

Laboratory Testing Services, As The Practice Of Medicine, Cannot Be Regulated As Medical Devices

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Executive Summary

Laboratory-developed testing services are an integral and longstanding component of the practice of medicine and have made immeasurable contributions to public health and the treatment of rare and complex diseases. They are developed and performed by thousands of authorized laboratories in the United States to help physicians diagnose diseases and assist them in deciding on a course of treatment.

For decades, laboratory-developed testing services have been comprehensively regulated by both state regulators and the Centers for Medicare and Medicaid Services (“CMS”). CMS administers the detailed requirements Congress enacted in the Clinical Laboratory Improvement Amendments of 1988 (“CLIA”) that were specifically tailored to and targeted at clinical laboratories and their tests.

Nonetheless, despite nearly three decades of comprehensive CMS oversight, the Food and Drug Administration (“FDA”) has recently asserted authority to regulate clinical laboratories and their tests pursuant to the Federal Food, Drug, and Cosmetic Act (“FDCA”). Specifically, FDA has issued “Guidance” documents that assert sweeping authority to treat laboratory-developed testing services as medical “devices” under its jurisdiction and purport to impose all manner of newly-imposed requirements on those services. FDA claims that Congress granted it this expansive and previously unexercised power *nearly 40 years ago*, through provisions that (unlike CLIA) do not even *mention* laboratories or laboratory testing services and expressly disclaim any intent to regulate the practice of medicine.

FDA’s novel effort to expand its jurisdiction is foreclosed by the plain text of the FDCA. Congress gave FDA the authority to regulate medical devices, and laboratory-developed testing services are not devices. Moreover, FDA’s effort to expand its jurisdiction will directly interfere with the practice of medicine, and will disrupt the ability of doctors to obtain the laboratory tests they need to provide the best possible care to their patients.

Recognizing the futility of asking Congress to grant it the unprecedented authority it now seeks to assert, FDA has proceeded on its own. But, whatever the rationale for its current approach, it is a dramatic overreach. FDA is attempting to saddle a dynamic and innovative industry with sweeping new regulatory burdens without any statutory basis. Worse still, FDA’s attempt to address laboratory-developed testing services as though they were medical devices is an impermissible effort to force a square peg into a round hole. The proper regulatory regime for manufactured articles of commerce—like drugs and medical devices—is simply not a suitable approach for laboratories that provide a service to individual physicians as part and parcel of the practice of medicine. To the contrary, laboratory testing services and medical devices raise completely different regulatory issues—as Congress itself recognized in enacting a distinct regulatory framework for clinical laboratory tests in CLIA, and in charging CMS rather than FDA with CLIA’s oversight of laboratories.

FDA’s attempt to impose burdensome requirements on laboratory-developed testing services through its Guidance documents is unlawful for a second reason as well: the effort violates bedrock principles of administrative law. In its haste to broaden its regulatory reach, FDA has bypassed the notice-and-comment procedures that are a prerequisite to the kind of binding rules that it seeks to impose on clinical laboratories. The agency’s use of Guidance documents in this setting is not some technical “foot fault.” It improperly circumvents the carefully crafted requirements of the Administrative Procedure Act—no mere bureaucratic enactment but a cornerstone, ever since 1946, of the administrative state. Courts and Congress alike have treated

broad delegations of power to executive agencies as permissible over the past six decades only because those agencies are duty-bound to comply with the APA. But FDA use of a Guidance document to effect substantive regulatory change lawlessly shields the agency from the congressional mandate that it meaningfully consider and respond to the comments it receives in the course of the public procedures Congress required. By proceeding via a Guidance approach, FDA is also impermissibly seeking to avoid assessing the enormous economic impact of its proposal and to avoid determining whether the benefits it would supposedly provide justify the costs it would undoubtedly impose. That is why the American Medical Association, American Hospital Association, and many leading medical providers have all requested that FDA withdraw its misguided Guidance proposal.

For all these reasons, FDA should withdraw its proposed Guidance.

Analysis

I. LABORATORY-DEVELOPED TESTING SERVICES ARE MEDICAL SERVICES

Laboratory-developed testing services are “in house” diagnostic tests developed, validated, and performed by highly trained professionals within a single clinical laboratory. Quite simply, physicians routinely depend on laboratory-developed tests in making crucial medical decisions for their patients. They are part and parcel of the practice of medicine. Therefore, it is not surprising that the American Medical Association and many leading medical providers have asked FDA to withdraw its proposed regulatory framework.

Laboratory-developed testing services are performed on blood, urine, tissue or other types of specimens at the request of an individual doctor, in the context of a specific doctor-patient relationship. Like the individual doctors themselves, the laboratories offer no physical product, but rather provide clinical information to physicians and their patients. A laboratory-developed testing service is a methodology or process—based on a laboratory’s unique knowledge of the protocols, performance characteristics, and means of analysis—by which the laboratory generates biochemical, genetic, molecular, or other forms of clinical information about a patient specimen that is provided to the treating physician.

Unlike a drug or device, which is a finished, packaged, off-the-shelf article of commerce accompanied by instructions for use by others, a laboratory-developed testing service is a proprietary methodology that is performed only by the developing laboratory. That service in turn generates a report of test results—for instance, whether the patient’s specimen contains a particular biomarker or analyte—that the laboratory transmits to the ordering physician. The testing service is not sold as a kit, and the protocol is not transferred in any manner to other laboratories, hospitals, or other facilities outside the developing laboratory entity; indeed, it is not distributed commercially at all. No physical product is sold. No article of personal property is transferred such that title passes from one party to another.

As FDA itself has recognized, such testing services are widely employed by doctors in their “clinical decision making and disease management, particularly in the context of personalized medicine.” FDA, Oversight of Laboratory Developed Tests, 75 Fed. Reg. 34,463 (June 17, 2010); *see also id.* (“they are often used ... to inform critical treatment decisions”) (emphasis added). In a hypothetical world of unlimited resources, doctors with access to cutting-edge scientific knowledge and equipment might in theory perform these tests in their own clinics, much like general practitioners might in theory perform specialized cardiac or neurological procedures in their own clinics. However, as with other medical specialties, referring these tests to professional laboratories is vastly more realistic and efficient and provides doctors and patients with access to a far larger and more up-to-date universe of potentially life-saving tests. Once a doctor receives the clinical information generated at that doctor’s request by the laboratory, the doctor reviews the results and makes his or her own diagnosis and treatment recommendations for the patient based on all the clinical information the doctor has obtained. Thus, unlike drugs or devices—which again are articles of commerce that are intended to be employed in the same way by any user, based on the manufacturer’s instructions—laboratory-developed testing services are developed by a laboratory for use only by that specific laboratory.

Doctors routinely rely on laboratory-developed testing services ranging from routine tests such as pap smears and gram stains, to the most advanced and sophisticated molecular and genetic sequencing tests for cancer, heart disease, and rare and infectious diseases. *See, e.g., Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013) (patent case addressing

laboratory-developed testing service for breast cancer risk by Myriad Genetics). While there are numerous, ready-made *in vitro* diagnostic test kits available in the marketplace, those commercially distributed kits address only a miniscule fraction of the situations in which laboratories can provide doctors with valuable diagnostic information. And even in situations in which commercially distributed test kits are available, the kits are frequently inadequate for patients who have particularized needs. For example, the FDA-approved BRAF test kit, used to characterize metastatic melanoma and other cancers, can detect mutated forms of the BRAF gene, but is unable to distinguish between two different mutational variants (V600E and V600K), each of which indicates very different treatments. Furthermore, for patients of Asian and Italian descent, there are additional genetic markers (*e.g.*, CKIT), not included in the FDA-approved test kit, which should be tested for in order to fully inform treatment decisions. Laboratory-developed tests have been formulated to meet these otherwise unmet clinical needs and provide physicians with the vital information they need to best treat their patients. In many instances, test kits are already outdated by the latest scientific knowledge upon their approval by FDA, and there are many biomarkers and analytes for which no standardized test kit yet exists. Where test kits would not generate the economies of scale necessary to justify a commercially marketed product—as with many rare diseases or conditions—laboratory-developed testing services are often the only available option. Such testing services include:

- “Gold standard” DNA sequencing and RNA expression tests, 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 tests, such as those used to detect leukemia, lymphoma, developmental delays, and mental retardation;
- Newborn screening tests for metabolic disorders;
- 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
- Child evaluation tests for developmental delays, such as Fragile X Syndrome testing and chromosome analysis.

