Laboratory Developed Tests
A Regulatory History and Update

Jonathan R. Genzen, MD, PhD

ASCLS Annual Meeting
August 1, 2017

DISCLOSURES

- **University of Utah**
  - Associate Professor (Clinical)
- **ARUP Laboratories**
  - Medical Director, ARUP Automated Core Laboratory
  - Vice President | Section Chief, Clinical Chemistry
  - Oversight over LDTs

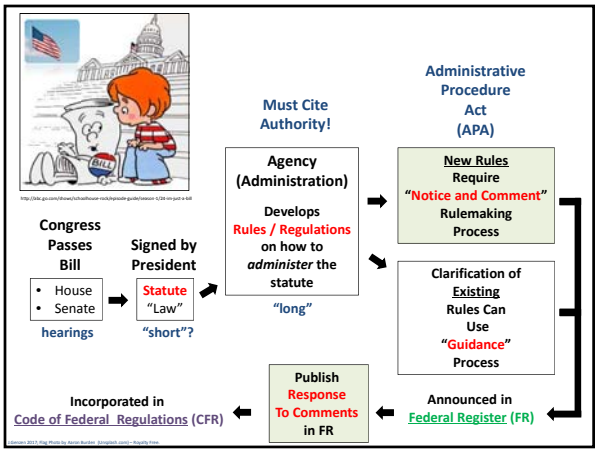
The views presented are my own and are not meant to be representative of my employer

OBJECTIVES

- **Identify regulatory authority for reagents under the Medical Device Amendments (MDA)**
- **Assess the requirements for assay validations under the Clinical Laboratory Improvement Amendments of 1988 (CLIA'88)**
- **Appraise current regulatory efforts regarding LDTs at the federal level**

OUTLINE

- **Background**
- **History of Federal Regulations**
  "How we got here"
  - **Medical Device Amendments of 1976 (MDA)**
  - **Clinical Laboratory Improvement Amendments of 1988 (CLIA'88)**
- **LDT Turning Point (1992-1998)**
- **Possible Regulatory Oversight (2010-2017)**
  "What Now?"



FDA

Federal Statutes

1906 **Pure Foods and Drugs Act**

1938 **Federal Food, Drug, and Cosmetic Act (FFDCA; "The Act")**

1976 **Medical Device Amendments (MDA)**

Pure Foods and Drugs Act

1906 **Pure Foods and Drugs Act**

Prohibited misbranded and adulterated foods, drinks, and drugs in interstate commerce

"Wiley Act"

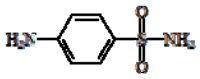
Dr. Harvey Washington Wiley

Chief Chemist
U.S. Department of Agriculture
Bureau of Chemistry

BUT - burden placed on the ***government*** to prove misbranding or adulteration

1937 - Sulfanilamide Tragedy

Source: www.the-scientist.com



ELIXIR
SULFANILAMIDE

Each fluidounce represents:
Sulfanilamide. 33 gr.

Dose, begin with 2 to 3 teaspoonfuls in water every four hours. Decrease in twenty-four to forty-eight hours to 1 or 2 teaspoonfuls and continue at this dose until recovery.

[Trade-mark]

THE S. E. MASSENGILL COMPANY
Manufacturing Pharmacists
BRISTOL, TENN.-VA.

Plus **Diethylene Glycol**

U.S. Races Death to Save 700 From Elixir

Federal Food, Drug, and Cosmetic Act

1938 **FFDCA**

Manufacturers were required to show that a drug was safe *before* it could be marketed

Regarding **DEVICES**

Prohibited ***misbranding*** and ***adulteration*** of "devices"

Defined **device** as:

Statute

"instruments, apparatus, and contrivances, including their components, parts, and accessories, intended (1) for use in the **diagnosis**, cure, mitigation, treatment, or prevention of disease in man or other animals; or (2) to affect the structure or any function of the body of man or other animals [Sec. 201(h)]

BUT, it did ***NOT*** provide a **comprehensive regulatory system** for medical device safety, efficacy, or evaluation

Federal Food, Drug, and Cosmetic Act. 52 STAT 1040. Public Law Number 75-717. June 25, 1938. http://legiscworks.org/sal/52/stats/STATUTE-52-Pg1040a.pdf Accessed 8/13/2016.

