice1Recalls@fda.hhs.gov – CT, DC, DE, IN, KY, MA, MD, ME, MI, NH, NJ, NY, OH, PA, RI, VA, VT, WV
  - ORADevice2Recalls@fda.hhs.gov – AL, FL, GA, IA, IL, KS, LA, MN, MO, MS, NC, ND, NE, PR, SC, SD, TN, US Virgin Islands, WI
  - ORADevice3Recalls@fda.hhs.gov - AK, AR, AZ, CA, CO, HI, ID, MT, NM, NV, OK, OR, TX, UT, WA, WY

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case studies

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Case Studies

Julie Ballard
Expert Consultant, NDA Partners

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case study #1 – lab personnel error

Issue	The ordering clinician calls the lab because the patient's test result was not consistent with patient's clinical data and symptoms.
Is this a complaint?	**Yes**. This complaint alleges a deficiency with the performance of the test. The lab records this as a complaint and initiates an investigation.
Investigation Results	Two specimens, one from Patient A and one from Patient B, were swapped by **lab personnel during testing**. Consequently, Patient A received Patient B's result and vice versa.
Is this a reportable event?	**Yes**, if the erroneous test result **may have caused or contributed to a death or serious injury** (e.g., Cancer diagnosis test that cause Patient A to receive unnecessary treatment and Patient B to not receive or delay treatment) **or** the error was **caused by a malfunction** (e.g., Test does not have proper process or safeguards to ensure specimen traceability). **No**, if this erroneous test result **did not cause or contribute to a death or serious injury** (e.g., Low-risk vitamin D level test).
Is a correction or removal required?	**Yes**. A correction is required to rectify the erroneous test result.
Is a recall required?	**Yes**. The original test report with the erroneous test result is recalled and replaced with a corrected test report with the correct test result.

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case study #2 – specimen collection error

Issue	The ordering clinician calls the lab because the patient's test result was not consistent with patient's clinical data and symptoms.
Is this a complaint?	**Yes**. This complaint alleges a deficiency with the performance of the test. The lab records this as a complaint and initiates an investigation.
Investigation Results	Two specimens, one from Patient A and one from Patient B, were swapped by **phlebotomy personnel during specimen collection at a blood draw site that is unaffiliated with the testing lab**. Consequently, Patient A received Patient B's result and vice versa.
Is this a reportable event?	**Yes**, if the erroneous test result **may have caused or contributed to a death or serious injury** (e.g., Cancer diagnosis test that cause Patient A to receive unnecessary treatment and Patient B to not receive or delay treatment). **No**, if this erroneous test result **did not cause or contribute to a death or serious injury** (e.g., Low-risk vitamin D level test).
Is a correction or removal required?	**No**. Even though a corrected test result report is required, the LDT was not the cause of the erroneous test result.
Is a recall required?	**No.** Even though a corrected test result report is required, the LDT was not the cause of the erroneous test result.

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case study #3 – reagent issue; test results reported

Issue	The ordering clinician calls the lab because the patient's test result was not consistent with patient's clinical data and symptoms.
Is this a complaint?	**Yes**. This complaint alleges a deficiency with the performance of the test. The lab documents this as a complaint and initiates an investigation.
Investigation Results	A reagent that passed QC testing and was subsequently used during testing was found to be contaminated, causing quantitative test results that were incorrectly higher for all specimens tested with that reagent.
Is this a reportable event?	**Yes**, if the erroneous test result **may have caused or contributed to a death or serious injury** (e.g., Cancer diagnosis test that cause Patient A to receive unnecessary treatment and Patient B to not receive or delay treatment) **or** the error was **caused by a malfunction** (e.g., Test does not have proper process or safeguards to prevent contamination). **No**, if this erroneous test result **did not cause or contribute to a death or serious injury** (e.g., Low-risk vitamin D level test).
Is a correction or removal required?	**Yes**. A correction is required to rectify this, and possibly other affected specimens, erroneous test result(s).
Is a recall required?	**Yes**. The original test report with the erroneous test result, and any other specimens that may have been affected, are recalled and replaced with a corrected test report with the correct test result.