History shows that tests are most often created in response to an otherwise unmet clinical need, or where the existing diagnostic tests are insufficient or fail to incorporate the most recent breakthroughs in scientific and medical research. Laboratories developed specialized tests for various cancer biomarkers, including KRAS (an oncogene frequently associated with colorectal, lung, pancreatic and other cancers), several years before FDA-approved test kits reached the general market. Laboratories likewise developed tests for emerging infectious diseases, such as HIV, SARS and H1N1, long before FDA-approved tests were available. In addition, laboratories validated a Western blot test to diagnose HIV-1 two years before an FDA-approved Western blot test became commercially available. Laboratory-developed testing services routinely represent the gold standard in facilitating the highest quality medical care.

In providing these medical services, laboratories are subject to comprehensive regulation by CMS, by state regulators, and often by “deemed authorities” under the CLIA program, including the Joint Commission on Oversight and the College of American Pathologists. These “deemed authorities” perform their own rigorous inspections to ensure that CLIA standards are

met and in some instances go even beyond those requirements. Laboratories regulated under CLIA are all required to be CMS-certified and state-certified as well. Those certifications ensure that the laboratories provide accurate information to doctors and that their testing processes are supervised by qualified personnel. For example, CLIA requires a qualified medical director to oversee all high-complexity clinical tests, and subjects each laboratory-developed test to analytical validity regulations to ensure that it does in fact accurately identify or measure the analyte (e.g., genotype, chemical, protein) that it purports to identify or measure. Nonetheless, precisely because the tests need *not* undergo the time-consuming premarket FDA approval process required of drugs and devices, laboratories are able to continually and rapidly innovate and improve their services. Laboratories have the flexibility and technical expertise to adapt in real time to the latest scientific advances. Laboratories continually modify and validate their tests to ensure that they reflect the most up-to-date technological know-how, scientific breakthroughs, and published research that will enable doctors to better serve their patients when the need arises, not when it is too late to be of use.

II. FDA’S SWEEPING ASSERTION OF JURISDICTION OVER LABORATORY-DEVELOPED TESTING SERVICES FLOUTS THE DECISIONS MADE BY CONGRESS

Both the text of the FDCA and the broader statutory context clearly foreclose FDA’s attempt to expand its jurisdiction to cover laboratory-developed testing services. Congress has expressly considered the unique regulatory issues raised by clinical laboratories and the tests they develop and perform. But it expressly addressed those issues through the comprehensive and entirely distinct statutory regime of CLIA, *not* through the FDCA. And Congress vested authority over those regulations in CMS, *not* in FDA. The text of the FDCA reflects this basic division of labor by granting FDA authority over “devices,” defined in terms that make clear that devices are articles of commerce, not the kinds of services performed by doctors and laboratories. Congress reinforced this division of labor by expressly precluding FDA from interfering with the practice of medicine. Moreover, multiple canons of construction, including the presumption against grants of controversial but long dormant regulatory authority and the rule of lenity, underscore that Congress did not *sub silentio* grant FDA the enormous regulatory power it seeks to exercise. FDA’s attempted expansion of its authority is flatly inconsistent with the statutory text, would transgress the explicit limitation against interfering with the doctor-patient relationship, and would raise serious constitutional questions that Congress itself sought to avoid.

A. FDA Has Asserted Sweeping Authority Over Laboratory-Developed Tests

Although laboratory-developed testing services have long been regulated both by the states and by CMS, FDA recently announced its own sweeping efforts to regulate those services via “Guidance” documents that purport to impose all manner of requirements through an elaborate, nine-year phased-in timetable. FDA’s assertion of regulatory authority is premised on the rather remarkable claim that the 1976 Medical Device Amendments (“MDA”) to the FDCA—enacted nearly four decades ago—rendered *all* laboratory-developed testing services “unapproved devices” under its jurisdiction. FDA posits that Congress took that dramatic step in provisions that did not mention laboratories, laboratory tests, or laboratory testing services, in a statute that specifically excludes from FDA’s jurisdiction any power to regulate the practice of medicine, and that is focused on the distinct problems concerning manufactured, mass-marketed, and widely-distributed drugs and devices moving in interstate commerce.¹

¹ The record shows that, in fact, the first time that FDA made a public claim about its supposed authority to regulate laboratory-developed testing services as devices was in a draft

The requirements FDA seeks to impose under its newly asserted authority are substantial. FDA’s so-called Guidance documents seek to impose significant, binding requirements on private parties that provide laboratory-developed testing services. In seeming recognition that FDA lacks the resources to regulate the entire range of laboratory-developed testing services over which it belatedly claims jurisdiction, the Guidance announces a risk-based, phased-in approach to a “Framework for Regulatory Oversight of Laboratory Developed Tests.” The main elements of this new Framework include numerous obligations that laboratories must observe in order to comport with numerous medical device regulations. These obligations include:

- Giving notification to FDA about, or registering and listing of, laboratory-developed testing services (and “significantly” changed laboratory-developed testing services) under 21 C.F.R. Part 807, to assist FDA in determining their risk classification and what premarket review requirements to enforce against which tests;
- Reporting of “adverse events” involving laboratory-developed testing services under 21 C.F.R. §803.50, whenever a laboratory that develops in-house tests or significantly modifies FDA-approved test kits becomes aware of any information that reasonably suggests that their test may have caused or contributed to death or serious injury;
- Submitting for premarket review “high-risk” and “moderate-risk” laboratory-developed testing services to assess their clinical validity, *see* 21 C.F.R. Part 814;
- Complying with Quality System Regulations, including the device-related design control procedures of 21 C.F.R. §820.30(a)-(j); and
- Demonstrating the “clinical validity” of laboratory-developed testing services.

These requirements are not uniformly imposed on all laboratory-developed testing services. Instead, FDA would classify laboratory testing services and, based on that classification, FDA would phase in requirements over a nine-year period after the Guidance is finalized. The Guidance documents thus envision that the contemplated regulatory regime will not be fully in place until 2024, at the earliest.

B. FDA’s Interpretation Is Foreclosed By The FDCA’s Plain Text

FDA’s assertion of authority over laboratory-developed testing services is clearly foreclosed by FDA’s own authorizing statute, the FDCA. On the face of the statute, laboratory-developed tests fall outside the ambit of FDA’s authority for at least three reasons: (1) they are not “devices” under 21 U.S.C. §321(h); (2) they are not “introduc[ed] into interstate commerce for commercial distribution” under 21 U.S.C. §360(k); and (3) they directly implicate the practice of medicine exempted under 21 U.S.C. §396.

1. Laboratory Testing Services Are Plainly Not “Devices”

Compliance Policy Guide in 1992. After objections, FDA removed any reference to laboratory tests in the final Compliance Policy Guide, released in 1996. It was not until 1996 that FDA announced in the Federal Register that it believed it had authority to regulate laboratory-developed testing services but was not exercising that power as a matter of discretion. Clinical laboratories and others filed comments challenging FDA’s assertion that it had the authority to oversee such testing services for twenty years but simply never used that authority. In any event, the legal analysis in this memorandum would not be affected even if FDA had consistently asserted the authority to regulate laboratory-developed tested services.

With the FDCA, Congress authorized FDA to protect the public health by regulating the safety and effectiveness of “any food, drug, device, tobacco product, or cosmetic” that is “introduc[ed] into interstate commerce.” 21 U.S.C. §331(a). Under the FDCA, therefore, FDA has authority to regulate manufacturers only of commercially distributed medical “devices,” including devices used to perform standardized clinical tests (so-called “test kits”). But laboratory-developed testing services are *processes* and *methodologies* that are qualitatively and categorically different from the tangible goods that FDA may regulate as “devices.” Statutory text, basic principles of interpretation, and common sense leave no doubt that laboratory-developed testing services are not medical “devices” under the FDCA.

In common usage, a “device” is a *physical article or product*. See *Oxford Dictionary of English* (3d ed.) (2010) (defining “device” as “a thing made or adapted for a particular purpose, especially a piece of mechanical or electronic equipment”); *American Heritage Dictionary* (5th ed. 2014) (defining “device” as “[a]n object designed and manufactured to perform one or more functions”). Laboratory-developed testing services are self-evidently not “devices.” Such in-house tests are proprietary *methodologies* rather than physical *products*. That is, laboratories provide a purely informational service, using their unique knowledge of the protocols, the performance characteristics, and the means of analyzing each test, to generate clinical information about a specimen for the ultimate use of the treating physician.

