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American Clinical Laboratory Association

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Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane
Room 1061
Rockville, MD 20852

CITIZEN PETITION

The American Clinical Laboratory Association (ACLA) submits this petition under the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) to request the Commissioner of Food and Drugs to take the actions described in Section A with respect to laboratory developed tests (LDTs). ACLA is a not-for-profit association that represents the nation's leading providers of clinical laboratory services, including local, regional, and national laboratories throughout the United States. All ACLA members develop and perform LDTs.

As referred to in this petition, LDTs are in vitro assays that clinical laboratories develop, validate, and perform as testing services. Laboratories create LDTs by establishing procedures for performing the tests with reagents and laboratory equipment. The laboratory receives test orders for specific patients, performs the test according to its own procedures, and reports the test results to the authorized persons who ordered them. LDTs thus differ from in vitro diagnostic test kits (IVD test kits), which commonly are products containing all or most of the components needed to perform a test, such as reagents and equipment, that are packaged and commercially distributed to laboratories, other providers, and, in some cases, consumers.

A. Actions Requested

ACLA respectfully requests that the Food and Drug Administration (FDA or the agency): (1) refrain from issuing draft or final guidance or a proposed or final rule purporting to regulate LDTs as devices under the FDCA; and (2) confirm in response to this citizen petition that LDTs are not devices under the FDCA.

B. Statement of Grounds

I. Executive Summary of Grounds

Since 1967, a comprehensive federal statutory scheme has governed laboratory services. The Clinical Laboratories Improvement Act of 1967 (CLIA '67), as amended by the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88), requires certification of laboratories and mandates their compliance with detailed quality standards, including the "standards to assure consistent performance . . . of valid and reliable laboratory examinations and

other procedures." This statutory scheme not only ensures the validity and reliability of LDTs, but also has furthered the public health. CLIA allows laboratories the flexibility to develop and validate LDTs quickly to respond to public health needs. Laboratories are able to update LDTs regularly as medicine advances, so that patients have access to the most advanced testing. Indeed, some LDTs represent the standard of care. LDTs are also used to diagnose and assess diseases and disorders for which no FDA-authorized test kit currently exists, *e.g.*, where disease prevalence and market circumstances do not justify development costs, or where no kit has yet completed the FDA authorization process. In summary, under CLIA, laboratories have fulfilled critical public health functions. Over the past few decades, health care providers have ordered millions of LDTs for their patients with few problems documented.

Although the agency has occasionally asserted that it has authority to regulate LDTs as "devices" under the FDCA, FDA has, for years, declined to do so. Instead, FDA has claimed it is exercising enforcement discretion over LDTs in recognition of their public health benefits and the adequacy of their regulation under CLIA. Moreover, because the agency has not acted to regulate LDTs, the clinical laboratory industry has not challenged FDA's assertion of jurisdiction in court, although it has objected to FDA's assertions of jurisdiction in each instance.

Recently, FDA issued a notice of its intent to regulate LDTs as devices under the FDCA.[1] FDA has indicated that it plans to regulate LDTs as devices through guidance documents, which are expected to require that LDTs comply with the FDCA's premarket controls (including the need for premarket clearance or approval) and its "general controls" for devices, including establishment registration and device listing requirements, the Quality System Regulation (QSR), medical device reporting requirements, and FDA promotional limitations.

ACLA believes that FDA cannot and should not regulate LDTs as medical devices under the FDCA. *First*, FDA cannot implement its new proposal, through guidance or otherwise, because the agency lacks the requisite statutory authority. For several reasons, FDA has no jurisdiction to regulate LDTs under the FDCA.

- LDTs are not "devices" as defined in the Act. As the text and legislative history of the "device" definition show, this term encompasses only articles. LDTs are proprietary procedures for performing a diagnostic test using reagents and laboratory equipment. They are essentially know-how, not articles. Therefore, they are not subject to regulation under the FDCA.

- FDA's assertion of jurisdiction over LDTs is incompatible with CLIA '88 and its legislative history. In amending CLIA, Congress explained its intent to regulate laboratory testing under a single statute: the amended CLIA. To that end, Congress created a comprehensive statutory framework for precisely the services that FDA now seeks to regulate under the device authorities of the FDCA. Congress made no mention of FDA having any authority to regulate LDTs under the previously enacted "device"

[1] 75 Fed. Reg. 34463, 34463 (June 17, 2010).

definition, even though a major goal of CLIA '88 was to strengthen oversight of Pap testing, which was a specific LDT.

- LDTs do not present a prerequisite for FDA jurisdiction under the Act: commercial distribution. FDA has defined "commercial distribution" in various contexts to require that a product be delivered, distributed, or placed on the market. As non-tangible know-how and testing services at clinical laboratories, LDTs do not meet any of these conditions.

Second, FDA regulation of LDTs would be contrary to the public health. Numerous critical tests are available only as LDTs, including many "gold standard" DNA sequencing assays, newborn screening tests, and tests for rare diseases. If FDA were to require clearance or approval for LDTs, laboratories may be unable to continue offering them. Some testing currently performed at laboratories as LDTs will never generate the financial returns needed to justify the costs of obtaining FDA clearance or approval. Patients served by these tests would be left with no testing options. Similarly, critical testing would be unavailable in the "lag time" between development of new tests and FDA authorization of them. The impact would be contrary to the agency's mandate to promote the public health.[2] Pursuant to CLIA, laboratories have served a crucial role in medicine. Physicians rely on laboratory test results every day to make medical decisions for patient care.

Third, FDA regulation of LDTs as devices would result in numerous unintended consequences with significant economic repercussions for the United States laboratory industry.

Finally, to the extent that stakeholders have concerns about possible regulatory gaps under CLIA, the most logical and appropriate solution would be to amend CLIA and/or its regulations – not to impose an additional layer of regulation based on a different statute designed for products rather than laboratory testing. FDA's contemplated new oversight will superimpose a new bureaucracy on an already highly-regulated industry that serves highly-trained physicians and professionals.

II. Background

A. The Draft Compliance Policy Guide, ASR Rule, and Enforcement Discretion Policy

In the sixteen years that followed enactment of the 1976 Medical Device Amendments (MDA) to the FDCA,[3] FDA did not assert jurisdiction to regulate LDTs as "devices" under that Act. This was appropriate, given Congress' prior enactment of legislation expressly regulating laboratory testing, CLIA '67,[4] and its subsequent revisions to that legislation

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[2] FDCA § 1003(b)(1).