Regulatory Standards (1940-1970)

DRUGS

Devices

Microsoft Clipart Library

1969 - Bacto-Unidisk Case

U.S. Supreme Court

United States v. Bacto-Unidisk
394 U.S. 784
(1969)

Chief Justice Earl Warren

Antimicrobial Susceptibility Disk

The Secretary of Health, Education, and Welfare **had the authority to regulate the device as a drug** such that the "*Secretary can subject it to pre-market clearance regulations*"

1969 – Consumer Protection

Special Message to Congress on Consumer Protection

October 30, 1969

President Richard Nixon

"certain ***minimum standards*** should be established for such devices" and "a thorough study of ***medical device regulation***" would be undertaken by the Department of Health, Education, and Welfare

1970 - "Cooper Committee Report"

Study Group on Medical Devices
Department of Health, Education, and Welfare.
Medical Devices: A Legislative Plan.
September 1970.

Dr. Theodore Cooper (1929-1993)
Director of the National Heart and Lung Institute

Proposed broad recommendations for **review** and **categorization** of **medical devices** and establishment of **performance standards**.

1970s – Food and Drug Administration

January 1972 **FDA NOTICE Released**

They would "in the near future propose regulations governing ***in vitro* diagnostic products**" which include "**reagents, instruments, and kits**"

August 1972 **FDA NOTICE OF PROPOSED RULEMAKING**

Asserted jurisdiction over **in vitro diagnostic products** stating that they are medical *drugs or devices* under FFDCA

1970s – Food and Drug Administration

1973 **FDA Releases Response to Comments of Proposed Rules**

Reiterated its authority

1973 **FDA Incorporates Procedural Regulations into Code of Federal Regulations** (21 CFR § 167)

- Re-codified in **March 1974** [21 CFR § 328]
- Re-codified in **February 1976** [21 CFR § 809]
- Amended in **February 1980** [45 FR 7484]

Who Cares?

In Vitro Diagnostic Product

***Definition:* "*In Vitro* Diagnostic Product"**

Regulation

"**reagents**, **instruments**, and **systems** intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the **collection**, **preparation**, and **examination** of **specimens** taken from the human body. **These products are devices** as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the act)…"

1973 - Senate Hearings

U.S. SENATE - September 1973

Hearings before the Subcommittee on Health of the Committee on Labor and Public Welfare United States Senate

"**Medical Device Amendments, 1973**"

3 Proposed Bills – S. 2368; S. 1446; S. 1337

- **Strong** focus on **conventional devices** (IUDs)
- There was testimony that ***in vitro* diagnostics** were **devices**
- "**Custom devices**" were discussed (in the context of dental implants)
- **The concepts of LDTs or "home-brew" testing NOT discussed**

1975 – House of Representatives

U.S. House - September 1975

Hearings before the Subcommittee on Health and the Environment of the Committee on Interstate and Foreign Commerce.

Similar content to 1973 Senate hearings

Testimony from Dr. Theodore Cooper

Opinion

"it should also be made clear that FDA would be able to take necessary action to curb a practitioner's use of a ***custom device*** as a course of conduct on a number of patients, where **this use is repeated to such an extent that the practitioner is in effect conducting unsupervised experiments, or allowing the marketing of a product that would otherwise be unlawful**"

LDTs or "home-brew" testing NOT discussed

Medical Device Amendments of 1976

An act "to amend the Federal Food, Drug, and Cosmetic Act [FFDCA; 1938] to provide for the **safety** and **effectiveness** of **medical devices** intended for human use, and for other purposes"

- Authorized FDA to regulate **in vitro diagnostic devices**
- Established Device Classes (risk based):
  - **Class I**, General Controls (**lowest risk**)
  - **Class II**, Performance Standard (**moderate risk**)
    - Subject to General and Special Controls
    - Premarket notification (510k) "*clearance*"
  - **Class III**, Premarket Approval (**highest risk**); PMA; "*approval*"

Medical Device Amendments of 1976

- Includes Amendment to Section 201
  - (B) Section 15(d) of the **Federal Trade Commission Act** is amended to read as follows:
  - (d) the term '**device**'…means an instrument, apparatus, implement, machine, contrivance, implant, **in vitro reagent**, or other similar or **related *article***…., which is:
    - (2) **intended for use in the diagnosis of disease or other condition, or in the cure, mitigation, treatment, or prevention of disease**, in man or other animals…

Statute

In Vitro Reagents are Devices

Medical Device Amendments of 1976

*The **statute**…*

- **DOES NOT** specifically discuss the "concept" of LDTs
- **DOES** include several concepts that should be considered if the FDA *were* to regulate LDTs
  - **1) Records and reporting requirements**
  - **2) Custom devices**

1) MDA – Records and Reports

Prescribed regulations…

Statute

"shall not impose requirements **unduly burdensome** to a device manufacturer, importer, or distributor taking into account his **cost** of complying with such requirements and **the need for the protection of the public health** and the implementation of this Act…" [SEC. 519 (a)].

