FDA's Proposed Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)

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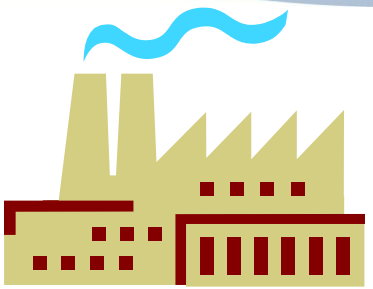
Overview

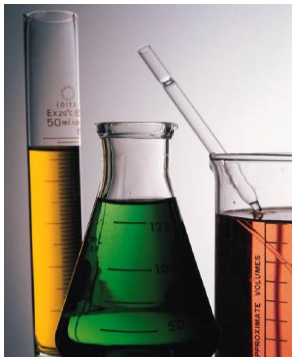
- **Initial public feedback in 2010**
  - Oversight framework suggestions
- **FDA's current proposal**
  - Continued enforcement discretion in some areas
  - Timeframe for enforcement in other areas
- **Next Steps**
  - Discussion of FDA's current proposal

Despite new public health risks, today's LDTs are still marketed under enforcement discretion by FDA.



"test kit" manufacturer

Performed in CLIA-certified lab



CLIA-certified lab

FDA "Enforcement Discretion"

Performed within same lab that developed test

Initial FDA Approach

- **Long-running discussion on need for oversight of LDTs**
  - SACGHS and other recommendations for oversight in last 10-15 yrs
- **Piecemeal approach**
  - ASR
  - IVDMIA

Risk Based Approach

- **Announcement in a 2010 Public Meeting**
- **Subsequent meetings with stakeholders**
  - Registration
  - Rare Disease
  - Unmet Needs
  - Certain tests are deeply rooted in the expertise of the laboratorian

Initial Public Feedback (2010)

- **Oversight Framework Suggestions**
  - Process should allow for stakeholder input and leverage external experts
  - Should use risk-based, phased-in strategy
  - Should provide reasonable transition period
  - Should provide clear definition of LDTs
  - Registry of all tests
    - Partnerships with other agencies
  - Process to address emerging diseases/emergency situations

Initial Public Feedback (2010)

- **Oversight Framework Suggestions (continued)**
  - Less oversight for certain categories of tests
    - Rare Diseases
    - No FDA approved/cleared alternative
    - Hospital based tests
    - Tests with extensive peer review
    - Tests performed in accredited lab or already approved by NY state
  - Post-Market Surveillance needed to protect public health
  - Significant Education/Outreach needed

FDA's Current Proposal

1. Enforce R&L with option for notification (no-fee alternative to R&L) to collect basic information on LDTs
2. Enforce Adverse Event Reporting
3. Use public process (including advisory panel) to obtain input on risk and priority for oversight
4. Phase-in enforcement of premarket review and QS requirements over ~9 years based on risk
5. Continue some enforcement discretion for specific categories.

"Traditional" LDTs

- **Proposed oversight:**
  - Enforcement discretion for premarket review and QS
  - Enforcement of R&L (with option for notification) and MDR
- **Proposed factors for enforcement discretion:**
  - Whether it is an LDT (designed, manufactured and used within a single lab);
  - Whether it is manufactured and used by a health care facility lab (such as one located in a hospital or clinic) for a patient that is being diagnosed and/or treated at that same health care facility or within the facility's healthcare system;
  - Whether it is comprised only of components and instruments that are legally marketed for clinical use; and
  - Whether it is interpreted by qualified laboratory professionals without the use of automated instrumentation or software for interpretation.

LDTs for Rare Diseases

- **Proposed oversight:**
  - Enforcement discretion for premarket review and QS
  - Enforcement of R&L (with option for notification) and MDR
- **Proposed factors for enforcement discretion:**
  - Whether it is an LDT (designed, manufactured and used within a single lab); and
  - Whether it meets the definition of a Humanitarian Use Device (HUD) under 21 CFR 814.102(a)(5) (i.e., number of persons who may be tested is fewer than 4,000 per year in the United States)

LDTs for Unmet Needs

- **Proposed oversight:**
  - Enforcement discretion for premarket review and QS
  - Enforcement of R&L (with option for notification) and MDR
- **Proposed factors for enforcement discretion:**
  - Whether it is an LDT (designed, manufactured and used within a single lab);
  - Whether there is no cleared or approved IVD available for the specific intended use; and
  - Whether it is manufactured and used by a health care facility lab (such as one located in a hospital or clinic) for a patient that is being diagnosed and/or treated at that same health care facility or within the facility's healthcare system.