[3] Pub. L. No. 94-295, 90 Stat 539 (1976).

[4] Pub. L. No. 90-174, § 5, 81 Stat. 533, 536 (1967).

in CLIA '88.[5] Moreover, for many years, the Secretary of Health and Human Services (HHS) principally has delegated authority to administer CLIA to the Centers for Medicare and Medicaid Services (CMS) and its predecessor, not to FDA.[6]

To ACLA's knowledge, FDA first asserted that it had authority to regulate LDTs as devices in a 1992 draft Compliance Policy Guide (CPG). In this document, FDA stated that "laboratories have been manufacturing [LDTs] . . . and utilizing these unapproved products for diagnostic purposes."[7] The draft CPG further asserted that "[t]hese products are subject to the same regulatory requirements as any unapproved medical device."[8] Industry objected to this assertion of jurisdiction over LDTs. For example, Hyman Phelps & McNamara filed a citizen petition explaining why FDA lacked jurisdiction over LDTs and requesting that the agency not regulate LDTs as devices.[9] Following controversy over the draft CPG, FDA did not finalize it or attempt to actively regulate LDTs. Instead, the agency asserted a position of enforcement discretion with respect to LDTs.[10] When FDA released a revised draft CPG a few years later, it contained no language claiming that FDA had jurisdiction over LDTs.[11]

FDA next asserted that it had jurisdiction over LDTs in its 1996 rulemaking to adopt the "ASR rule" governing analyte specific reagents (ASRs). In the preamble to the proposed rule, FDA stated that it had not "actively regulated" LDTs, but might do so in the future.[12] ACLA and other stakeholders filed comments challenging FDA's assumption that it had authority to regulate LDTs under the FDCA.[13] When FDA finalized the ASR rule the next year, the agency contended: "FDA believes that clinical laboratories that develop [LDTs] are

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[5] Pub. L. No. 100-578, 102 Stat. 2903 (1988).

[6] *See, e.g.*, 69 Fed. Reg. 22849, 22849 (Apr. 27, 2004); 49 Fed. Reg. 35247, 35249 (Sept. 6, 1984). CMS previously was known as the Health Care Financing Administration. FDA has received only a narrow role in administering CLIA: to "implement CLIA's complexity categorization provisions as they apply to commercially available tests." 69 Fed. Reg. at 22849.

[7] FDA, Draft Compliance Policy Guide: Commercialization of Unapproved In Vitro Diagnostic Devices Labeled for Research and Investigation (Aug. 1992), at 4.

[8] *Id.* FDA also issued a subsequent, undated version of this draft CPG that omitted the second quoted statement and replaced it with a description of the "circumstances" that FDA should consider before taking action against LDTs. FDA, Draft Compliance Policy Guide: Commercialization of Unapproved In Vitro Diagnostic Devices Labeled for Research and Investigation (undated), at 4; FDA Response to Hyman Phelps & McNamara, P.C., Citizen Petition, Docket No. 92P-0405 (Aug. 12, 1998), at 2-3.

[9] Hyman Phelps & McNamara, P.C., Citizen Petition, Docket No. 92P-0405 (Oct. 22, 1992); *see also* Hyman Phelps & McNamara, P.C., Supplemental Citizen Petition, Docket No. 92P-0405 (Dec. 2, 1992).

[10] *See, e.g., IVD Policy Will Not Include Exemptions for "Standard-of-Care" Tests*, THE GRAY SHEET (Oct. 11, 1993) (Exhibit 1); Draft Compliance Policy Guide: Commercialization of Unapproved In Vitro Diagnostic Devices Labeled for Research and Investigation (undated), at 4.

[11] *See* FDA, Draft Compliance Policy Guide 7124.32, Commercialization of In Vitro Diagnostic Devices (IVDs) Labeled for Research Use Only and Investigational Use Only (May 1996).

[12] 61 Fed. Reg. 10484, 10484 (Mar. 14, 1996).

[13] *See, e.g.*, Comments of ACLA to Docket 96N-0082 (June 4, 1996), at I-2 n.1; Comments of Mayo Clinic to Docket 96N-0082 (June 11, 1996), at 1.

acting as manufacturers of medical devices and are subject to FDA jurisdiction under the act."[14] FDA also recognized, however, that LDTs had "contributed to enhanced standards of medical care in many circumstances," and that "significant regulatory changes in this area could have negative effects on the public health."[15] Moreover, FDA stated its belief that "existing mechanisms for laboratory oversight under the mandate of CLIA are sufficient in most cases to assure proper test control."[16] Therefore, the agency declined to regulate LDTs.[17] Instead, FDA again claimed that it was exercising enforcement discretion with respect to LDTs.

Subsequently, FDA continued to assert that it had jurisdiction over LDTs but maintained its policy of enforcement discretion.[18] For example, in denying the Hyman Phelps petition in 1998, the agency stated that it "may regulate assays developed by clinical reference laboratories strictly for in-house use as medical devices."[19] ACLA continued to voice its opposition to FDA's position, but because FDA did not act to apply the medical device authorities of the FDCA to LDTs, ACLA did not challenge FDA's assertion of jurisdiction in court.

B. Mid-2000s: Case-by-Case Regulation and IVDMIA Draft Guidance

In 2006 and 2007, the agency issued two draft guidance documents purporting to regulate as devices a subset of LDTs, which FDA referred to as in vitro diagnostic multivariate index assays (IVDMIAs).[20] As defined in the second draft guidance, IVDMIAs are tests that combine multiple variables to produce a single, patient-specific result (*e.g.*, a "score") that is "non-transparent" and cannot be independently derived by the user.[21] FDA stated that its longstanding policy of enforcement discretion did not apply to IVDMIAs, because these assays include elements that are not typical in LDTs, such as "complex, unique interpretation functions."[22] Around the same time, FDA attempted to impose premarket regulatory

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[14] 62 Fed. Reg. 62243, 62249 (Nov. 21, 1997).

[15] *Id.*

[16] *Id.* at 62250.

[17] *Id.* at 62249.