Exemption from reporting…

Statute

"any practitioner who is **licensed by law** to prescribe or administer devices intended for use in humans and who manufactures or imports devices **solely for use in the course of his professional practice**…" [17; SEC. 519 (b) (1)].

What is the professional practice of clinical pathology?

2) MDA – Custom Devices

Statute

"**in order to comply with the order of a physician or dentist**" [or other specially qualified person designated under regulations…] "necessarily deviates from an otherwise applicable performance standard…if

•The device is **not generally available** in finished form for purchase or for dispensing upon prescription ***AND*** is **not offered through labeling or advertising by the manufacturer, importer, or distributor thereof for commercial distribution**, ***AND***

•Such device---

(A)(i) is intended for use by an **individual patient** named in such order of such physician or dentist (or other specially qualified person so designated) ***AND*** is to be made in a specific form for such patient, ***OR***

(ii) is intended to **meet the special needs of such physician** or dentist (or other specially qualified person so designated) in **the course of the professional practice** of such physician or dentist (or other specially qualified person so designed, ***AND***

(B) is ***NOT* generally available to or generally used by other physicians** or dentists (or other specially qualified persons so designated)" [17; SEC. 520 (b)]

1977 Final Rule – Establishment Registration

Regulation

Persons EXEMPT from Registration

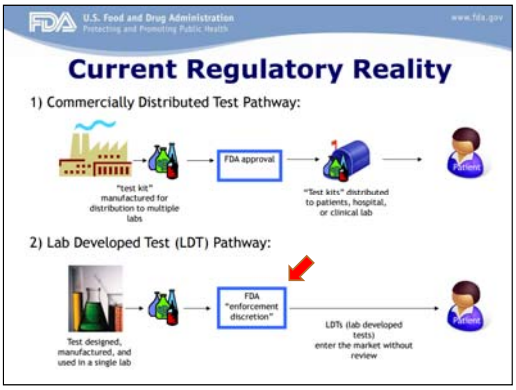
"(i) Persons who dispense devices to the ultimate consumer or whose **major responsibility is to render a service** necessary to provide the consumer (i.e. patient, physician, laymen, etc.) with a device or the benefits to be derived from the use of a device; for example, a…**clinical laboratory**"

"Is LDT Notification *de facto* registration?"

If YES, then Draft Guidance can't change this – requires Notice and Comment Rulemaking.

1976-1992

- For **16 years** after passage of the Medical Device Amendments, the **FDA did not** (at least publically) **assert *any* authority over LDTs**
- In practice, there were two "pathways" for laboratory testing:
  - **Commercially Distributed Pathway** (*regulated by the FDA*)
  - **LDTs** (*not regulated by the FDA*)



CLIA'88

1967 – Partnership for Health Amendments

Clinical Laboratory Improvement Act of 1967

- Licensing program for clinical laboratories involved in **interstate commerce**

"No person may **solicit** or **accept** in interstate commerce, directly or indirectly, any specimen for laboratory examination or other laboratory procedures, unless there is in effect a license…" [p536]

CLIA'67 - Consequences

- **Fragmented** system
- Didn't apply to ALL clinical laboratories
- **Physician office laboratories** were excluded

Different **quality requirements** for different types of laboratories led to **growing national concern over laboratory quality** (e.g. PAP smears)

1988 – House of Representatives #1

U.S. House - 1988

Hearings before the Subcommittee on **Regulation and Business Opportunities of the House Committee on Small Business**

"Deadly Mistakes: Are Laboratory Results Reliable"

LDTs not discussed!

1988 – House of Representatives #2

U.S. House - 1988

Hearings before the Subcommittee on **Oversight and Investigations of the House Committee on Energy and Commerce**

"Clinical Laboratories"

LDTs not discussed!