Consistent with the plain, common-sense meaning of “device,” the FDCA defines that term as “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory,” that satisfies various specified criteria.² 21 U.S.C. §321(h). The words grouped in §321(h) are, without exception, *physical articles* that move in interstate commerce. “The traditional canon of construction, *noscitur a sociis*, dictates that words grouped in a list should be given related meaning.” *Dole v. United Steelworkers of Am.*, 494 U.S. 26, 36 (1990) (“*noscitur a sociis*” literally means “it is known by the company it keeps”). Here, the statutory text itself reflects and reinforces that traditional canon by employing an inclusive catch-all term that uses the word “article.” In-house laboratory testing services are not physical “articles,” much less articles moving in commerce, and are categorically different from the items Congress enumerated as “devices.” Sweeping proprietary *methodologies* and *processes* into a list that includes only tangible articles would contravene the basic rule of construction that “words ... are known by their companions.” *Gutierrez v. Ada*, 528 U.S. 250, 255 (2000).

FDA asserts that Congress’ addition of “in vitro reagents” to §321(h) in the 1976 MDA was intended to sweep in all laboratory-developed testing services. But a testing service is not a “reagent.” Reagents are chemical substances or mixtures, *i.e.*, physical articles, that are separate and distinct from services that make use of them as part of their procedures. Indeed, the inclusion of reagents as an additional statutory example of a “device” cuts *against* FDA’s interpretation because it confirms that Congress focused its device definition on *physical articles*. See H.R. Rep. No. 94-853, at 14 (1976) (new definition “retain[ed] (in somewhat more precise detail) provisions

² A “device” must be: (1) “recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,” “intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals,” *or* “intended to affect the structure or any function of the body of man or other animals,” *and* (2) “not achieve its primary intended purposes through chemical action within or on the body of man or other animals and ... not [be] dependent upon being metabolized for the achievement of its primary intended purposes.” 21 U.S.C. §321(h).

of existing law that a device is *an article or component thereof*) (emphasis added). Had Congress wished to defy the ordinary conventions of the English language and define a “device” as “any process that *uses* a reagent,” it could easily have done so. It did not, and nothing in the Act suggests that Congress subjected clinical laboratory methodologies to the FDCA’s “device” regulations.

When the statutory text is this clear, there is no need for resort to legislative history. See *Ratzlaf v. United States*, 510 U.S. 135, 148 (1994). But here, the legislative history underscores that Congress used “device” in its ordinary sense and that the 1976 MDA did not introduce any sweeping change in the statute’s device coverage. To the contrary, the House Reports repeatedly referred to “devices” as “products” and “articles.” See H.R. Rep. No. 94-1090, at 62, 65 (1976) (Conf. Rep.); H.R. Rep. No. 94-853, at 6 (1976).

It is far-fetched to suppose that laboratory-developed testing services *become* medical devices in their own right merely because they sometimes *utilize* other medical devices. FDA’s own regulations recognize the distinction between a service that uses devices and a device itself. For example, the FDA regulation excluding laboratories from device registration requirements specifically recognizes that laboratories’ “primary responsibility to the ultimate consumer is to ... provide a service *through the use* of a previously manufactured device.” 21 C.F.R. §807.65(i) (emphasis added). Laboratories may well draw on both reagents and laboratory equipment of many kinds in executing their clinical testing services, but that plainly does not render the services these laboratories perform *themselves* “medical devices.” A contrary view would mean that all surgical procedures and physical examinations that may *use* devices—*i.e.*, virtually *every* medical procedure (except perhaps those few procedures that use only a physician’s own eyes, ears, and hands)—would be deemed “devices” subject to the FDCA’s regulations. For example, every time a radiologist reads an x-ray, he or she is providing a service that depends on a medical device—the x-ray machine. However, the radiologist is rendering a service, and is not subject to regulation under the FDCA. It is plainly not the law that a surgical procedure like an appendectomy is itself a “device” merely because it *uses* devices such as surgical instruments, sutures, and other medical equipment. Cf. *Nixon v. Mo. Mun. League*, 541 U.S. 125, 138 (2004) (courts should not construe statutes to produce absurd results).

Nor does it matter that a particular laboratory-developed testing service may be *functionally similar* to some kind of device. FDA heavily emphasizes, for example, that *in vitro* diagnostic (“IVD”) test kits perform clinical testing functions that are *similar* to laboratory-developed testing services. See FDA Denial of ACLA Citizen Petition (“FDA Denial”) at 4-5. But IVD test kits are devices by any plausible reading of the statutory definition; laboratory testing services do not become “devices” because they allow physicians to accomplish similar ends. FDA ignores the fact that the statute does not classify based on functionality, but on whether something is a physical article that a manufacturer commercially distributes in interstate commerce. Not only does a functional approach have no basis in the statutory text, but it would be completely unworkable in practice. Most medical devices are designed to allow a treating physician to perform some function more effectively, and many are substitutes for a service that the doctor would otherwise perform. For example, a sophisticated medical device may obviate the need for a more invasive or riskier form of surgery, but the functional similarity of a doctor’s service to a medical device does not thereby turn the doctor’s service into a device.

Once again, the legislative history confirms what the text makes clear. Congress had IVD *products* in mind (unlike in-house laboratory testing *services*) in enacting the MDA amendments to the “device” definition. The Senate Report specifically noted that the “in-vitro diagnostic *products*” covered by the new definition “include those *products* which are not ingested and which are used to assist in the diagnosis of disease or other conditions of the body.” S. Rep. No. 94-33,

at 17 (1975) (emphases added). Where the statute itself draws a distinction between devices and non-devices, FDA may not conjure up regulatory gaps based on functional resemblances and then use that purported similarity to expand its own jurisdiction.³

At bottom, plain text, basic principles of statutory interpretation, and common sense foreclose FDA's assertion of authority over laboratory-developed testing services. FDA jurisdiction over those services would require not merely a "broad" reading of section 321(h), but a rewriting of the statute.⁴

2. Laboratory-Developed Testing Services Are Not Introduced Into Interstate Commerce for Commercial Distribution

Section 510(k) of the FDCA, which applies FDA's approval and clearance requirements only to devices that *both* move in interstate commerce *and* are commercially distributed, further underscores that Congress did not remotely mean to grant FDA authority to regulate laboratory-developed testing services. Section 510(k) provides:

Each person who is required to register under this section and who proposes to begin the introduction or delivery for introduction into 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 360d [related to performance standards] or 360e [related to premarket approval] which are applicable to the device.

21 U.S.C. §360(k). FDA has defined "commercial distribution" to mean "any distribution of a device intended for human use which is held or offered for sale," 21 C.F.R. §807.3(b), and to generally require delivery to purchasers or consignees. FDA Manual of Compliance Policy Guides §300.600 (1978, reissued 1987) ("CPG").

Laboratory-developed testing services obviously do not move in interstate commerce. Indeed, FDA itself acknowledged this fact in the preamble to its rule governing analyte specific reagents ("ASRs"), stating that the focus of its rule was "the classification and regulation of ASR's *that move in commerce*, not tests developed in-house by clinical laboratories." Medical Devices; Classification/Reclassification; Restricted Devices; Analyte Specific Reagents, 62 Fed. Reg. 62,243, 62,249 (Nov. 21, 1997) (emphasis added). Unlike IVD test kits, which are mass-produced, mass-distributed products delivered to numerous laboratories and consumers, the laboratory-developed testing services are not commercially distributed. The testing services are performed in-house and the proprietary methodologies employed in the in-house testing are specific to the individual laboratory entity and never leave its confines. And while the results of the testing services do leave the laboratory, they are not commercially distributed, but rather are communicated to the requesting physician and patient. None of this is to suggest that Congress could not regulate the laboratories and their testing services as a valid exercise of its commerce power. Indeed, Congress has done just that in other statutes. But the Medical Device

³ FDA regulations that define "devices as defined in section [321](h)" as including several "[i]n vitro diagnostic *products*" only confirm that the "device" definition covers products, not services. 21 C.F.R. §809.3(a) (emphasis added).

⁴ Even the sole district court case that FDA cites as supporting a "broad" understanding of "device" involved a physical instrument, and does not sweep nearly as broadly as FDA's current theory. *See United States v. 22 Rectangular Or Cylindrical Finished Devices*, 714 F. Supp. 1159, 1165 (D. Utah 1989) (upholding FDA's determination that a sterilizing *instrument* that did not come into direct contact with patients was a "device").

Amendments of 1976 were, as their name suggests, directed at devices, which Congress understood to be physical articles that can be introduced into commerce and commercially distributed. The fact that laboratory-developed testing services are not commercially distributed is just one more indication that Congress did not intend to reach those services in the MDA.

