Proposed Regulatory Framework for Laboratory Developed Tests

Alberto Gutierrez, PhD
Director, Office of In Vitro Diagnostics and Radiological Health
FDA Center for Devices and Radiological Health

CLIAC

November 6, 2014

IVD Regulation

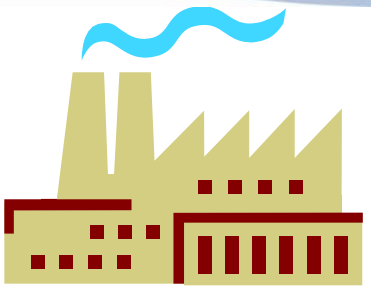
- In Vitro Diagnostic tests (IVDs) are a critical component of current clinical care, influencing *ca.* 80% of all clinical decision-making

- Through the 1976 medical device amendments to the FFDCA, FDA has the authority to regulate all laboratory tests, regardless of whether they are commercially distributed or developed by a laboratory

- FDA is charged with ensuring that IVDs are safe and effective (do what they say they will do) for their intended use so that patients are not unnecessarily harmed

Benefits of FDA Oversight

- Independent Premarket Review
  - Independent assessment occurs prior to clinical use of test
  - Ensures test limitations are described
  - Ensures test performance claims are supported
- Clinical Validation
  - Provide assurances that test provides clinically meaningful results
- Post Market Surveillance and Post Market Controls
  - Mechanism to assist manufacturers and FDA in identifying problems with tests and assuring the performance of the IVD through out its life cycle
- Oversight of Investigational-Stage Devices
  - Ensures patients and physicians understand the scientific evidence supporting use of a diagnostic test



"test kit" manufacturer

Performed in CLIA-certified lab

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

CLIA-certified lab

FDA "Enforcement Discretion"

Performed within same lab that developed test

Public Health Need for Greater Oversight

- Evolution of LDT technology, marketing, and business models has:
  - Increased risk associated with LDTs
  - Created gaps in LDT Oversight
- Consequences
  - Significant adverse health consequences
  - Unnecessary healthcare costs
  - Uneven playing field
  - Could undermine progress of personalized medicine, which depends on tests that work

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

U.S. Food and Drug Administration
Protecting and Promoting Public Health
www.fda.gov

FDA's Current Proposal

Upcoming draft guidance is intended to initiate discussions with all stakeholders on a framework that will ***best serve public health***

U.S. Department of Health and Human Services

U.S. Food and D
Protecting and Promo

Home | Food | Drugs | Medical Devices

News & Events

Home > News & Events > Newsroom > Press Announcements

FDA News Release

FDA takes steps to help ensure certain diagnostic tests

Reinforces agency's commitment to fostering personalized me

For Immediate Release July 31, 2014

Release Today, the U.S. Food and Drug Administ
certain tests used by health care profes
provide accurate, consistent and reliable

First, the FDA is issuing a final guidance

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

JUL 31 2014

The Honorable Tom Harkin
Chairman
Committee on Health, Education, Labor and Pensions
United States Senate
Washington, D.C. 20510

Dear Mr. Chairman:

As required by Section 1143 of the Food and Drug Administration Safety and Innovation Act (FDASIA), signed into law by the President on July 9, 2012, the Food and Drug Administration (FDA) is providing notification to the Committee on Health, Education, Labor and Pensions and the House Committee on Energy and Commerce of its intent to issue draft guidance entitled *Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)* (Framework Guidance) and an accompanying draft guidance document entitled *FDA Notification and Medical Device Reporting for Laboratory Developed Tests (LDTs)*. The anticipated details of these draft guidance documents are included in this notification and are found in the enclosure to this notification.