1988 – Senate Hearings

U.S. Senate - 1988

Hearings before the Subcommittee on **Oversight of Government Management of the Senate Committee on Governmental Affairs**

"Health Care Financing Administration's Management of Medical Laboratories"

LDTs discussed **once** in testimony!

***12 years* after MDA passage!**

1988 – Senate Hearings

U.S. Senate - 1988

Hearings before the Subcommittee on **Oversight of Government Management of the Senate Committee on Governmental Affairs**

Written testimony of **Dr. Herbert W. Dickerman**
Director of the **New York State Wadsworth Center for Laboratories and Research**

Describing the Federal program for laboratory regulation…

"while FDA requirements must be met if a kit or reagent is to be commercially marketed, **labs that use their own techniques and reagents need no approval**" [p235].

Testimony / Opinion

Clinical Laboratory Improvement Amendments of 1988 (CLIA '88)

"An amendment to the Public Health Services Act [PHSA] in which Congress revised the federal program for certification and **oversight of clinical laboratory testing**"

- Quality standards
- Certification program

- "**All facilities** in the United States that perform **laboratory testing** on **human specimens** for **health assessment or the diagnosis, prevention, or treatment of disease** are regulated under [CLIA]"

CLIA – PERFORMANCE SPECIFICATIONS

42 CFR 493.1253 - Standard: **Establishment and verification of performance specifications**

(2) ***Establishment of performance specifications.*** Each laboratory that **modifies an FDA-cleared or approved test system**, or **introduces a test system not subject to FDA clearance or approval** (including **methods developed in-house** and standardized methods such as text book procedures), or uses a test system in which performance specifications are not provided by the manufacturer ***must, before reporting patient test results, establish for each test system the performance specifications for the following performance characteristics, as applicable:***

(i) Accuracy.
(ii) Precision.
(iii) Analytical sensitivity.
(iv) Analytical specificity to include interfering substances.
(v) Reportable range of test results for the test system.
(vi) Reference intervals (normal values).
(vii) Any other performance characteristic required for test performance.

Regulation NOT Statute

Time	Source	Verbiage
Pre-CLIA'88	Examples: 39 C.F.R. § 405.1317 (1974); 42 C.F.R. § 74.20 (1987); 42 C.F.R. § 405.1317 (1988)	"(a) *Standard; general.* Quality controls imposed and practiced by the laboratory must provide for and assure: (1)…validation of methods"
Pre-CLIA'88 1988	*Proposed rule:* Medicare, Medicaid and CLIA Programs; Revision of the Laboratory Regulations for the Medicare, Medicaid, and Clinical Laboratories Improvement Act of 1967 Programs. 53 Fed. Reg. 29590 (August 5, 1988) (to be codified at 42 C.F.R. pt 493).	*Proposed* § 493.235 "The laboratory must have a written protocol and documentation of the validation of each method that verified that the method products test results within the laboratory's stated performance characteristics… (c) A method used by the laboratory must be validated before it is used and documentation of the validation must be available…"
CLIA'88 1988	Clinical Laboratory Improvement Amendments of 1988. Pub. L. 100-578. 102 Stat. 2903. 31 October, 1988.	*Authorization:* "(f) Standards; (1) In General – **The Secretary shall issue standards to assure consistent performance by laboratories**…of valid and reliable laboratory examinations…(A) to maintain a quality assurance and quality control program adequate and appropriate for the **validity and reliability of the laboratory examinations** and other procedures of the laboratory…"
1990	*Final rule with comment period:* Medicare, Medicaid and CLIA Programs; Revision of the Laboratory Regulations for the Medicare, Medicaid, and Clinical Laboratories Improvement Act of 1967 Programs. 55 Fed. Reg. 9538 (March 14, 1990)	"The laboratory must have a written protocol and documentation for the validation of each method that verifies that the method produces test results within the laboratory's stated performance characteristics. Method validation must be performed before a test procedure is placed into routine use…"
1992	*Final rule with comment period:* Medicare, Medicaid and CLIA Programs; Regulations Implementing the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 57 Fed. Reg. 7002 (February 28, 1992) (codified at 42 C.F.R. § 493.1213 (1992))	"After September 1, 1992, a laboratory that introduces a new procedure for patient testing using: **a method developed in-house; a modification of the manufacturer's test procedure; or a method (instrument, kit, or test system) that has not been cleared by the FDA** as meeting the CLIA requirements for general quality control, must, prior to reporting patient test results…"
2003	*Final rule:* Medicare, Medicaid and CLIA Programs; Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications. 68 Fed. Reg. 3640 (January 24, 2003) (codified at 42 C.F.R. § 493.1253 (2003))	"Each laboratory that modifies an FDA-cleared or approved test system, or introduces a test system not subject to FDA clearance or approval (included methods developed in-house and standardized methods such as text book procedures, Gram stain, or potassium hydroxide preparations), or uses a test system in which performance specifications are not provided by the manufacturer must, before reporting patient test results, establish for each test system the performance specifications for the following performance characteristics…"
2003	*Final Rule; correction:* 68 Fed. Reg. 50722 (August 22, 2003) (to be codified at 42 C.F.R pt. 493).	Deleted "Gram stain, or potassium hydroxide preparations" from above text.