FDA argues that the “commercial distribution” requirement is satisfied here because laboratory-developed tests “are *offered* commercially for use in the diagnosis/treatment of patients,” such as through “promot[ion] ... on their website.” FDA Denial at 13 (emphasis added). Mere promotion, however, is not sufficient to establish commercial distribution. Nobody would describe an interstate advertisement as the “commercial distribution” of either the words comprising the advertisement or of the goods or services the advertisement describes and promotes. The legislative history of the MDA confirms this commonsense conclusion by specifically noting that “commercial distribution” does *not* include “mere announcements of intent to market a device.” H.R. Rep. 94-853, at 36 (1976). Even FDA’s own Compliance Policy Guide, moreover, has clarified that offering a device for sale is not enough; a 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. CPG §300.600. Indeed, far from being commercially distributed, laboratory-developed testing services are often required precisely because the same clinical information *cannot* be obtained from commercially distributed test kits. And, of course, the promotion of a service is very different from the distribution of an article—as different, indeed, as the provision or advertisement of medical advice is from the sale of a stethoscope or a syringe.

In short, the statute’s commercial distribution requirement underscores the FDCA’s focus on problems arising in connection with manufactured, mass-marketed, and widely-distributed drugs and devices—yet another indication of Congress’ intent to regulate products far afield from the informational in-house services of laboratories to meet the needs of individual patients.

3. Regulating Laboratory Testing Services As Devices Would Interfere With The Practice Of Medicine

That laboratory-developed testing services fall outside of the FDCA’s device definition is further confirmed by Congress longstanding reluctance to interfere with the practice of medicine, which is underscored by an express statutory disclaimer of such interference. Congress enacted the FDCA and its “device” definition in 1938 against a well-established background understanding that “direct control of medical practice in the states is beyond the power of the federal government.” *Linder v. United States*, 268 U.S. 5, 18 (1925); *see also Rush Prudential HMO, Inc. v. Moran*, 536 U.S. 355, 387 (2002) (establishing “standards of reasonable medical care” is a “quintessential[] state-law” function). As the Act’s sponsor, Senator Royal Copeland, explained, “the bill is not intended as a medical practices act and will not interfere with the practice of the healing art by [persons] in the States where they are licensed by law to engage in such practice.” S. Rep. No. 74-361, at 3 (1935). In fact, a bill seeking to clarify that the definition of “drug” did not encompass any “medicine prepared and dispensed by a physician in the course of his professional practice” was rejected as superfluous because there was “nothing in the [FDCA] which would interfere at all with the ordinary legal practice of medicine.” Peter Barton Hutt, *Regulation of the Practice of Medicine Under the Pure Food and Drug Laws*, 33 Q. Bull. Ass’n of Food & Drug Off. 1, 8 (1969).

In 1997, Congress added a provision making *explicit* what had always been implicit: that the FDCA does not regulate the practice of medicine. Section 1006 provides: “Nothing in this chapter shall be construed to limit or interfere with the authority of a health care practitioner to

prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship.” 21 U.S.C. §396. That provision, as the Supreme Court has recognized, reinforces that FDA’s “mission [is] to regulate ... without directly interfering with the practice of medicine.” *Buckman Co. v. Plaintiffs’ Legal Comm.*, 531 U.S. 341, 350 (2001). “FDA is charged with the difficult task of regulating the marketing and distribution of medical devices without intruding upon decisions statutorily committed to the discretion of health care professionals.” *Id.*

However, laboratory-developed testing services are part and parcel of the practice of medicine. To regulate the generation of information that a physician asks a consultant or a consulting laboratory to provide—by performing tests on specimens provided by the physician in order to assist that physician in diagnosing the patient’s illness or in prescribing a course of treatment—interferes with that physician’s decisions of what to prescribe or administer to his or her patient. In fact, in a hypothetical world of unlimited resources, highly-trained doctors with access to cutting-edge scientific knowledge and equipment might in theory perform these tests in their own clinics, much in the same way that a general practitioner in a hypothetical world of unlimited resources might in theory be able to perform specialized cardiac or neurological procedures in their own clinics. However, as with other medical specialties, referring these tests to professional laboratories is far more realistic and efficient and provides doctors and patients with access to a far larger and more up-to-date universe of potentially life-saving tests.

For instance, clinical laboratories routinely perform tests that are premised on new scientific developments, are used to test for unique or complicated conditions, or are more sensitive and sophisticated than off-the-shelf FDA-approved test kits. That referral of responsibility, however, does not change the fact that the tests are merely an extension of the *doctor’s* favored methods for evaluating a patient and diagnosing the problem. Whether outsourced or not, the testing methodology is part and parcel of the doctor’s practice of medicine, not materially different from the same doctor’s consultation of an up-to-date, peer-reviewed medical journal or clinical examination of their own patient. The laboratory offers the doctor an objective array of factual information—for instance, a patient’s genetic predisposition to a particular disease—from which the doctor draws his or her *own* interpretation, diagnosis, and treatment recommendations.

In this respect, laboratory-developed testing services are fundamentally different from drugs and devices—products that *themselves* promise to yield a particular diagnosis or treatment upon application to the patient and that are accompanied by instructions for use. Laboratory-developed testing services, by contrast, are developed and performed at the request of an individual doctor, within the context of a doctor-patient relationship, to inform the doctor’s independent diagnosis and treatment decisions. The laboratories provide no physical product. They provide a *medical service*, just as physicians do.

Regulating laboratory-developed testing services as devices, as FDA seeks to do, would thus fundamentally “interfere with the authority of ... health care practitioner[s]” to make diagnosis and treatment decisions. 21 U.S.C. §396.

Remarkably, FDA does not dispute that its actions will interfere with the diagnosis and treatment decisions of doctors. Instead, FDA contends that section 1006 only protects doctors’ right to administer “legally marketed” devices, not “unapproved” devices. But FDA’s contention is hopelessly circular: the question to be answered here is whether laboratory-developed testing services are “devices” subject to approval by FDA, and the fact that treating them as such would interfere with the practice of medicine is itself an important reason for concluding that they are not. Similarly, the mere possibility that a laboratory-developed testing service could potentially *use* an “unapproved” device—such as an unauthorized reagent, over which FDA *does* have

jurisdiction—does not and cannot bring the *services themselves* within FDA’s regulatory reach. Just as a doctor’s use of an unapproved device in treating a patient would not render the doctor’s medical services “devices” under the FDCA, so too a laboratory’s hypothetical use of an unapproved reagent in conducting a testing service would not suddenly transform its testing service into a “device”—particularly because, in both cases, the assertion of FDA authority would be a brazen interference with the practice of medicine.

In all events, FDA’s premise—that doctors, in relying on laboratories and their testing processes in their practice of medicine, are using “unapproved” devices—only underscores the extreme implications of FDA’s broad interpretation of the FDCA: that the entire medical profession has, unbeknownst to doctors, been involved in the widespread illegal distribution of unapproved medical devices since 1976. Under FDA’s theory, every doctor who sends a specimen for analysis via a laboratory-developed testing service is really soliciting an unlawful medical device. See 21 U.S.C. 331(c) (prohibiting receipt of a misbranded medical device). Moreover, FDA’s theory necessarily means that an entire laboratory-testing industry has been unwittingly operating in violation of a number of criminal statutes for decades, spared from prosecution only by FDA’s grace. As the Seventh Circuit concluded in rejecting a similarly sweeping government theory in a different context, the far “more plausible hypothesis” is that the industry’s practice is simply not unlawful. *Yi v. Sterling Collision Centers, Inc.*, 480 F.3d 505, 510-511 (7th Cir. 2007).

In sum, the FDCA’s practice-of-medicine exception is further evidence that Congress did not intend to treat in-house tests developed by laboratories as “devices.” Both doctors and patients would ultimately suffer the adverse consequences of subjecting laboratory-developed tests to FDA’s clearance and approval requirements. Because obtaining FDA pre-approval is often not financially feasible for tests that serve only small patient populations, and because obtaining FDA re-approval is not workable for laboratories that continually modify thousands of in-house tests, the end result would be less laboratory-generated clinical information that doctors can use to assess and care for their patients. Nothing in the FDCA remotely contemplates, let alone compels, this harmful and potentially life-threatening interference with the practice of medicine.

C. Bedrock Principles of Statutory Construction Reinforce The Conclusion That FDA Lacks Jurisdiction

Two bedrock principles of statutory interpretation further reinforce the conclusion that FDA lacks the sweeping authority over laboratory-developed testing services it now belatedly asserts.

First, Congress is presumed not to address issues of great “economic and political significance” in a “cryptic ... fashion.” *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 160 (2000). Congress “does not, one might say, hide elephants in mouseholes.” *Whitman v. Am. Trucking Ass’n*, 531 U.S. 457, 468 (2001). For decades, countless clinical laboratories have openly developed in-house tests—up to thousands of in-house tests per laboratory—without seeking premarket approvals from FDA, and have also modified FDA-approved test kits without reapplying for new approvals. Innumerable doctors have widely employed such laboratory-developed testing services to obtain clinical information to help them diagnose and treat their patients. It is late in the day indeed to conclude that all these laboratories and physicians have been unlawfully utilizing unregistered medical devices for all these years based on a statutory provision no one understood to have this dramatic effect. It is little wonder then that the American Medical Association, together with American Hospital Association, Coalition for 21st Century Medicine, Emory University, LabCorp, Mayo Clinic, Miraca Life Sciences, Quest Diagnostics and Seattle Children’s Hospital, have separately expressed grave concern about FDA’s proposal.