FDA's Current Proposal

1. Collect basic information on all LDTs through new notification process (i.e., no-fee alternative to R&L)
2. Use public process (i.e., advisory committees) to obtain input on risk and priority for regulation
3. Phase-in regulatory framework over ~9 years based on risk
4. Continue some enforcement discretion for specific categories determined by FDA to be in the best interest of public health

Continued Enforcement Discretion

	Notifi-cation	MDRs	Pre-market Review	QSRs	R&L
LDTs used solely for **forensic** purposes	X	X	X	X	X
LDTs used in CLIA –certified, high-complexity histocompatibility labs for **transplantation**	X	X	X	X	X
low risk medical devices, including **low risk** LDTs			X	X	X*
LDTs used for **rare diseases** per HUD definition			X	X	X*
"**Traditional**" LDTs			X	X	X*
LDTs for **unmet needs** when no FDA cleared/approved alternative exists			X	X	X*

*enforcement discretion will be applied to R&L provided notification is completed

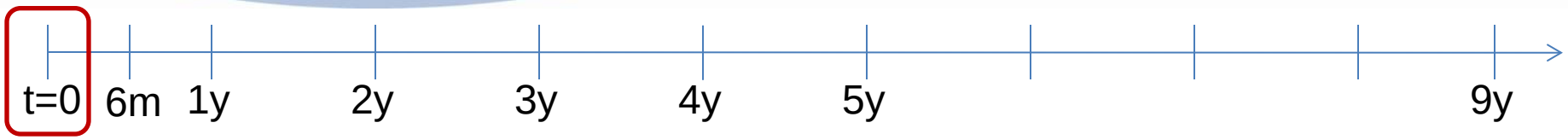
Notification and AE Reporting *only*

	Notifi-cation	MDRs	Pre-market Review	QSRs	R&L
LDTs used solely for **forensic** purposes	X	X	X	X	X
LDTs used in CLIA –certified, high-complexity histocompatibility labs for **transplantation**	X	X	X	X	X
low risk medical devices, including **low risk** LDTs	6m	6m	X	X	X*
LDTs used for **rare diseases** per HUD definition	6m	6m	X	X	X*
"**Traditional**" LDTs	6m	6m	X	X	X*
LDTs for **unmet needs** when no FDA cleared/approved alternative exists	6m	6m	X	X	X*

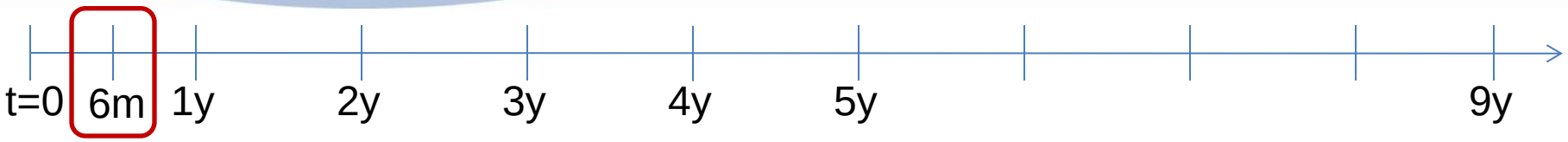
*enforcement discretion will be applied to R&L provided notification is completed

Risk-Based, Phased-In Enforcement

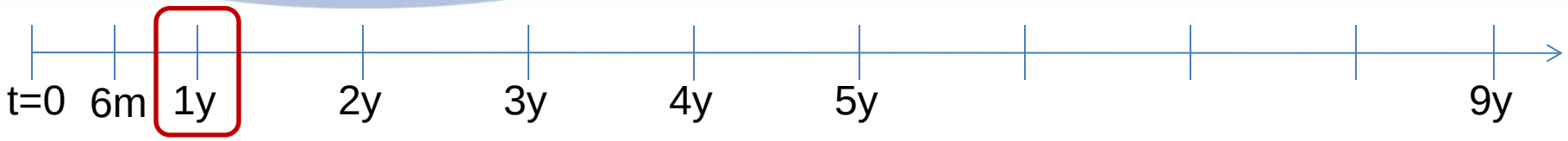
	Notifi-cation	MDRs	Pre-market Review	QSRs	R&L
Highest risk LDTs already on market • LDTs with same intended use as cleared/approved companion diagnostics • LDTs with same intended use as approved Class III medical devices • Certain LDTs for determining safety and effectiveness of blood or blood products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