Summarizing FDA vs CMS "Roles"

FDA

- *Authority:* FFDCA / MDA
- **Safety** and **Effectiveness** of Devices / Reagents
- Quality of **Design** and **Manufacture**
- **Analytical** *and* **Clinical Validity**

CMS

- *Authority:* CLIA
- Quality of **Clinical Testing Process**
- Quality of the **Laboratory**
- Requirements to **Assess Performance**
- **Analytical Validity**

Regulation of Clinical Tests: In Vitro Diagnostic (IVD) Devices, Laboratory Developed Tests (LDTs), and Genetic Tests; Congressional Research Service; 7-5700 R43638 (Burke, Gitter) & Consumer Genetic testing, testimony on July 22, 2010

1992

1992 – FDA Draft CPG

Aug 3, 1992 - FDA released **draft Compliance Policy Guide (CPG):**

"Commercialization of Unapproved *In Vitro* Diagnostic Devices Labeled for Research and Investigation"

Draft CPG

"It has **come to the attention** of the FDA that laboratories have been **manufacturing**, "**home brew**" products, either from products already on the market, or from components, and utilizing these unapproved products for diagnostic purposes. **These products are subject to the same regulatory requirements as any unapproved medical device** not identified in Attachment A".

Commercialization of Unapproved In Vitro Diagnostic Devices Labeled for Research and Investigation (Draft Compliance Policy Guide). Food and Drug Administration. Center for Devices and Radiological Health. August 3, 1992. Rockville, MD.

1992 – Citizen Petition to CPG

October/December 1992 – **Citizen Petition** filed by **Hyman, Phelps & McNamara** (law firm representing "laboratories that would be affected")

"…***request that the Commissioner of Food and Drugs not regulate as medical devices assays developed by clinical reference laboratories strictly for in-house use***"

Grounds

- **Inconsistent with CLIA**
- FDA **lacks Statutory Authority** to Regulate In-House Assays
- CPG Would Violate the **Administrative Procedure Act**
- CPG Would **Diminish the Quality of Health Care**

Oct 22, 1992 Citizen Petition, Law Offices of Hyman, Phelps, & McNamara, to Food and Drug Administration (FOI-0603)

1997 – Analyte Specific Reagent (ASR)

Federal Register 21 CFR Parts 809 and 864; Medical Devices; **Classification / Reclassification; Restricted Devices; Analyte Specific Reagents (FINAL RULE)**

III. Response to Comments

General Comments, Comment 9 (about device classification)

"FDA…appreciates the concerns raised about the **development of in-house tests** and the current marketing of test services based on tests that have not been reviewed independently for safety and effectiveness. **FDA believes that clinical laboratories that develop such tests are acting as manufacturers of medical devices and are subject to FDA jurisdiction under the act**."

Response to Comment in Federal Register

Federal Register / Vol. 62, No. 225 / Friday, November 21, 1997 / Rules and Regulations 62249

Audience Questions

How many of you work in clinical laboratories?

How many of you work in manufacturing facilities?

Does your lab offer laboratory developed tests?

2010

2010 – July 19-20th, FDA Public Meeting

Jeffrey Shuren, Director of the Center for Devices and Radiological Health, announced that **FDA intends on regulating all LDTs**

- Moving from "**enforcement discretion**" to "**exercise oversight**"
- FDA plans to issue **Guidance Document** instead of **Notice and Comment Rulemaking**

RATIONALE PROVIDED

- Volume and types of LDTs have **grown**. Now commercial labs and/or biotechnology companies.
- LDTs have **evolved** to be more like commercial *in vitro* devices. Not just regional with direct contact to ordering clinician.
- LDT route to market presents a favorable **business model** and driving venture capital funding for clinical diagnostics; competitive disadvantage to FDA premarket review.
- Some LDTs **aggressively marketed** directly to clinicians via Internet.
- **Public needs assurances** that LDTs are sound and reliable.