[18] *See, e.g., Unwilling to Regulate Homebrews, FDA Inches Forward on ASRs, Microarrays*, THE GRAY SHEET (Sept. 15, 2003) (quoting Director of the Office of In Vitro Diagnostics (OIVD), Steven Gutman, and OIVD's Joseph Hackett, as stating that "FDA does not plan to exert regulatory authority over homebrews") (Exhibit 2).

[19] FDA Response to Hyman Phelps & McNamara, P.C., Citizen Petition, Docket No. 92P-0405 (Aug. 12, 1998), at 1.

[20] FDA, Draft Guidance for Industry, Clinical Laboratories, and FDA Staff: In Vitro Diagnostic Multivariate Index Assays (July 2007) (2007 IVDMIA Draft Guidance); FDA, Draft Guidance for Industry, Clinical Laboratories, and FDA Staff: In Vitro Diagnostic Multivariate Index Assays (Sept. 2006) (2006 IVDMIA Draft Guidance); 71 Fed. Reg. 52800, 52800 (Sept. 7, 2006).

[21] 2007 IVDMIA Draft Guidance, at 3-4.

[22] *Id.* at 4. FDA stated that it had exercised enforcement discretion over "standard LDTs," *i.e.*, those that primarily use ASRs, general purpose reagents and laboratory equipment, controls, and other laboratory instrumentation. *Id.*; *see also* 2006 IVDMIA Draft Guidance, at 2-3.

requirements on several individual LDTs, including LDTs that FDA believed met its definition of an IVDMIA, on a case-by-case basis.[23]

ACLA objected to the draft guidance in several comments to the docket.[24] Similarly, in 2006, the Washington Legal Foundation (WLF) filed a citizen petition requesting that FDA confirm that it will not regulate LDTs as medical devices.[25] WLF noted that "both the facts and the law ha[d] changed materially" since FDA ruled on the Hyman Phelps petition. WLF emphasized that FDA "ha[d] begun taking action against individual clinical laboratories offering [LDTs], seeking to regulate them as medical devices."[26] FDA has not yet responded to the WLF petition.[27] Nevertheless, the agency continued to issue enforcement letters to companies, such as those that offer genetic testing services directly to consumers.[28]

C. Notice of Intent to Regulate LDTs

On June 17, 2010, FDA announced its intention to abandon an enforcement discretion policy and begin to regulate LDTs as devices under the FDCA.[29] The agency cited numerous factors influencing its conclusion, including concerns about the validity of the tests and the fact that "an increasing number of LDT manufacturers are corporations rather than hospitals or public health laboratories."[30] FDA stated its intent to propose a risk-based oversight framework that it would "phase in . . . over time," based on the risk presented by various tests.[31] The agency also pledged to "move forward expeditiously to develop a draft oversight framework for public comment to provide predictability as quickly as possible."[32] In its comments to FDA's

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[23] *See, e.g.*, Letter of Steven I. Gutman, Director, OIVD, to Agendia B.V. (Apr. 6, 2005), *available at* http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm125133.htm (asserting that in-house gene expression profiling test system for breast cancer prognosis, MammaPrint, was a device).

[24] *See, e.g.*, ACLA, Comments to Docket No. 2006D-0347 (now Docket FDA-2006-D-0233) (Feb. 28, 2007); ACLA, Comments to Docket No. 2006D-0347 (now Docket FDA-2006-D-0233) (Feb. 8, 2007); ACLA, Comments to Docket No. 2006D-0347 (now Docket FDA-2006-D-0233) (Mar. 5, 2007).

[25] Washington Legal Found., Citizen Petition, Docket No. 2006P-0402 (now Docket No. FDA-2006-P-0149) (Sept. 28, 2006), at 1.

[26] *Id.* at 3.

[27] In 2008, Genentech filed a citizen petition requesting that FDA apply the same scientific and regulatory standards to LDTs and IVD test kits used in drug or biologic therapeutic decision making. Genentech, Citizen Petition, Docket No. FDA-2008-P-0638 (Dec. 5, 2008). ACLA filed comments to the docket opposing the petition. ACLA Comments to Docket No. FDA-2008-P-0638 (Feb. 18, 2009).

[28] *See* FDA, Letters to Manufacturers Regarding Genetic Tests, http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm219582.htm.

[29] 75 Fed. Reg. 34463, 34463 (June 17, 2010). Following this announcement, FDA indicated that it does not intend to finalize the IVDMIA draft guidance, but instead will focus on regulation of all LDTs. Turna Ray, *FDA Shelves IVDMIA Final Guidelines in Order to Focus on Overall LDT Regulation*, GENOME WEB (June 23, 2010) (Exhibit 3).

[30] 75 Fed. Reg. at 34463.

[31] *Id.* at 34464.

[32] *Id.*

docket on this notice, ACLA again noted the existence of legal issues regarding FDA's authority to regulate LDTs.[33]

During 2011 negotiations regarding medical device user fee legislation, the agency stated that it plans to release three guidance documents to implement its LDT regulatory framework.[34] One will address the overall risk-based framework and presumably will address the necessity of obtaining clearance and approval for LDTs and the tests that FDA will phase-in initially. The second guidance will address the interplay between the QSR applicable to devices and the quality requirements under CLIA.[35] The third guidance reportedly will call for registration and listing of LDT developers and their tests.[36]

Congress responded with section 1143 of the Food and Drug Administration Safety and Innovation Act (FDASIA), enacted in July 2012. This provision prohibits FDA from "issu[ing] any draft or final guidance on the regulation of [LDTs] under the [FDCA]" without providing 60 days' notice to two Congressional committees.[37] As part of this notice, FDA must include "the anticipated details of such action."[38]

III. FDA Lacks Authority to Regulate LDTs under the FDCA

A. LDTs are not "devices" as defined in the FDCA

Section 201(h) of the FDCA defines "device" in relevant part to mean "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is . . . intended for use in the diagnosis of disease or other conditions."[39] This definition describes objects. For example, the dictionary defines "contrivance" as "*a thing* that is created skillfully and inventively to serve a particular purpose."[40]

Similarly, the legislative history of the MDA generally refers to devices as "products" and "articles."[41] For example, the Senate Report states that "the Committee reported

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[33] Comments of ACLA to Docket No. FDA-2010-N-0274 (Sept. 15, 2010), at 10 n.2.