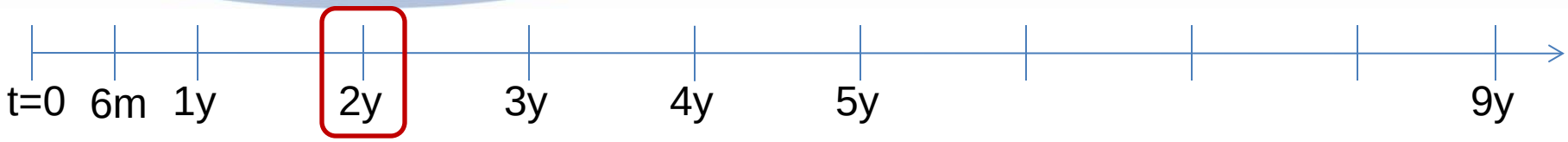
- Premarket review for all **NEW** (i.e., not currently marketed) IVDs that:
  - Have the same intended use as cleared/approved companion diagnostics
  - Have the same intended use as approved Class III medical devices
  - Certain LDTs for determining safety and effectiveness of blood or blood products



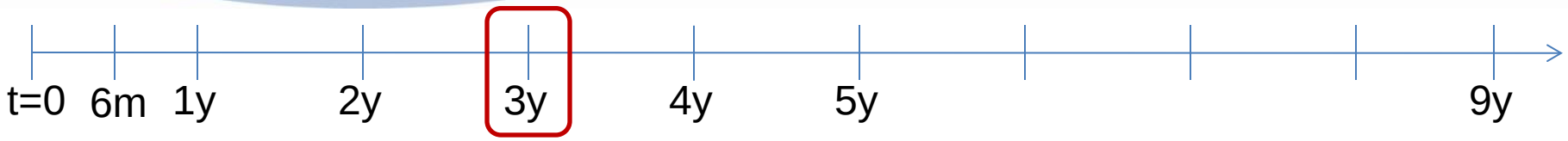
- By 6m: Notification and adverse event reporting for all **currently marketed** LDTs except:
  - those used solely for forensic purposes
  - those used in CLIA –certified, high-complexity histocompatibility labs for transplantation
- After 6m: Begin requirement for notification of all **NEW** LDTs prior to marketing
  - Includes notification for significant changes to existing LDTs



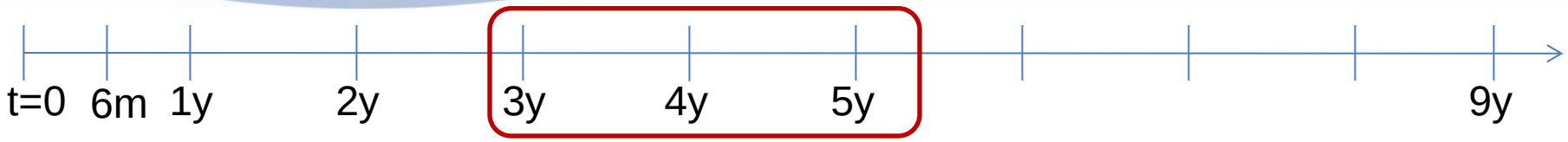
- Premarket review for **currently marketed IVDs** that:
  - **Have the same intended use as cleared/approved companion diagnostics**
  - **Have the same intended use as approved Class III medical devices**
  - **Certain LDTs for determining safety and effectiveness of blood or blood products**
- Subject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



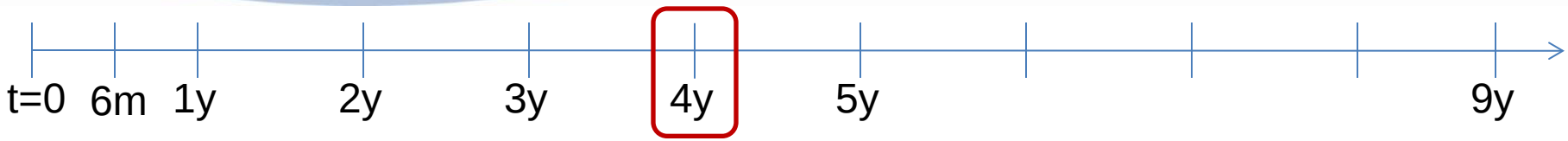
- Publication of priority list for remaining high-risk LDTs
  - Based on public process including advisory panels
  - Publication in FDA guidance