Draft Guidance vs Notice and Comment

(5) DR. SHUREN: Sure. The reason why
(6) not for notice and comment rulemaking is
(7) because the requirements actually already
(8) apply now. The law is in effect. We have
(9) simply, as a matter of policy, determined not
(10) to exercise or not to enforce that authority
(11) as of right now.

2010

Policy vs Practice

Clearly had a *practice* of not exercising oversight

Timeline
- Claim that authority existed since 1976
- Did not recognize issue until 1992
- Did not announce intention until 2010

Therefore **Guidance Process** Since Not Creating "New Rules"

2010-2014

- **2010** onward – FDA Created Draft Guidelines
- **August 2013** – Nine Democratic Congressmen wrote letter to OMB urging release:
  "We have reached a critical point in the development of advanced diagnostics at which it has become essential that FDA move this guidance forward to ensure appropriate and efficient oversight of safe and effective diagnostics."
- **July 11, 2014** – Five Democratic Senators wrote letter to OMB urging release, stating
  "for years this draft guidance has languished at OMB causing continued unpredictability and uncertainty"
- **July 31, 2014** – FDA Notified Congress of its intent to release the Draft Guidance documents

OMB review not publically available

October 3, 2014

Framework for Regulatory Oversight

- **"Notification"** to FDA of all LDTs
- **Medical device reporting** (e.g., adverse events)
- Enforcement discretion for **forensic LDT** and **HLA/transplant**
- Enforcement discretion (with respect to premarket review requirements) for **low-risk LDTs**, "Traditional LDTs", LDTs used for rare diseases, and "LDTs for Unmet Needs"
- Risk-based, phased-in approach to enforcing the premarket review requirements for other **high-risk** and **moderate-risk LDTs**
- Use of **clinical literature** to support a demonstration of clinical validity
- **Third-party review** for many moderate risk LDTs
- Phased-in approach to enforcing the **Quality System** (QS) regulation

January 8-9, 2015 – FDA Public Workshop

"Laboratory Developed Tests"

FDA Public Workshop (Bethesda, MD)

- Overview of Proposed Framework
- Components of a Test and LDT Labeling Considerations
- Clinical Validity and Intended Use
- Categories for Continued Enforcement Discretion
- Notification and Adverse Reporting
- Public Process for Classification and Prioritization
- Quality System Regulation
- Public Comments (~40 different individuals/organizations)

U.S. House of Representatives

Subcommittees

Passed by the House July 10, 2015

Sep 9, 2014	Hearing on FDA Draft Guidance
Dec 2014	White Paper Seeking Feedback for 21st Century Cures (11 Q's)
Jun 2015	Draft Bill Circulated for IVCT Regulation (i.e. **DTWG**)
Oct 2015	Updated IVCT Draft Bill (would create new FDA center for IVCT)
Nov 17, 2015	FDA* - Jeffrey Shuren**
	CMS – Patrick Conway, Dep. Admin, CMS Office Admin

"The FDA is committed to developing a final policy for oversight of LDTs…"

*24 hrs prior released "20 Case Studies"

UNITED STATES SENATE

U.S. SENATE COMMITTEE ON
Health, Education
Labor & Pensions
(HELP Committee)

04.06.16

Senate Health Committee Approves Last of 19 Bipartisan Bills, Completing Work on Companion to House-Passed 21st Century Cures Act

Lamar Alexander (R, TN; Committee Chair)

"I would like to take the proposals we've passed here, along with a bipartisan agreement on the NIH Innovation Fund with Senator Murray, and put them in Senator McConnell's hands as the Senate's contribution to a 21st Century Cures Act.

*We'll have an opportunity for more debate on the floor, including…**[t]he issue of lab developed tests, which are vitally important to get right to ensure precision medicine and cancer moonshot are a success**."*

The U.S. House of Representatives
COMMITTEE ON APPROPRIATIONS
Chairman Hal Rogers

April 19, 2016

Mr. ADERHOLT, from the Committee on Appropriations, submitted the following

REPORT

(To accompany H.R. XXXX)

The Committee on Appropriations submits the following report in explanation of the accompanying bill making appropriations for Agriculture, Rural Development, Food and Drug Administration, and Related Agencies for fiscal year 2017.