[34] *See, e.g.*, Minutes from Negotiation Meeting on MDUFA III Reauthorization: June 27, 2011, at 3, *available at* http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/ucm263026.htm.

[35] *See id.*

[36] *See, e.g., id.*

[37] Pub. L. No. 112-144, § 1143(a)(1), 126 Stat. 993, 1130 (2012).

[38] *Id.* § 1143(a)(2).

[39] FDCA § 201(h).

[40] Oxford U.S. English Dictionary, Entry for "contrivance," http://oxforddictionaries.com/definition/american_english/contrivance (last accessed May 23, 2013) (emphasis added) (Exhibit 4).

[41] *See, e.g.*, H.R. Rep. No. 94-1090, at 62, 65 (1976) (Conf. Rep.) (referring to devices as "products" and "articles") (Exhibit 5); H.R. Rep. No. 94-853, at 6 (1976) (referring to devices as "products," "machines" and "articles") (continued...)

bill has carefully defined 'device' so as to specifically include implants, in-vitro diagnostic *products* and other similar or related *articles*."[42] It elaborates as follows: "In vitro diagnostic *products* include those *products* which are not ingested and which are used to assist in the diagnosis of disease or other conditions of the body."[43]

Even though the MDA added several items to the list of articles qualifying as devices — including in vitro reagents — the legislative history clarifies that this amendment did not expand the device definition beyond its tie to tangible articles. Instead, the House Report explains that "[t]he new definition retains (in somewhat more precise detail) provisions of existing law that a device is an article or component thereof," while making changes to distinguish drugs and devices by reference to chemical action and metabolism.[44] The prior definition, which had listed "instruments, apparatus, and contrivances, including their components, parts, and accessories," encompassed "purely mechanical devices" such as shoulder braces and scales used to weigh patients.[45] When Congress added in vitro reagents to the device definition, the definition was still tied to an "article."

LDTs are not devices as described in section 201(h) or its legislative history. LDTs are not products or articles. Laboratories create LDTs by establishing procedures for performing the tests with reagents and laboratory equipment. Performing an LDT might involve use of ASRs, general purpose reagents, general purpose laboratory equipment, and controls, which are devices under FDA regulations.[46] The LDT therefore represents a laboratory's proprietary procedure for performing the test – essentially its knowledge or know-how. When the test is ordered for a specific patient, the laboratory performs the test according to this proprietary procedure and reports the test result as a service to the authorized person who ordered the test. No product is shipped. Indeed, FDA's device establishment registration regulations provide that laboratories are exempt from registration because their "primary responsibility to the ultimate consumer is to . . . provide a service through the use of a previously manufactured device."[47] Therefore, LDTs do not fall within the device definition.

The fact that laboratory testing entails use of tangible articles does not change this conclusion. Congress did not intend that FDA would regulate every clinical service as a medical

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(Exhibit 6); *id.* at 14 (noting that, "generally the term 'device' is used in the bill to *refer to an individual product or to a type or class of products*," except where one device is indicated for multiple intended uses) (emphasis added).

[42] S. Rep. No. 94-33, at 17 (1975) (emphases added) (Exhibit 7).

[43] *Id.* (emphases added).

[44] H.R. Rep. No. 94-853, at 14.

[45] *See* 79 Cong. Rec. 4841, 4842 (1935) (statement of Sen. Clark) (Exhibit 8); *Foods, Drugs, and Cosmetics: Hearing on H.R. 6906, H.R. 8805, H.R. 8941, and S. 5 Before a Subcomm. of the H. Comm. on Interstate & Foreign Commerce*, 74th Cong. 55 (1935) (statement of Walter G. Campbell, Chief, FDA) (Exhibit 9); *see also* 80 Cong. Rec. 10236 (1936) (statement of Rep. Chapman) (in discussing device provisions, noting that "[t]here are hundreds of worthless *contrivances* being sold to and used by gullible people") (emphasis added) (Exhibit 10).

[46] 21 C.F.R. §§ 864.4020, 862.2050, 862.1660; 21 C.F.R Part 864, Subpart D.

[47] 21 C.F.R. § 807.65(i).

device simply because the service involves the use of tangible articles which themselves may be subject to FDA regulation. Otherwise, every surgical procedure or physical examination that is performed on a patient using tangible devices would be subject to FDA regulation. Congress made clear in FDCA section 1006 that FDA has no authority to regulate the practice of medicine, which includes the practice of laboratory medicine.[48]

Other aspects of the MDA's legislative history compel the conclusion that LDTs are not devices. Nowhere in this history did Congress suggest it was granting FDA authority to regulate LDTs. According to FDA's theory, in enacting the MDA, Congress decided to impose device requirements on LDTs, in addition to the regulatory controls already applicable to them under CLIA '67, without acknowledging that fact. If FDA were correct, the MDA would have rendered all LDTs unapproved medical devices, but Congress did not mention that either.[49] As the Supreme Court stated in *Brown and Williamson*, "Congress could not have intended to delegate a decision of such economic and political significance to an agency in so cryptic a fashion."[50] FDA's assertion of jurisdiction over LDTs based on the "device" definition therefore is unjustified.

B. Regulation of LDTs under the FDCA is inconsistent with CLIA and its legislative history

In CLIA, Congress created a separate statutory framework for the precise testing that FDA intends to regulate under the device authorities of the FDCA. FDA regulation of LDTs as devices would be inconsistent with the detailed CLIA scheme and Congress' intent in fashioning it.

Under FDA's view of its authority, when CLIA '88 was enacted, the agency already had authority to regulate LDTs as devices for twelve years, beginning with the MDA of 1976. Yet, neither CLIA '88 nor it legislative history refer to FDA as having *any* authority to regulate LDTs, let alone the sweeping authority that FDA asserts. Moreover, a major goal of the legislation was to strengthen oversight over Pap testing, which is typically performed as an LDT. In describing the legal landscape in place at the time, the House Report stated that laboratories were "governed by two separate and distinct statutes, Medicare and CLIA."[51] Moreover, the Report's section on the "Current Regulatory System" did not mention FDA.[52] Instead, testimony by the HHS Inspector General, Richard Kusserow, supported the conclusion that FDA had authority only over the laboratory equipment used in tests, not the tests themselves.[53] Therefore,

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[48] *See* FDCA § 1006.