Oversight Framework Proposal

	Notifi-cation*	MDRs	Premarket Review	QS Reg.	R&L **
LDTs used solely for **forensic** purposes					
LDTs used in CLIA-certified, high-complexity histocompatibility labs for **transplantation**					
Low-risk (Class I) LDTs	√	√			
LDTs used for **rare diseases** per HUD definition	√	√			
"**Traditional**" LDTs	√	√			
LDTs for **unmet needs** when no FDA cleared/approved alternative exists	√	√			

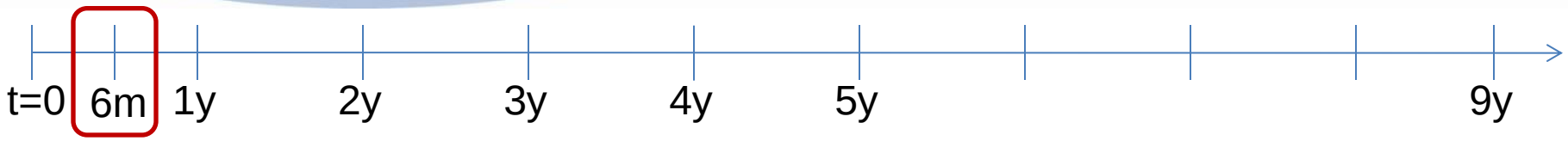
* Notification is not a requirement but an option to R&L.
**FDA intends to continue exercising enforcement discretion for R&L provided notification is completed.

Proposed Phase-In
(based on final guidance publication)

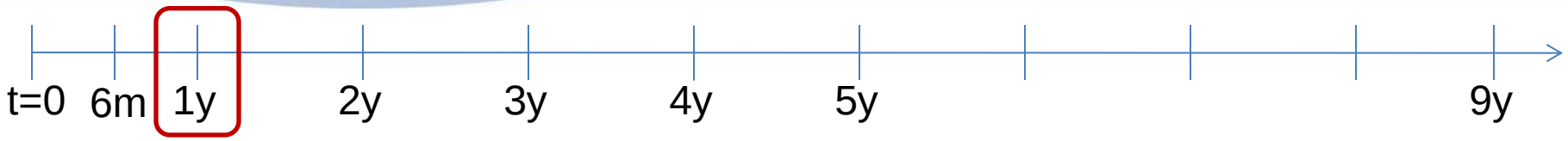
	Notifi-cation*	MDRs	Premarket Review	QS Reg.	R&L
Highest risk LDTs already on market • LDTs with same intended use as cleared/approved companion diagnostics • LDTs with same intended use as approved Class III medical devices • Certain LDTs for determining safety or effectiveness of blood or blood products	6m	6m	1y	Upon PMA submission	Upon PMA approval
Subsequent high risk LDTs in priority order developed with input through public process	6m	6m	2-5y	Upon PMA submission	Upon PMA approval
Moderate risk LDTs in priority order developed with input through public process	6m	6m	5-9y	Upon 510k clearance	Upon 510k clearance

* Notification is not a requirement but an option to R&L.

- Premarket review for all **NEW** (i.e., not currently marketed) LDTs that:
  - Have the same intended use as cleared/approved companion diagnostics
  - Have the same intended use as approved Class III medical devices
  - Certain LDTs for determining safety or effectiveness of blood or blood products

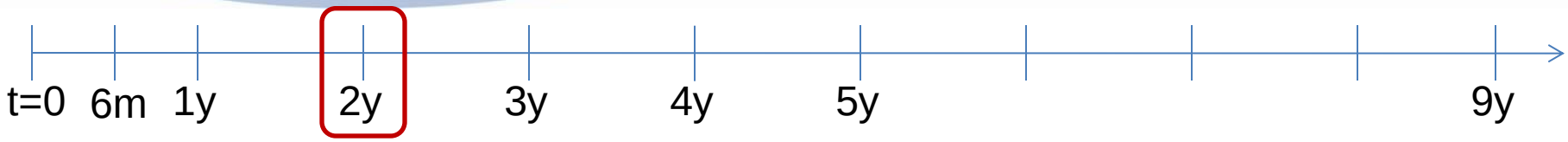


- By 6m: Notification (or R&L) and adverse event reporting for all **currently marketed** LDTs except:
  - those used solely for forensic purposes
  - those used in CLIA-certified, high-complexity histocompatibility labs for transplantation
- After 6m: Notification (or R&L) of all **NEW** LDTs prior to marketing
  - includes notification for significant changes to the marketed intended use of existing LDTs