Non-Binding

Laboratory Developed Tests.—The FDA's draft guidance issued on October 3, 2014, titled "Framework for Regulatory Oversight of Laboratory Developed Tests" (LDTs), puts forth a proposed regulatory framework that is a significant shift in the way LDTs are regulated. Such a shift deserves input from the public, and Congress has been working with stakeholders, constituencies, and the FDA to find common ground on regulating LDTs. **The FDA's guidance circumvents the normal rulemaking process and changes expectations for patients, doctors, and laboratories for the first time since the Clinical Laboratory Improvement Amendments Act was passed in 1988. The Committee directs the FDA to suspend further efforts to finalize the LDT guidance and continue working with Congress to pass legislation that addresses a new pathway for regulation of LDTs in a transparent manner**.

CAP
www.cap.org

AMP Association for Molecular Pathology
www.amp.org

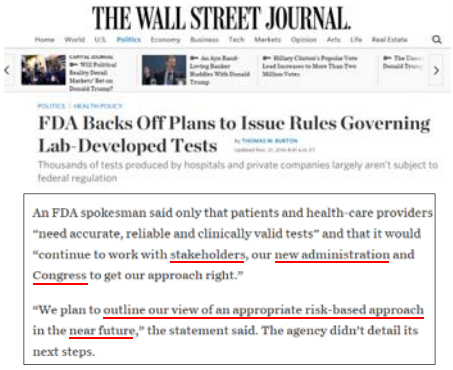
ACLA American Clinical Laboratory Association

AACC Better health through laboratory medicine
www.aacc.org

DTWG
Diagnostic Test Working Group

ASCP American Society for Clinical Pathology
www.ascp.org

November 18, 2016



THE WALL STREET JOURNAL.

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POLITICS | HEALTH POLICY

FDA Backs Off Plans to Issue Rules Governing Lab-Developed Tests

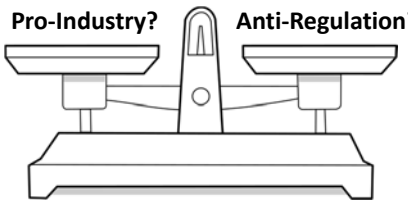
By THOMAS M. BURTON

Thousands of tests produced by hospitals and private companies largely aren't subject to federal regulation

An FDA spokesman said only that patients and health-care providers "need accurate, reliable and clinically valid tests" and that it would "continue to work with stakeholders, our new administration and Congress to get our approach right."

"We plan to outline our view of an appropriate risk-based approach in the near future," the statement said. The agency didn't detail its next steps.

2017- Trump Administration



On the issue of FDA regulation of LDTs, can you be both?

Early 2017

- **January 2017**
  - ***Discussion Paper on Laboratory Developed Tests (LDTs)***, FDA's "synthesis of feedback" received during the public comment period and stakeholder engagement; FDA's "current thoughts"
- **March 2017**
  - ***Diagnostic Accuracy and Innovation Act (DAIA)*** Discussion draft was made available for public comment from two members of the House Energy and Commerce Committee, Subcommittee on Health

Diagnostic Accuracy Innovation Act (DAIA)

In Vitro Clinical Tests (IVCTs)

FDA Jurisdiction

Test Development and Manufacturing

Finished Products	**Laboratory Protocols**
(test kits and platforms)	(LDTs)

CMS/CLIA Jurisdiction

Laboratory Operations

Laboratory Testing

(Finished Products AND Laboratory Protocols)

Diagnostic Accuracy Innovation Act (DAIA)

Risk Classification

High Risk Medium Risk Low Risk

- Would a clinically significant **inaccurate result** for the intended use cause **serious harm**?
- Do **risk reducing factors** have the capacity to **prevent or detect** such inaccurate result or otherwise mitigate the risk?
- Is the **risk** of adverse patient impact **remote**?
- **Reasonable assurance** of analytical and clinical validity?
- **Valid scientific evidence**?

The End?

ACKNOWLEDGEMENTS

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Teneille R. Brown, JD (S.J. Quinney College of Law)

*ASCP Science, Technology, & Policy Fellowship
**Center for Law and Biomedical Sciences Fellows

Questions

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