[49] *See* Comments of Hyman, Phelps, & McNamara, P.C., Docket No. 2006P-0402 (Mar. 23, 2007), at 8-9.

[50] *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 160 (2000).

[51] H.R. Rep. No. 100-899, at 12 (1988) (Exhibit 11).

[52] *Id.* at 11.

[53] *Deadly Mistakes: Are Laboratory Results Reliable?: Hearing Before the Subcomm. on Regulation and Business Opportunities of the H. Comm. on Small Business*, 100th Cong. 71 (1988) (statement of Richard Kusserow, Inspector Gen., Dep't of Health and Human Servs.) ("From all the literature and evidence that is available, it does show that modern laboratory analyzers, as a rule, produce consistently good test results . . . . But also the fact that (continued...)

the legislative history shows that FDA had no jurisdiction over LDTs at the time CLIA '88 was enacted.

Furthermore, CLIA '88 is a comprehensive framework for laboratory regulation that did not leave residual authority under other federal laws. The objective of this legislation was to replace the "patchwork of inconsistent and overlapping standards" of CLIA, the Medicare statute, and state regulation with a "unified regulatory mechanism."[54] As Representative Dingell explained in discussing CLIA '88:

> The legislation essentially directs the Department of Health and Human Services to regulate all laboratories *under a single statute.* It should end duplicative and confused regulation under a tangled web of statutory authorities.[55]

Thus, Congress opted to strengthen federal oversight over laboratory testing, including LDTs, through amendments to CLIA – not by granting FDA authority over these LDTs under the FDCA. This was the case even though "[t]he bill respond[ed] to atrocious abuses in the area of [P]ap [testing]," an LDT.[56] If FDA had jurisdiction over LDTs, Congress surely would have mentioned this. Yet nothing in the legislative history of CLIA '88 indicates that FDA could regulate LDTs. Again, "Congress could not have intended to delegate a decision of such economic and political significance to an agency in so cryptic a fashion."[57]

CLIA's detailed statutory framework further belies the notion that Congress could have intended for FDA device regulation to apply to LDTs in addition to CLIA. CLIA '88 comprehensively regulates clinical laboratories, defined as any facility for "examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings."[58] Under CLIA, a laboratory must obtain a certificate prior to soliciting or accepting specimens for these laboratory examinations or procedures.[59] Laboratories also must comply with personnel qualification requirements and "standards to assure consistent performance . . . of valid and reliable laboratory examinations and other procedures."[60] These standards require laboratories to maintain adequate quality control and quality assurance programs to assure the "validity and reliability" of the tests and "the proper collection,

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another part of our Department, FDA, also evaluates the equipment. Therefore, thus far in our study, we couldn't help but conclude that that problem is really with the user of the equipment [*i.e.*, the laboratory] and not the equipment itself") (Exhibit 12).

[54] H.R. Rep. No. 100-899, at 12; S. Rep. No. 100-561, at 3 (1988) (Exhibit 13).

[55] 134 Cong. Rec. 23606 (1988) (statement of Rep. Dingell) (emphasis added) (Exhibit 14).

[56] *Id.*

[57] *Brown & Williamson*, 529 U.S. at 160.

[58] Public Health Service Act (PHSA) § 353(a).

[59] *Id.* § 353(b).

[60] *Id.* § 353(f)(1).

transportation, and storage of specimens and the reporting of results."[61] CLIA also requires laboratories to participate in regular proficiency testing.[62] Congress chose to fashion and apply these requirements, instead of the FDCA's premarket controls and quality requirements, to LDTs.

CLIA's enforcement provisions reinforce this conclusion. CLIA requires laboratories to submit to inspections of their "facilities, equipment, materials, records, and information" to verify compliance,[63] and the FDCA similarly authorizes inspections of device establishments.[64] CLIA includes a detailed enforcement framework providing for a variety of civil and criminal penalties for noncompliant laboratories, including enforcement powers paralleling those in the FDCA, such as injunction and criminal penalties.[65] Congress would not have included these similar enforcement authorities in CLIA if it understood the FDCA to already provide them.

C. FDA regulation of LDTs is inconsistent with CMS regulations under CLIA

CMS regulations expressly recognize a distinction between laboratory tests that use FDA-cleared or -approved products and those that do not. Further, for tests not subject to FDA clearance or approval, the CLIA regulations provide enhanced requirements for validation of tests.[66] Specifically, 42 C.F.R. § 493.1253(b)(2) applies to "[e]ach 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 . . .)." This regulation requires the laboratory to establish performance specifications and calibration and control procedures. Any FDA guidance regulating LDTs as devices, and requiring clearance and approval of these assays, would conflict with this validly promulgated regulation of its sister agency.

D. Laboratories do not commercially distribute LDTs

LDTs do not entail the prerequisite for FDA jurisdiction under the Act: commercial distribution. Under section 510(k) of the Act, the premarket controls of the FDCA apply only to devices that both move in interstate commerce and are commercially distributed. This provision states:

> Each person who is required to register under this section and who proposes to begin the introduction or delivery for introduction into

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[61] *Id.* § 353(f)(1)(A).

[62] *Id.* § 353(f)(1)(D) & (f)(3). If a proficiency testing program is not available or required for a particular test or procedure, the laboratory must verify the accuracy of that test or procedure at least twice per year using alternative assessment methods. 42 C.F.R. § 493.1236(c).

[63] PHSA § 353(g).

[64] FDCA § 704(a)(1)(B).

[65] *See, e.g.*, PHSA § 353(j), (l); *see also* FDCA §§ 303, 304.

[66] 42 C.F.R. § 493.1253(b)(2).