FDA's position—that Congress in 1976 *sub silentio* subjected in-house laboratory tests to FDA premarket clearance and approval requirements—would have a breathtaking economic impact on traditional laboratory practices, on the physicians who rely on laboratory medicine to facilitate their diagnostic and treatment decisions, and on the allocation of regulatory authority between FDA and CMS. “When an agency claims to discover in a long-extant statute an unheralded power to regulate ‘a significant portion of the American economy,’ we typically greet its announcement with a measure of skepticism.” *Util. Air Regulatory Grp. v. E.P.A.*, 134 S. Ct. 2427, 2444 (2014). Congress is presumed not to have dramatically upended a well-settled regulatory landscape without some clear indication in the relevant statutory text and history. *See id.*; *Brown & Williamson*, 529 U.S. at 160). FDA's assertion of an “unheralded authority” to regulate thousands of laboratories already subject to regulation by CMS and state regulators “falls comfortably within the class of authorizations that we have been reluctant to read into” statute in the absence of unambiguous text. *Util. Air Regulatory Grp.*, 134 S. Ct. at 2444.

Second, the “rule of lenity” requires that when a statute carries criminal penalties, “less constrained” constructions must be rejected absent “Congress’ clear instruction otherwise.” *Skilling v. United States*, 561 U.S. 358, 411 (2010). Basic principles of due process require that a federal statute define the conduct it proscribes with specificity so that ordinary persons are on notice of what conduct is prohibited and required. *United States v. Lanier*, 520 U.S. 259, 266 (1997).

That tenet squarely applies to the FDCA, which provides for both civil *and criminal* penalties for violations, *see* 21 U.S.C. §331, 333(a), and must be interpreted consistently in both contexts. *See Clark v. Martinez*, 543 U.S. 371, 380 (2005); *Leocal v. Ashcroft*, 543 U.S. 1, 11-12 n.8 (2004). Moreover, “where, as here, an agency’s announcement of its interpretation is preceded by a very lengthy period of conspicuous inaction, the potential for unfair surprise is acute.” *Christopher v. SmithKline Beecham Corp.*, 132 S. Ct. 2156, 2168 (2012). FDA’s theory would mean that the innumerable laboratories that have openly bypassed FDA’s device regulations over the past four decades, and the countless doctors who have widely employed such “unapproved devices” in diagnosing and treating individual patients, have been spared criminal penalties only by the grace of a decades-long exercise of enforcement discretion. Where a federal agency has “never initiated any enforcement actions ... or otherwise suggested that it thought the industry was acting unlawfully,” it is highly unlikely that the industry has been operating unlawfully for decades—instead, “the ‘more plausible hypothesis’ is that the [agency] did not think the industry’s practice was unlawful.” *Id.* (quoting *Yi*, 480 F.3d at 510-511). Any construction of the FDCA that would render thousands of CMS- and state-regulated laboratories and hundreds of thousands of doctors a professional class of unwitting, unprosecuted violators of federal criminal law rests on a highly implausible interpretation of what Congress did and what it intended and must accordingly be rejected.

D. FDA’s Interpretation Is Foreclosed By The Broader Regulatory Scheme

The FDCA itself makes plain that laboratory-developed testing services do not fall within FDA’s delegated authority. Where “the intent of Congress is clear and unambiguously expressed by the statutory language at issue, that [is] the end of our analysis.” *Zuni Pub. School Dist. No. 89 v. Dep’t of Educ.*, 550 U.S. 81, 93–94 (2007). Nonetheless, here, “the broader context of the [statutory scheme] as a whole,” *Robinson v. Shell Oil Co.*, 519 U.S. 337, 341 (1997), makes crystal clear what is already evident from the face of the FDCA: Congress’ enactment of CLIA’s 1988 amendments leaves no doubt that the FDCA does not bear the weight of FDA’s reading. That is, there is no need to speculate as to why Congress did not bring laboratory-developed testing services under FDA’s authority in the FDCA. When Congress expressly considered and addressed

the unique issues posed by laboratory-developed testing services, it opted to do so in a different statute (CLIA) administered by a different agency (CMS).

Clinical laboratories have been regulated by the federal government in various ways, going back to at least 1967, and yet at no time was there any suggestion of the FDA's ability to regulate laboratory-developed testing services. For example, laboratories engaged in interstate commerce were initially regulated under the Clinical Laboratory Improvement Act of 1967. Pub. L. 90-174, 81 Stat. 536 (1967). At the same time, laboratories participating in Medicare also had to meet separate regulatory requirements established in Medicare's Conditions of Participation or Conditions of Coverage applicable to the particular type of laboratory involved. *See* 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. 9538-39. However, there is nothing in those regulations to suggest that FDA, rather than CMS (referred to then as HCFA, the Health Care Financing Administration) had authority over laboratory-developed testing. In fact, when HCFA revised the Medicare and 1967 CLIA regulations in 1990, it noted that FDA *did* have authority over blood bank programs, but made no mention of authority over laboratory-developed testing services. *Id.*

In CLIA's 1988 amendments—passed 12 years after the 1976 MDA—Congress created an even more detailed statutory framework specifically to govern clinical laboratories and their tests. Congress centralized oversight, moreover, under the auspices of HHS (in turn, CMS)—*not* FDA. CLIA requires the certification of 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.” 42 U.S.C. §263a(a). CLIA prohibits these laboratories from soliciting or accepting specimens for laboratory tests until the laboratories are CMS-certified. *Id.* §263a(b). CLIA further provides that CMS “shall issue standards” to ensure quality control, including standards “adequate and appropriate for the validity and reliability of the laboratory examinations” and standards for the personnel “qualifications ... for the direction, supervision, and performance of examinations and procedures within the laboratory.” *Id.* §263a(f)(1)(A), (C). CLIA also requires laboratories to participate in regular “proficiency testing.” *Id.* §263a(f)(1)(D).

The very enactment of the CLIA amendments in 1988 would be well-nigh inexplicable if Congress had intended in the 1976 MDA, as FDA asserts, to subject laboratory-developed testing services to the FDCA's device regulations. Under FDA's theory, by the time Congress amended CLIA in 1988, FDA *already* had authority to regulate *the very same tests*—authority that it was simply declining in its discretion to exercise. But that theory cannot be sustained without rendering CLIA utterly pointless. Instead, Congress passed the CLIA amendments precisely because Congress did not share FDA's interpretation of the MDA.

Indeed, neither CLIA's statutory text nor legislative history in 1988 makes any reference to preexisting FDA authority to regulate laboratory-developed testing services, let alone the sweeping authority to regulate such services as “medical devices.” Since Congress was prompted to action by concerns about the inadequate regulation of pap testing (a laboratory-developed testing service), if FDA possessed pre-existing authority that it had failed to tap, there is little doubt that FDA officials would have been in the proverbial “hot seat” before Congress. Instead, FDA was unmentioned.

Making the absence of FDA references all the more noteworthy, Congress' avowed objective in CLIA's 1988 amendments was to replace the “patchwork of inconsistent and overlapping standards” regulating clinical laboratories to date with a “unified regulatory mechanism.” S. Rep. No. 100-561, at 3 (1988); H.R. Rep. No. 100-899, at 12 (1988); *see also* 134 Cong. Rec. 23606 (1988) (statement of Rep. Dingell) (“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.”). Accordingly, the legislative history is replete with references to the overlapping standards of CLIA, of the Medicare statute, and of state regulation—but strikingly devoid of any references to FDA or the FDCA. For instance, the House Report stated that clinical laboratories had, to date, been “governed by two separate and distinct statutes, *Medicare and CLIA*,” and included a section entitled “Current Regulatory System” that contained no mention whatsoever of FDA. H.R. Rep. No. 100-899, at 11-12 (1988). Thus, even as Congress took deliberate steps to streamline and strengthen federal regulations over clinical laboratory testing, it made no acknowledgement of any parallel FDA standards.

In fact, Congress armed CMS with enforcement authorities under CLIA that, on FDA’s theory, would be wholly redundant with FDA’s enforcement authorities under the FDCA. For instance, CLIA requires laboratories to submit to inspections of their “facilities, equipment, materials, records, and information” to verify compliance with CMS standards, 42 U.S.C. §263a(g)—a provision that, on FDA’s reading, would be rendered superfluous by FDCA’s requirement that device establishments submit to inspections, 21 U.S.C. §374(a)(1)(B).