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case study #4 – reagent issue; test results not reported

Issue	Lab personnel using a new lot of controls report that the positive and negative controls for a quantitative test repeatedly fails. No patient test results were reported. Another acceptable lot of controls was subsequently used for patient testing. Patient test results were reported using the acceptable controls.
Is this a complaint?	**No**. The test using the failed lot of controls was not distributed (i.e., test result was not reported.).
Investigation Results	The controls were found to be contaminated, causing it to fail acceptance criteria. This lot was quarantined and subsequently discarded.
Is this a reportable event?	**No**. The test using the failed lot of controls was not distributed (i.e., test result was not reported).
Is a correction or removal required?	**No**. The test using the failed lot of controls was not distributed (i.e., test result was not reported).
Is a recall required?	**No**. The test using the failed lot of controls was not distributed (i.e., test result was not reported).

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case study #5 – LIMS issue; test result reported

Issue	The ordering clinician calls the lab because the patient's test result was not consistent with patient's clinical data and symptoms.
Is this a complaint?	**Yes**. This complaint alleges a deficiency with the performance of the test. The lab documents this as a complaint and initiates an investigation.
Investigation Results	The test was performed correctly. However, due to a defect with the lab's validated commercial laboratory information system (LIMS), the incorrect test result was reported.
Is this a reportable event?	**Yes**, if the erroneous test result **may have caused or contributed to a death or serious injury** (e.g., Cancer diagnosis test that cause Patient A to receive unnecessary treatment and Patient B to not receive or delay treatment) **or** the error was **caused by a malfunction** (e.g., LIMS was not properly tested to ensure there were no defects). **No**, if this erroneous test result **did not cause or contribute to a death or serious injury** (e.g., Low-risk vitamin D level test).
Is a correction or removal required?	**No**. The erroneous test result must be corrected for CLIA purposes but the correction does not have to be reported to FDA since the commercial LIMS is not part of the LDT (device).
Is a recall required?	**No**. The erroneous test result must be corrected but no recall is required since the commercial LIMS is not part of the LDT (device).

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case study #6 – turnaround time

Issue	A patient calls the lab and states that the test turnaround time (TAT) is too long.
Is this a complaint?	**Yes**. This complaint alleges a deficiency with the quality of the test.
Investigation Results	The labeling for the test states that the TAT for the test is 10 days. The patient called to complain after only five days. While this complaint is not valid, it must still be recorded and investigated.
Is this a reportable event?	**No**. This was not an erroneous test result that may have caused or contributed to a death or serious injury, and it was not a malfunction.
Is a correction or removal required?	**No**. A correction or removal is not required since the LDT is being performed as stated in its labeling and instructions for use.
Is a recall required?	**No**. A recall is not required since the LDT is being performed as stated in its labeling and instructions for use.

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case study #7 – complaint to salesperson

Issue	An office assistant mentions to a lab's salesperson on Oct. 1st that several patients have stated that they don't like having to give four EDTA tubes of blood for the test because removing that much blood makes them feel faint. The salesperson relays this information to the lab's complaint handling department on Oct. 15th.
Is this a complaint?	**Yes**. This is an oral complaint that alleges a deficiency with the safety of the test. If the manufacturer (which includes all employees, not just lab personnel) of the LDT (device) becomes aware of any complaint, it must be treated as such.
Investigation Results	The lab's LDT was developed and validated using four EDTA tubes of whole blood. Specimen collection requirements and precautions for the test (e.g., ensure patient is hydrated when collecting specimens) are stated in its labeling and instructions for use. While this complaint is not valid, it must still be recorded as a complaint and investigated.
Is this a reportable event?	**No**. This was not an erroneous test result that may have caused or contributed to a death or serious injury, and it was not a malfunction. Note: If this had been a reportable event, the deadline to report to the FDA would be Oct. 30th (within 30 days of first becoming aware of the complaint), not Nov. 15th.
Is a correction or removal required?	**No**. A correction or removal is not required since the LDT is being performed as stated in its labeling and instructions for use.
Is a recall required?	**No**. A recall is not required since the LDT is being performed as stated in its labeling and instructions for use.

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Questions

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