> interstate commerce *for commercial distribution* of a device intended for human use shall, at least ninety days before making such introduction or delivery, report to the Secretary . . . action taken by such person to comply with requirements under section 514 [related to performance standards] or 515 [related to premarket approval] which are applicable to the device.[67]

The House Report to the MDA provides that "'[c]ommercial distribution' is the functional equivalent of the popular phrase 'on the market'" and does not include "mere announcements of intent to market a device."[68] By regulation, FDA has defined "commercial distribution" to mean "any distribution of a device intended for human use which is held or offered for sale."[69] Similarly, in a CPG, FDA has interpreted "commercial distribution" to generally require delivery to purchasers or consignees.[70] Under this CPG, FDA will consider a device in commercial distribution without deliveries only if the manufacturer can establish that, among other things, it had accepted or been prepared to accept at least one purchase order before enactment of the MDA "generally with delivery to occur immediately or at a promised future date."[71] A court has upheld this CPG's interpretation of "commercial distribution."[72]

LDTs are not distributed, delivered, or placed into the market. Although the reagents, components, and specimens used in performing LDTs, may meet these criteria, the LDTs themselves do not. FDA acknowledged this fact in the preamble to its rule governing analyte specific reagents (ASRs), stating: "The focus of this rule is the classification and regulation of ASR's *that move in commerce*, not tests developed in-house by clinical laboratories."[73] FDA's regulation exempting clinical laboratories from registration requirements also is consistent with this fact, because it recognizes that laboratories offer services, not products.[74] Thus, FDA's claim of authority to regulate LDTs as devices is inconsistent with the statutory prerequisite of commercial distribution and its prior interpretation of this requirement.

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[67] FDCA § 510(k) (emphasis added).

[68] H.R. Rep. No. 94-853, at 36 (1976).

[69] 21 C.F.R. § 807.3(b).

[70] FDA, CPG § 300.600 (1978, reissued 1987).

[71] *Id.* Advertisement of a device alone is not sufficient to establish commercial distribution. To establish commercial distribution under the CPG, the manufacturer must show that: (1) it advertised, displayed, or offered the device for sale; (2) the device was not offered or accepted only for research or investigational use; *and* (3) the manufacturer had accepted or was prepared to accept a purchase order, generally with delivery to follow. *Id.*

[72] *U.S. v. An Article of Device Consisting of 1,217 Cardboard Boxes*, 607 F. Supp. 990, 995 (W.D. Mich. 1985).

[73] 62 Fed. Reg. 62243, 62249 (Nov. 21, 1997) (emphasis added).

[74] 21 C.F.R. § 807.65(i). Laboratories also are exempt from premarket notification requirements, which apply only to firms required to register. *See* FDCA § 510(k); 21 C.F.R. § 807.81(a).

E. FDA may not regulate LDTs through guidance documents

While FDA lacks authority to regulate LDTs for the reasons discussed above, an attempt to regulate LDTs through guidance documents would be inappropriate for additional reasons. Directing clinical laboratories to register as device establishments would violate the existing FDA regulation that exempts clinical laboratories from registration, and that regulation may not be amended without notice-and-comment rulemaking.[75] In addition, FDA would be asserting jurisdiction over an entire industry sector, which would have a major impact on the economy.[76]

Moreover, as discussed below, regulating LDTs under the FDCA could subject clinical laboratories to FDA's burdensome device-authorization requirements and to the medical device tax, potentially negating laboratories' financial incentives to develop innovative new tests and to market important testing services. FDA regulation of LDTs therefore presents important public health issues of critical importance to patients, physicians, and clinical laboratories that rely on their services, and other stakeholders. Those issues are most appropriately addressed through legislation and rulemaking.[77]

IV. FDA Regulation of LDTs Is Contrary to the Public Health

FDA's regulation of LDTs as devices would adversely affect patient care in the United States. LDTs are critical to timely and effective patient care. Relying on flexibility afforded under the CLIA statute, laboratories perform LDTs to serve patient populations for which there are no FDA-approved or -cleared test kits. LDTs reflect the latest research and scientific developments and allow rapid diagnosis and assessment of emergent infectious diseases, among other diseases and conditions. FDA regulation of LDTs as devices would preclude them from serving these critical public health purposes.

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[75] *See* 21 C.F.R. § 807.65(f) (exempting from registration "[p]ersons who manufacture, prepare, propagate, compound, or process devices solely for use in research, teaching, or analysis and do not introduce such devices into commercial distribution"); *id.* § 807.65(i) (exempting from registration "[p]ersons ... whose major responsibility is to render a service necessary to provide the consumer (*i.e.*, patient, physician, layman, etc.) with a device or the benefits to be derived from the use of a device; for example, a ... clinical laboratory ... whose primary responsibility to the ultimate consumer is to dispense or provide a service through the use of a previously manufactured device"); *see also Nat'l Family Planning & Reproductive Health Ass'n v. Sullivan*, 979 F.2d 227, 235 (D.C. Cir. 1992).

[76] *Thomas v. New York*, 802 F.2d 1443, 1447 n.* (D.C. Cir. 1986) (Scalia, J.) (It is "clear that the impact of an agency statement upon private parties is relevant ... to whether it is ... a general statement of policy and thus does not require notice and comment ...." (internal citation omitted)); *see, e.g., Gen. Elec. Co. v. EPA*, 290 F.3d 377 (D.C. Cir. 2002) (invalidating under the Administrative Procedure Act a "Guidance Document" that "reasonably led [affected private parties] to believe that failure to conform [would] bring adverse consequences"); *Chamber of Commerce of the U.S. v. U.S. Dep't of Labor*, 174 F.3d 206 (D.C. Cir. 1999) (notice-and-comment rulemaking required where the agency's policy "will have a substantial impact" upon regulated entities regardless of whether the policy has the force of law).

[77] *See, e.g., Syncor Int'l Corp. v. Shalala*, 127 F.3d 90 (D.C. Cir. 1997).

A. LDTs are the sole available tests for many patient populations

Many tests are available only as LDTs. The reasons vary. In some cases, there is no financial incentive to perform clinical trials and seek FDA approval or clearance of a test for a well-accepted, clinically recognized biomarker, because the test will serve only a small patient population, *e.g.*, a rare disease or condition. In other cases, a kit has not yet completed the FDA authorization process. For example, the following tests currently are available only as LDTs:

- Numerous "gold standard" DNA sequencing assays and RNA expression analysis, including those for Gaucher disease, Canavan disease, Niemann Pick disease, multiple endocrine neoplasia, hereditary nonpolyposis colon cancer (HNPCC), breast cancer, and hereditary deafness;

- Karyotype/chromosome/cytogenetic analyses, such as those used to detect leukemia/lymphoma and developmental delay/mental retardation;

- Newborn screening tests that identify inborn metabolic disorders, which many States require for newborns;

- Tests for rare diseases, including many tests used in Ashkenazi Jewish screening (*e.g.*, tests for Tay-Sachs disease) and tests for herpes simplex encephalitis, muscular dystrophies, hereditary hemochromatosis, Prader-Willi/Angelman syndromes, neurofibromatosis (types 1 and 2), and congenital adrenal hyperplasia; and

- Tests involved in the evaluation of children with developmental delay/mental retardation, including Fragile X Syndrome testing and chromosome analysis.