Worse still, CMS laboratory test regulations would *conflict* with FDA device regulations. CMS, for example, has distinguished laboratory tests that use FDA-approved products from laboratory tests that use products that have not undergone the FDA approval process. For the latter, CMS requires enhanced performance specifications, obligating laboratories to establish every test system’s “analytical sensitivity,” “analytical specificity to interfering substances,” and other additional performance characteristics “before reporting patient test results.” 42 C.F.R. §493.1253(b)(2). Any FDA guidance requiring this latter category to undergo premarket device approval processes would thus be flatly irreconcilable with the prescriptions in §493.1253(b)(2). Similarly, CMS allows laboratories to continually update their tests to reflect new scientific developments as long as they appropriately validate and document any modifications. But FDA’s device regulations would, in sharp contrast, require supplemental filings and FDA authorizations for any and all modifications—an utterly impractical mandate given the constantly evolving and dynamic nature of laboratory-developed testing services.

In sum, CLIA’s 1988 amendments leave no doubt that Congress intended *not* to regulate laboratory-developed testing services in the 1976 MDA. To the extent more regulation is required, CLIA makes clear that Congress’ approach has been to enhance oversight by CMS, not to grant new and duplicative authority to FDA.

E. Even If The FDCA Were Ambiguous, FDA’s Interpretation Would Be Objectively Unreasonable

FDA’s view that laboratory-developed testing services can be regulated as medical “devices” is “clearly contrary to the intent of Congress.” *Edward J. DeBartolo Corp. v. Fla. Gulf Coast Bldg. & Constr. Trades Council*, 485 U.S. 568, 574 (1988). In any event, even if there were some ambiguity in the FDCA, FDA’s view would be an objectively unreasonable and substantively indefensible interpretation of the statute. It would mean that Congress, in exceptionally cryptic fashion, rendered *all* laboratory-developed testing services (if not *all* services that utilize a medical device) unapproved medical devices, even though such services do not entail any physical product. It would mean that Congress did so in a statute that was concerned with the “commercial distribution” of mass-produced physical articles moving in interstate commerce, when individualized in-house laboratory tests never even leave the confines of the laboratory, let alone move across state borders—and when Congress specifically addressed the entirely distinct issues of clinical laboratory tests in a wholly different statute, CLIA, overseen by a different agency, CMS. And it would mean that Congress, in the FDCA, interfered with the

practice of medicine in contravention of the FDCA's own explicit disclaimer of such intent. That far-fetched interpretation of Congress' actions cannot withstand scrutiny. See *Commissioner v. Brown*, 380 U.S. 563, 571 (1965) (courts have "some scope for adopting a restricted rather than a literal or usual meaning of [statute's] words where acceptance of that meaning would lead to absurd results").

In fact, construing the FDCA to authorize FDA's regulation of and interference with the practice of medicine and the doctor-patient relationship could well raise nettlesome constitutional questions both about federal intrusion into the medical domain and about heavy-handed governmental regulation of a sensitive personal and professional relationship. See, e.g., *Rust v. Sullivan*, 500 U.S. 173, 200 (1991) ("It could be argued by analogy that traditional relationships such as that between doctor and patient should enjoy protection under the First Amendment from Government regulation..."); *Colautti v. Franklin*, 439 U.S. 379, 387 (1979) (citing "the central role of the physician" and "the importance of affording the physician adequate discretion in the exercise of his medical judgment"); *Planned Parenthood of Central Mo. v. Danforth*, 428 U.S. 52, 67 n. 8 (1976) (condemning regulations tending to "confine the attending physician in an undesired and uncomfortable straitjacket in the practice of his profession"). FDA should avoid any interpretation that raises such constitutional questions. The doctrine of "[c]onstitutional avoidance trumps even *Chevron* deference, and easily outweighs any lesser form of deference [a court] might ordinarily afford an administrative agency."⁵

As a practical matter, moreover, FDA is manifestly not equipped to bear the massive regulatory burden it claims that Congress intended it to shoulder. FDA has projected that it would take nearly *a decade* for it to phase in its asserted regulatory authority over laboratory-developed testing services. That it would take that many years to handle the full scope of the administrative responsibilities it asserts is yet another indication that Congress never intended for FDA's preexisting (and ill-suited) regulations over drugs and devices in interstate commerce to sweep in laboratory-developed testing services. Just last Term, the Supreme Court rejected a similar effort by a federal agency to claim newfound regulatory authority in ways that would overburden the agency's resources. See *Util. Air Regulatory Grp.*, 134 S. Ct. at 2444. As the Court explained, the fact that an expansive interpretation of regulatory authority "would place plainly excessive

⁵ *Union Pac. R.R. Co. v. U.S. Dep't of Homeland Sec.*, 738 F.3d 885, 893 (8th Cir. 2013) (discussing *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984)); see also *Edward J. DeBartolo Corp. v. Florida Gulf Constr. Coast Bldg. and Trades Council*, 485 U.S. 568, 574-75 (1988) (noting that a "statutory interpretation by the Board would normally be entitled to deference" but not deferring to the Board's interpretation because it would raise a serious constitutional issue that could be avoided through an alternative interpretation); see also *Solid Waste Agency of N. Cook Cty. v. U.S. Army Corps of Eng'r*, 531 U.S. 159, 174 (2001) (court chose to "read the statute as written to avoid the significant constitutional and federalism questions raised by [the Army Corps of Engineers'] interpretation, and therefore [to] reject the request for administrative deference"); *U.S. West, Inc. v. FCC*, 182 F.3d 1224, 1231 (10th Cir. 1999) ("[I]f we determine that [agency's] rule presents a serious or grave constitutional question, we will owe the [agency] no deference, even if its . . . regulations are otherwise reasonable, and we will apply the rule of constitutional doubt."); *Campbell on Behalf of Campbell v. Shalala*, 1994 WL 163719, at *4 (D. Me. Mar. 16, 1994) ("Such an interpretation of the Secretary's income counting provisions [in agency regulations] is obviously to be avoided," because it "would implicate Fifth Amendment equal treatment concerns."); *Moreland v. Sullivan*, 765 F. Supp. 970, 975 (C.D. Ill. 1991) ("The court is aware that it generally must defer to an administrative agency's interpretation of its own regulations. Yet the court is also aware that it must avoid a regulatory interpretation that presents serious constitutional difficulties.").

demands on limited government resources is alone a good reason for rejecting it.” *Id.* But the agency’s felt need to impose limits on its newly-claimed jurisdiction—limits found nowhere in the statute itself—to make the program administrable provides further evidence that the agency has exceeded its statutory authority. *See id.* at 2446 (“We are not willing to stand on the dock and wave goodbye as [the agency] embarks on this multiyear voyage of discovery.”).

Indeed, “[t]hree recent studies” from the FDA Science Board, the National Academies Institute of Medicine, and the GAO have all concluded that FDA “suffers from serious scientific deficiencies and is not positioned to meet current or emerging regulatory responsibilities” and “lacks the resources needed to accomplish its large and complex mission.” *Wyeth v. Levine*, 555 U.S. 555, 578 n.11 (2009). A former FDA chief counsel has observed that FDA suffers from “the hollow government syndrome—an agency with expanded responsibilities, stagnant resources, and the consequent inability to implement or enforce its statutory mandates.” Peter Barton Hutt, *The State of Science at the Food and Drug Administration*, 60 ADMIN. L. REV. 431, 431 (2008). An FDA advisory panel has observed that, since 1938, when the FDCA was enacted, Congress has adopted “125 statutes that directly impact FDA’s regulatory responsibilities,” by requiring “the development of implementing regulations, guidance or other types of policy, and some require the establishment of entire new regulatory programs.” FDA Science Board, *FDA Science and Mission at Risk: A Report of the Subcommittee on Science and Technology* §2.1 (2007). Virtually all of those statutory mandates “require some type of scientific knowledge or expertise for the agency to address them.” *Id.* The report found that, despite the addition of all of these requirements, Congress has not provided “an appropriation of new personnel and increased funding designed to allow adequate implementation.” *Id.* The report concluded that “[t]he scientific demands on the Agency far exceed its capacity to respond” and that FDA has “serious scientific deficiencies and is not positioned to meet current or emerging regulatory responsibilities.” *Id.*, at §1.1, pp. 2-3.