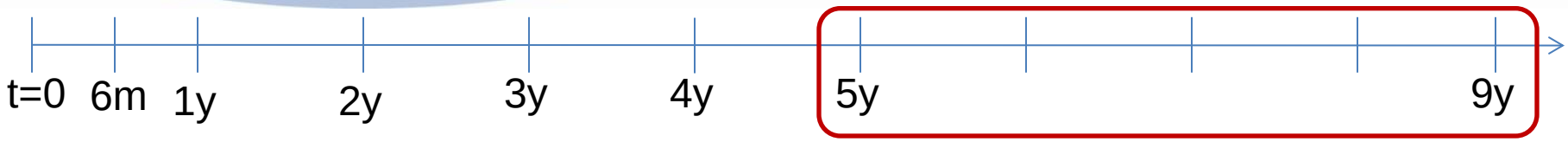
- Premarket Review for **first prioritized high-risk group** which FDA anticipates may include:
  - Devices that act like companion diagnostics
  - Screening devices for serious diseases/conditions intended for use in asymptomatic patients without other confirmation
  - Diagnostics for certain infectious diseases with high-risk intended uses
- Subject to QS reg at time of PMA submission
- Subject to R&L upon PMA approval



- Premarket Review for all **remaining high-risk LDTs** according to priority list announced at year 2
- Subject to QS reg at time of PMA submission
- Subject to R&L upon PMA approval

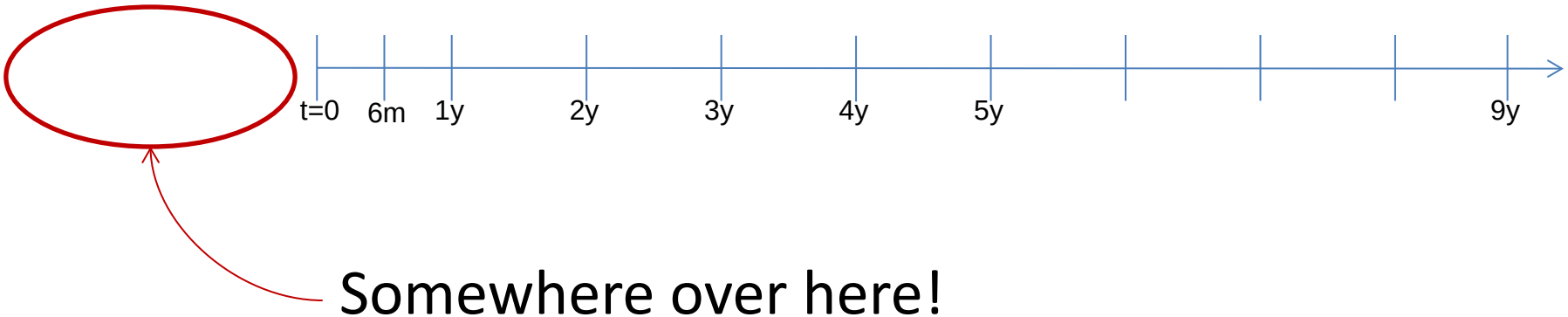


- Publication of priority list for moderate-risk LDTs
  - Based on public process including advisory panels
  - Publication in FDA guidance



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

Where are we today?



No implementation will begin prior to publication of final guidances.

What's Next

- Publication of *DRAFT* guidances
- Solicitation of Public Input via FR Notice announcing:
  - 90 day public comment period
  - Public Workshop

  Goal: to work with all stakeholders to determine a framework for regulation that is in the best interest of public health
- Analysis of public input and edits to guidances

Acronym List

SACGHS	Secretary's Advisory Committee on Genetics, Health, and Society
ASR	Alternative Summary Reporting
IVDMIA	In Vitro Diagnostic Multivariate Index Assay
FFDCA	Federal Food, Drug, and Cosmetic Act
IVDs	In Vitro Diagnostic tests
HUD	Humanitarian Use Device