With evolving medical technology, clinical laboratories are well positioned to develop more novel LDTs that will diagnose or otherwise allow evaluation of other diseases and conditions for which there is no available IVD test kit. But if FDA moves forward in regulating this testing under its device authorities, many of the tests will become unavailable, with adverse effects on patient care. Some of these tests will never generate the financial returns needed to justify the costs of obtaining FDA clearance or approval, notwithstanding well-accepted and recognized clinical support in the form of peer-reviewed research and/or laboratory-based studies. Clinical laboratories currently are filling a significant gap for individuals with these diseases, and FDA regulation would preclude them from serving these medical needs. Even if some laboratories elect to pursue the FDA authorization process rather than discontinuing their tests, they would need significant time to generate data needed to support a submission and to obtain approval of that submission. During this time, FDA regulation could preclude availability of these LDTs, which would compromise patient care.

One of the most critical public health purposes of LDTs has been to provide patient testing services during the lag time between scientific development of a test and FDA authorization of a test kit. The history regarding HIV testing is illustrative. No HIV-1 antibodies confirmatory test was available when the HIV-1 screening test was first introduced in 1985. Clinical laboratories developed and validated an LDT version of the Western blot to meet the

acute need to establish definitive diagnoses of HIV-1. The FDA-approved HIV-1 Western blot did not become available for another two years. Similarly, HIV viral load testing was first made available as an LDT around 1989-90, roughly six or seven years before FDA approved a kit to determine progression of disease in July 1996. These LDTs thus served an essential public health role in the lag time between test development and FDA approval. FDA regulation would preclude LDTs from filling these gaps and thus would harm the public health.

Likewise, LDTs served an unmet need to identify colorectal cancer patients who had KRAS gene mutations — and therefore were not expected to benefit from treatment with Erbitux — prior to FDA's approval of an IVD test kit for this use.[78] FDA had updated the Erbitux labeling in 2009 to reflect that the drug was not effective in patients with certain KRAS mutations, but only LDTs were available to detect those mutations in the three-year lag time before approval of the IVD test kit.

B. FDA regulation of LDTs also would slow the availability of novel tests, harming patient care

CLIA affords laboratories the flexibility to develop tests quickly and to update them regularly as medicine advances, so that patients have access to the most current diagnostic testing science. This flexibility would be lost under FDA regulation.

If FDA were to regulate LDTs as devices, its workload would increase exponentially. A single laboratory site may offer thousands of LDTs, and numerous laboratories may offer different LDTs for a single disease or condition. This immense workload would slow an already protracted premarket review process. The net result would be that new tests will reach patients much more slowly than they do under CLIA regulation.

Similarly, FDA regulation of LDTs as devices would slow improvements in existing tests. Under CLIA, laboratories may continually update their tests to reflect scientific developments, as long as they appropriately validate and document test modifications. Under the FDA regulatory scheme, these modifications often would require supplemental filings and authorizations from FDA.[79] Additional authorizations can take months to obtain, and in many cases, laboratories could not implement the modifications in the interim. Thus, FDA regulation would hinder scientific progress in the diagnostic testing field.

C. LDTs rapidly diagnose patients with emergent infectious diseases

The FDA approval/clearance process is not designed to allow for the rapid clearance or approval of tests for patients with emergent infectious diseases. Under the current regulatory framework, LDTs are used to respond in real time to these emergencies. Many clinical laboratories track world trends regarding infectious diseases and, in some cases, work

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[78] Turna Ray, *Qiagen Enters Companion Dx Market with Approval of KRAS Test Kit for Erbitux; LDT Impact Unknown*, Genome Web (July 11, 2012) (Exhibit 15).

[79] *See, e.g.*, FDCA § 515(d)(6), 21 C.F.R. §§ 807.81(a)(3), 814.39.

directly with HHS' Centers for Disease Control and Prevention (CDC) to develop tests for devastating infectious diseases, such as SARS, H1N1, and Avian Influenza. Diagnostic testing for many such diseases first became available through LDTs.[80] This immediate or near-immediate response time is critical to the welfare of these patients and the public health. In these situations, waiting for manufacturers to develop test kits and obtain FDA approval or clearance of them would take far too long, to the detriment of the public health and with potentially catastrophic consequences.[81]

V. FDA Regulation of LDTs as Devices Would Result in Numerous Unintended Consequences with Significant Economic Repercussions for the United States Laboratory Industry

FDA's regulation of LDTs as devices could trigger legal obligations far beyond the FDA requirements – requirements not envisioned by Congress. These downstream effects of FDA regulation could be felt by both independent laboratories and laboratories within hospitals and physician group practices. These examples illustrate the unintended consequences of applying the "device" definition to laboratory testing – a service it was never meant to reach.

First, FDA's action could subject laboratories to duplicate taxes by application of the federal medical device tax.[82] Congress imposed the device tax to ensure that device manufacturers helped to offset the costs of health care reform, since they are not directly reimbursed by Medicare and therefore would not have been able to contribute through cuts in Medicare reimbursement. In contrast, laboratories *are* directly reimbursed by Medicare. The laboratory industry worked closely with key House and Senate committees to identify cuts that would be acceptable to the industry to help fund their fair share of the costs associated with health care reform. In other words, the laboratory industry has already made its contribution to offsetting the costs of health care reform. If FDA were to require laboratories to list their LDTs as devices, however, the device tax could apply to LDTs – doubling the economic impact of health care reform on clinical laboratories. Congress never envisioned this result.

Second, regulation of LDTs as devices could trigger application of additional state liability laws, thus imposing substantial unintended economic burdens for laboratories. Under many current state laws, laboratories are subject to negligence standards. If FDA were to require

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[80] *See, e.g.*, Jan A. Nowak, M.D., Ph.D., and Karen L. Kaul, M.D., Ph.D., *The Role of Community Molecular Diagnostics Laboratories in the HINI Pandemic*, 11(5) J. MOL. DIAGN. 369, 369-70 (2009) (editorial) (Exhibit 16).