FDA’s proposed actions, moreover, would have numerous adverse public health repercussions fundamentally inconsistent with its mission. As an initial matter, FDA oversight of laboratory-developed testing services would sharply curtail the number and range of tests available to doctors and their patients. Currently, a wide swath of critical diagnostic tests are available only as in-house laboratory tests, including many “gold standard” DNA sequencing assays, newborn screening tests, and tests for rare diseases. The prohibitive costs of obtaining FDA premarket clearance or approval for each such test would leave many laboratories unable to continue offering them, despite patient need and physician demand. Even where supported by well-accepted, peer-reviewed research and scientific studies, “low-volume” tests designed for individual patients or small patient populations often generate only modest financial returns for laboratories. In turn, the patients who benefit from the valuable clinical information generated by these tests would be left with no alternatives.

FDA oversight would also render critical testing, particularly for patients with emergent infectious diseases, unavailable in the “lag time” before FDA approval. The FDA approval process is protracted and not designed for the rapid clearance of tests. Many clinical laboratories track world trends regarding infectious diseases and have demonstrated immediate or near-immediate responses to infectious diseases ranging from SARS to H1N1 and Avian Influenza. In these fast-moving, life-or-death situations, awaiting the development of manufactured test kits and the completion of FDA’s clearance procedures could entail potentially catastrophic delays, with disastrous consequences for patient care.

In the long run, moreover, FDA oversight would stunt and stifle innovation and competition in the diagnostic testing field. Laboratory tests are constantly evolving in response to scientific advances. Laboratories continually develop, refine, and validate their tests to ensure

that they reflect the most up-to-date scientific literature and advanced diagnostic testing technologies. Furthermore, laboratories routinely modify FDA-approved and FDA-cleared *in vitro* diagnostic test kits in order to improve performance, expand diagnostic capabilities, or to incorporate the latest scientific research and discoveries to benefit patients. Regulating laboratory-developed testing services as devices, however, would dramatically slow not only the initial premarket approval of new tests, but also improvements to existing tests, delaying access to new and improved diagnostic testing services for patients and clinicians. In the long run, such regulation would impede clinical laboratories' ability to meet public health needs.

* * *

In sum, FDA's asserted jurisdiction over laboratory-developed testing services lacks any statutory basis and embodies a misguided attempt to fit a square peg in a round hole. FDA's strained reading of its preexisting authority under the FDCA defies bedrock principles of statutory interpretation, common sense, and longstanding industry practice. Indeed, the FDCA—a statute targeted at mass-produced, mass-marketed, and mass-distributed drugs and devices moving in interstate commerce—is a poor fit for the distinct issues raised by laboratories that provide vital diagnostic tools for doctors as part and parcel of the practice of medicine. And this is not just a question of FDA attempting to fill a regulatory gap or administer a statute in the face of congressional silence. The more fundamental problem is that Congress has *already* considered the distinct issues raised by laboratory-developed testing services in CLIA, and chose to address those issues by vesting regulatory authority *not* in FDA, but in CMS. CLIA thus reflects Congress' clear and unmistakable intent to regulate laboratory-developed testing services under a statutory framework that is emphatically *not* the FDCA.

FDA's theory, moreover, necessarily implies that the entire laboratory industry (and the entire medical profession that has outsourced diagnostic tests to those laboratories) has operated for decades as a professional class of unwitting, unprosecuted violators of federal criminal laws. It renders inexplicable FDA's decades-long purported exercise of enforcement discretion, as FDA, by its own admission, has *never* before sought to enforce the FDCA laws against clinical laboratories. And it means that FDA itself will require nearly a full decade to restore "law and order" to that industry, and adapt to the enormous administrative burdens that its asserted jurisdiction would entail. Those implausible implications make plain that FDA's power grab does not effectuate, and instead flouts, Congress' intent.

III. FDA MAY NOT REGULATE LABORATORY-DEVELOPED TESTING SERVICES BY MEANS OF "GUIDANCE" DOCUMENTS RATHER THAN NOTICE-AND-COMMENT RULEMAKING

The FDCA as it now stands does not permit FDA to regulate laboratory-developed testing services, and FDA has not gone to Congress to seek the dramatic overhaul and fundamental redirection of the FDCA that such action would necessitate. But the problems with FDA's attempt to regulate laboratory-developed testing services do not end there. FDA has also failed to undertake the notice-and-comment procedures that would be required to create the binding rules that it seeks to impose, even if it had the statutory authority to do so. That is, FDA has bypassed not only Congress and its plan for regulating this vital area of public health but also proper rulemaking procedures, seeking impermissibly—and in defiance of the framework established by Congress as long ago as 1946 to subject the administrative state to the rule of law—to enlarge its control over laboratory-developed testing services through mere informal "Guidance" documents.

A. FDA's "Guidance" Imposes Binding, Substantive Obligations on Private Parties

FDA has issued so-called Guidance documents that go well beyond providing helpful guidance. Instead, they seek to impose significant, binding requirements on private parties that provide laboratory-developed testing services. The Guidance announces a risk-based, phased-in approach to a “Framework for Regulatory Oversight of Laboratory Developed Tests.” The main elements of the Framework include extensive obligations that laboratories must observe in order to comport with numerous medical device regulations. As detailed above, *see supra* at 6, these obligations include: giving notification to FDA about, or registering and listing of, laboratory-developed testing services (and “significantly” changed laboratory-developed testing services) under 21 C.F.R. §807; classifying services by risk levels and assisting FDA in determining what premarket review requirements to enforce against which tests; reporting of “adverse events” under 21 C.F.R. §803.50; submitting to premarket review “high-risk” and “moderate-risk” laboratory-developed testing services to assess their clinical validity, *see* 21 C.F.R. §814; and complying with Quality System Regulations, including 21 C.F.R. §820.30(a)-(j).

These requirements are highly burdensome, and FDA’s effort to impose them by means of Guidance documents—without undertaking full notice and comment rulemaking—is an improper end run around its procedural obligations. Under the Administrative Procedure Act, an agency generally may issue “interpretive rules” and “general statements of policy” without notice and comment, but that is not the case for “substantive” rules. As the Act makes clear, an agency’s “substantive” rules are valid only if they are promulgated after proper notice and comment. *See* 5 U.S.C. §553.⁶ Here, for several reasons, FDA’s Guidance announces substantive rules subject to notice and comment.

To begin with, FDA’s Guidance has precisely the purpose and effect that characterizes a substantive legal rule rather than a merely helpful hint or a useful piece of advice: it “purports to impose legally binding obligations or prohibitions on regulated parties” and forms “the basis for an enforcement action.” *Nat’l Min. Ass’n*, 758 F.3d at 251.⁷ Specifically, FDA is seeking to establish a new “Framework for Regulatory Oversight” of clinical laboratories, which will saddle laboratories with binding legal obligations that have never before been applied to them. As a result, FDA’s actions will have dramatic effects on the way in which clinical laboratories operate. *See General Electric v. EPA*, 290 F.3d 377, 382 (D.C. Cir. 2002) (agency action with “binding effects on private parties or the agency itself with the ‘force of law’” is a substantive rule); *Nat’l Family Planning & Reprod. Health Ass’n v. Sullivan*, 979 F.2d 227, 238–39 (D.C. Cir. 1992) (rulemaking required when interpretation “produce[s] significant effects on private interests”). FDA’s pronouncements thus plainly amount to “lawmaking,” the hallmark of a substantive rule.⁸

⁶ FDA’s Guidance clearly meets the APA’s broad definition of a “rule”—an agency statement with “future effect” that is “designed to implement, interpret, or prescribe law or policy” or prescribe FDA’s “procedure, or practice.” 5 U.S.C. §551(4).

⁷ By contrast, an *interpretive* rule “merely interprets a prior statute or regulation, and does not itself purport to impose new obligations or prohibitions or requirements.” *Nat’l Min. Ass’n*, 758 F.3d at 251. Thus, an interpretive rule involves no “lawmaking” or “change in the legal norm.” *Syncor*, 127 F.3d at 94.