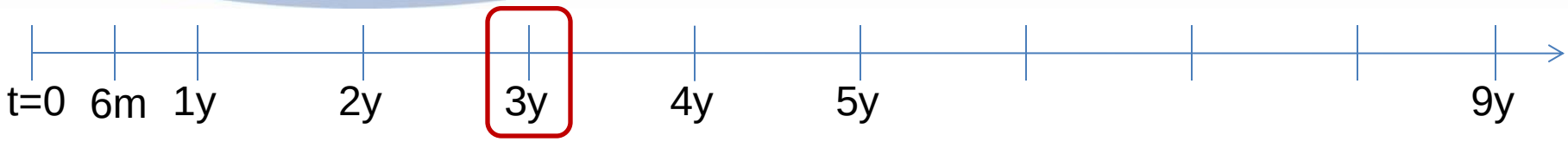


- Premarket submission for **currently marketed LDTs** that:
  - **Have the same intended use as cleared/approved companion diagnostics**
  - **Have the same intended use as approved Class III medical devices**
  - **Certain LDTs for determining safety or effectiveness of blood or blood products**
- Compliance with QS reg at time of PMA submission
- Compliance with R&L upon PMA approval

- Public process to get input on classification for existing LDTs
  - Will include use of advisory panel
  - Will issue draft guidance on LDT device classification for public comment
- Public process to get input on priority for remaining high-risk LDTs
  - Will include use of advisory panel

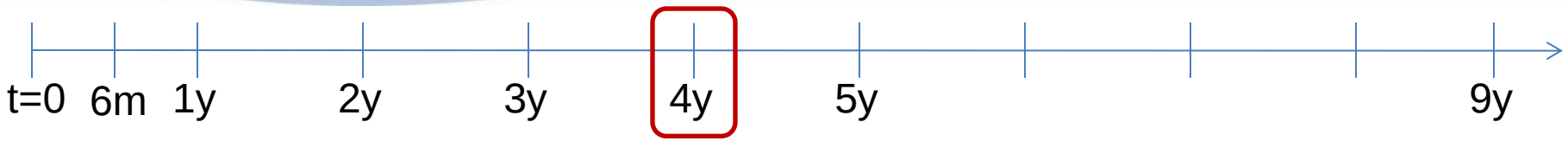


- Publication of a guidance on LDT device classification
- Publication of priority list for remaining high-risk LDTs



- Premarket submission for **first prioritized high-risk group**
  - Compliance with QS reg at time of PMA submission
  - Compliance with R&L upon PMA approval

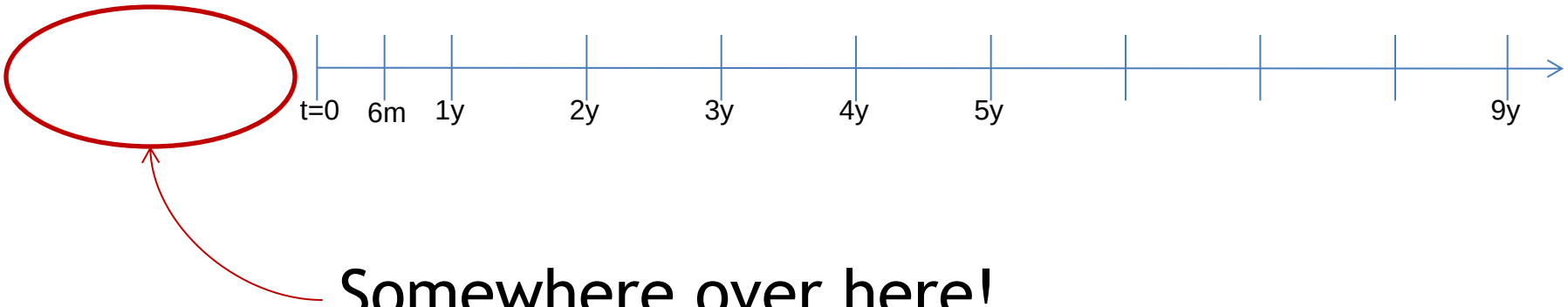
- Premarket submission for all **remaining high-risk LDTs** according to priority list announced at year 2
  - Compliance with QS reg at time of PMA submission
  - Compliance with R&L upon PMA approval
- Public process to get input on priority for remaining moderate-risk LDTs
  - Will include use of advisory panel



- Publication of priority list for moderate-risk LDTs
  - After considering input received through public process including advisory panel

- Premarket submission for all **moderate-risk LDTs** according to priority list announced at year 4
  - FDA anticipates use of third party reviewers
  - Compliance with QS reg at time of 510(k) clearance
  - Compliance with R&L at time of 510(k) clearance

Where are we today?



Somewhere over here!

FDA does not intend to implement the proposed enforcement policy for LDTs prior to publication of final guidances.

What's Next

- Public discussion of draft oversight framework
  - 120 day public comment period
  - Public Workshop in January

Goal: to work with all stakeholders to determine a framework for oversight that is in the best interest of public health

- FDA analysis of public input and incorporation of appropriate revisions in the final guidances
- Publication of final guidances (t=0 in timeline)
- Implementation

Questions?

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