[81] Although FDA may authorize use of a device pursuant to an emergency use authorization (EUA), this authority is available only upon declared emergencies or threats. Such declarations may be made only in situations involving: (1) a heightened risk of an attack on the U.S. with "a biological, chemical, radiological, or nuclear agent or agents"; (2) a potential or actual public health emergency that involves such an agent or a related disease or condition, and that has the potential to affect national security or the health and security of U.S. citizens living abroad; or (3) identification of a "material threat" from such an agent sufficient to affect national security or the health and security of U.S. citizens living abroad. FDCA § 564(b)(1).

[82] *See* 26 U.S.C. § 4191; 26 C.F.R. § 48.4191-2(a) (defining a taxable medical device as "any device, as defined in section 201(h) of the [FDCA] that is intended for humans," *i.e.*, "a device that is listed as a device with [FDA] under section 510(j) of the [FDCA] and 21 C.F.R. part 807, pursuant to FDA requirements").

laboratories to list LDTs as devices, plaintiffs could argue that laboratories also should be subject to the product liability standards applicable to product manufacturers. FDA regulation of LDTs as devices therefore could require laboratories to carry product liability insurance in addition to the professional liability insurance they already carry, increasing costs significantly for every laboratory in the country, including hospital-based laboratories and small or rural laboratories.[83]

Third, many medical device manufacturers also are subject to detailed disclosure requirements under the Physician Payments Sunshine Act for payments and other transfers of value made to physicians and teaching hospitals.[84] Compliance with the Sunshine Act is expected to be very resource-intensive.[85]

Finally, laboratories would bear substantial burdens in seeking to comply with FDA requirements applicable to devices, even if only a subset of LDTs were determined to be subject to premarket review. Laboratories likely would need to adopt wholly new procedures and processes to comply with FDA's QSR requirements, which would pose special challenges because FDA has not defined how QSR requirements would apply in the laboratory context. Laboratories also would need to comply with to adverse event reporting, labeling, and promotional requirements. These requirements would apply even if FDA regulated only one of a laboratory's LDTs. Laboratories also would be likely to encounter challenges in complying with both CLIA and the FDCA. For example, it could be difficult to comply with FDA promotional requirements while fulfilling CLIA requirements to offer consultation on interpreting test results. And although CLIA regulations require laboratories to provide pertinent updates on testing information as soon as it is available,[86] FDA requirements for obtaining approval or clearance of labeling changes could preclude this action. Laboratories also would encounter duplicative regulation, such as inspections by both FDA and CMS. This additional regulatory burden would be costly and unwarranted.

VI. Regulation of LDTs under CLIA Has Served the Public Health, and Sound Policy Favors Continuation of this Approach

CLIA is specifically tailored to laboratory testing and has been implemented through voluminous regulations governing essentially all aspects of laboratory practice.[87] The CLIA statute and regulations include safeguards to ensure that LDTs are appropriately validated. For example, the statute mandates compliance with standards to ensure the validity of testing.[88] The CLIA regulations require Laboratory Directors to ensure that "[t]he test methodologies

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[83] State FDCA laws and commercial codes covering products also could apply to LDTs, if FDA were to regulate them as devices.

[84] 42 U.S.C. § 1320a-7h.

[85] *See* Comments of Eli Lilly and Co., Docket No. CMS-2011-0191, File Code CMS-5060-P (Feb. 17, 2012), at 23 (Exhibit 17).

[86] 42 C.F.R. § 493.1291(e).

[87] *See* 42 C.F.R. Part 493.

[88] PHSA § 353(f)(1).

selected have the capability of providing the quality of results required for patient care," and that "[v]erification procedures used are adequate to determine the accuracy, precision, and *other pertinent performance characteristics* of the [test] method."[89] These standards can be met only if the tests results are clinically relevant to the tested population.

The CLIA framework has worked well. Over the past few decades, health care providers have ordered millions of LDTs for their patients with few problems. With regard to genetic tests, for example, the Secretary's Advisory Committee on Genetics, Health, and Society has stated that "there have been few documented cases in which patients experienced harm because of errors in a CLIA-regulated genetic test."[90] Even though laboratories are not required to report adverse events, litigation or other publicity likely would have revealed more widespread incidence of harm if such harm had in fact occurred. Thus, regulation of LDTs under CLIA has effectively protected the public health.

To the extent that stakeholders have concerns about possible gaps in the clinical validation of LDTs, the most logical and appropriate solution would be to amend CLIA and/or its regulations. It would be overly burdensome to superimpose a new bureaucratic regime on the laboratory industry which is already highly regulated under CLIA. It would also be like trying to fit a square peg into a round hole to impose an additional layer of regulation based on a statute designed for products (FDCA) rather than laboratory testing procedures (CLIA).

The current approach of regulating IVD test kits and LDTs differently is appropriate because an IVD test kit presents more risks than an LDT. IVD test kits are designed for sale to a large number of laboratories of various sizes and skills for those entities' use. In contrast, the entity performing an LDT is, by definition, the laboratory that developed it and thus is familiar with and responsible for its performance characteristics.

VII. Conclusion

For the foregoing reasons, ACLA believes that FDA lacks authority to regulate LDTs as medical devices. Therefore, ACLA respectfully requests that FDA refrain from issuing a proposed or final rule or guidance purporting to regulate LDTs as devices. We also ask that the agency's response to this petition confirm that LDTs are not devices under the FDCA.

C. Environmental Impact

The actions requested herein are subject to categorical exclusion under 21 C.F.R. § 25.30(h).

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[89] 42 C.F.R. §§ 493.1407(e)(3)(i) & (ii), 493.1445(e)(3)(i) & (ii) (emphasis added).

[90] Secretary's Advisory Committee on Genetics, Health, and Society, "U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services" (Apr. 2008), at 32, *available at* http://oba.od.nih.gov/oba/sacghs/reports/sacghs_oversight_report.pdf (Exhibit 18).

D. Economic Impact

Pursuant to 21 C.F.R. § 10.30(b), an economic impact statement will be submitted only at the request of the Commissioner.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

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