⁸ FDA’s inability to ground its regulation in the language of the FDCA is a further indication that it is making new law. Courts have noted that “[t]he distinction between an interpretative rule and substantive rule ... likely turns on *how tightly the agency’s interpretation is drawn linguistically* from the actual language of the statute,” *Paralyzed Veterans v. D.C. Arena L.P.*, 117 F.3d 579, 588 (D.C. Cir. 1997) (emphasis added), with a rule that is largely untethered to the statutory text falling on the substantive side of the line. Here, FDA’s strained interpretation equating laboratory-developed testing services to “devices” is certainly not obvious from, or

For the same reasons, FDA's Guidance cannot be viewed merely as a "general statement of policy" that "explains how the agency ... will exercise its broad enforcement discretion or permit discretion under some extant statute or rule." *Nat'l Min. Ass'n v. McCarthy*, 758 F.3d 243, 252 (D.C. Cir. 2014). The defining feature of a true policy statement is that it is "binding on neither the public ... nor the agency" and "does not affect the legal norm." *Syncor Int'l Corp. v. Shalala*, 127 F.3d 90, 94 (1997). It "imposes no obligations or prohibitions on regulated entities," such that they "may ignore the ... Guidance without suffering any legal penalties or disabilities." *Nat'l Min. Ass'n*, 758 F.3d at 252-53. Here, FDA's Guidance imposes binding norms, with no real basis in the statute. Read as a whole, this purported "guidance" does much more than guide: "[i]t commands, it requires, it orders, it dictates." *Appalachian Power Co. v. EPA*, 208 F.3d 1015, 1023 (D.C. Cir. 2000). Laboratories are now *obligated* to notify FDA of each laboratory-developed test and to provide basic information within 6 months of the final guidance. Laboratories are *obligated* to comply with FDA's risk classification and to seek premarket approval of "high risk" tests. And there is no question that FDA will bring enforcement actions and penalties against laboratories if they do not comply.

Although FDA has claimed that, by issuing its Guidance, it is doing no more than announcing a revised enforcement policy regarding laboratory-developed testing services, *see* 79 Fed. Reg. at 59778 ("guidance ... does not create or confer any rights for or on any person and does not operate to bind FDA or the public"), the "label an agency attaches to its action is not determinative." *Continental Airlines, Inc. v. CAB*, 522 F.2d 107, 124 (D.C. Cir. 1974); *see also Appalachian Power Co.*, 208 F.3d at 1024 ("an agency may not escape the notice and comment requirements ... by labeling a major substantive legal addition to a rule a mere interpretation"). To the contrary, "'it is the substance of what the [agency] has purported to do and has done which is decisive.'" *Chamber of Commerce v. Occupational Safety & Health Admin.*, 636 F.2d 464, 468 (D.C. Cir. 1980); *see also General Electric*, 290 F.3d at 383 (agency action requires rulemaking if it is "binding as a practical matter," regardless of agency's self-serving characterization).⁹ Here, the substance of FDA's actions—imposing a host of new mandatory obligations on laboratory-developed testing services—makes clear that it has gone well beyond simply stating its non-binding views about proper enforcement policy. A mere declaration by the agency to the contrary is not enough to change that basic fact.

Finally, FDA's foray into impermissible lawmaking is further demonstrated by the fact that its Guidance would fundamentally rewrite longstanding FDA regulations with respect to registration under the FDCA. FDA's existing regulations—first promulgated in 1977 after notice-and-comment rulemaking—have consistently stated that private entities need not comply with the

compelled by, the FDCA's very general language. *See Catholic Health Initiatives v. Sebelius*, 617 F.3d 490, 494 (D.C. Cir. 2010) (agency can avoid rulemaking only if "interpretation" flows from a "document whose meaning compels or logically justifies the proposition"). Indeed, that interpretation is all but foreclosed by the ordinary understanding of the FDCA's terms.

⁹ Numerous courts have rejected agencies' self-interested attempts to recharacterize substantive rules as mere interpretations. *See CropLife Am. v. EPA*, 329 F.3d 876, 881, 883 (D.C. Cir. 2003) (press release announcing that agency would no longer consider or rely on third-party human studies was binding regulation, rather than a mere policy statement, because it "reflects an obvious change in established agency practice," "creates a 'binding norm,'" and "clearly establishes a substantive rule"); *Barrick Goldstrike Mines Inc. v. Browner*, 215 F.3d 45, 47-49 (D.C. Cir. 2000) (guidance document was binding because it created "legal consequences" and "the prospect of hardship"); *Alaska Prof'l Hunters Ass'n, Inc. v. FAA*, 177 F.3d 1030, 1034 (D.C. Cir. 1999) (new rule announcing that fishing and hunting guides long exempt from commercial pilot restrictions would now be required to comply with such restrictions was substantive).

FDCA's device-registration requirements if their "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*." 21 C.F.R. §807.65(i); *see also* 21 C.F.R. §807.65(f) (exempting from registration persons who "do not introduce such devices into *commercial distribution*") (emphasis added). Moreover, the regulations explicitly set forth the *reason* that clinical laboratories (including those engaged in laboratory-developed testing services) are exempted from registration: the fact that "such registration is not necessary for the protection of the public health." 21 C.F.R. §807.65(i). Thus, FDA has long advised laboratories that they could meet their regulatory responsibilities without complying with the FDCA's device regulations. And, based on that settled understanding of the law, clinical laboratories have invested billions of dollars in developing innovative new testing services.

FDA's present about-face, therefore, upends nearly four decades of established practice. While an agency is not prohibited from changing its position, "recourse to notice-and-comment rulemaking" is a critical safeguard against the risk of unfair surprise for regulated parties. *Long Island Care at Home, Ltd. v. Coke*, 551 U.S. 158, 170-71 (2007); *see also Christopher*, 132 S. Ct. at 2168-69 (recognizing "potential for unfair surprise" when Labor Department's "announcement of its interpretation [wa]s preceded by a very lengthy period of conspicuous inaction" with "no [notice or] opportunity for public comment"). FDA's "current doubts about the wisdom of the regulatory system followed ... for more than thirty years does not justify disregarding the requisite procedures for changing that system." *Alaska Prof. Hunters Ass'n Inc. v. FAA*, 177 F.3d at 1035. Here, all of the reasons that FDA has advanced for its proposed change—the expanding importance of diagnostic tests in clinical decision making, the growing complexity of laboratory-developed testing services, and the increasing number of corporations in the industry—"are exactly the sorts of changes in fact and circumstance which notice-and-comment rulemaking is meant to inform." *Syncor*, 127 F.3d at 95. And the circumstantial nature of those reasons make clear that FDA has introduced "not a change in interpretation or in enforcement policy, but rather ... [a] fundamentally new regulation." *Id.*

B. FDA May Not Circumvent the Requirements of Rulemaking By Using a "Guidance" Document Instead

FDA may not use the "Guidance" process to avoid the vital protections guaranteed for nearly seven decades by the APA. In fact, FDA has attracted widespread criticism from Congress and commentators for its use of guidance documents as "a backdoor approach" to "sacrifice[] the procedural safeguards dictated" by the APA and "secure[] widespread adherence to its technically nonbinding policies." Lars Noah, *Governance by the Backdoor: Administrative Law(lessness?) at the FDA*, 93 NEB. L. REV. 89, 90 (2014).¹⁰ A congressional oversight committee, moreover, recently charged that "draft guidances are becoming default FDA policy." *GOP Senators Criticize FDA Delays in Finalizing Draft Guidances*, Drug Indus. Daily, May 9, 2014, available at 2014

¹⁰ *See also* Todd D. Rakoff, *The Choice Between Formal and Informal Modes of Administrative Regulation*, 52 ADMIN. L. REV. 159, 168 (2000) ("there has been a striking increase in the number of FDA-issued documents intended to give guidance to the regulated industry but not adopted through public procedures"); Lars Noah, *The Little Agency That Could (Act with Indifference to Constitutional and Statutory Strictures)*, 93 CORNELL L. REV. 901, 924 (2008) ("FDA evidently has institutionalized a practice of cavalierly ignoring legal constraints"); Kasey L. Martini, *A Historical Look at FDA's Approach to Regulation and Policymaking* (2009), available at <http://nrs.harvard.edu/urn-3:HUL.InstRepos:10139281> ("it is arguable that the FDA has developed and expanded the use of guidance as an alternative to notice and comment rulemaking more so than any other agency").

WLNR 12430760. As one FDA official has noted, proceeding by rulemaking is “a huge ordeal ... there are economic analyses of the impact [of the proposed regulation], notice and comment, involvement of [the Office of Management and Budget], etc.” See Erica Seiguer & John J. Smith, *Perception and Process at the Food and Drug Administration: Obligations and Trade-Offs in Rules and Guidances*, 60 Food & Drug L.J. 17, 24 (2005). But that “ordeal” is intentionally rigorous: FDA has a bedrock obligation to meaningfully consider and respond to comments and undertake economic analysis of the regulatory impact of its proposed action.

1. FDA May Not Use “Guidance” Documents To Evade the APA’s Notice-and-Comment Requirements

The APA establishes notice-and-comment procedures requiring an agency to “consider[]” the comments submitted to it. See 5 U.S.C. § 553(c). “Section 553 requires consideration of whatever data and views are submitted. Such consideration has been considered [necessary] to demonstrate an ‘open mind.’” *Mortgage Investors Corp. of Ohio v. Gober*, 220 F.3d 1375, 1379 (Fed. Cir. 2000). The requirement to consider public comment is no mere formality. Rather, it is “designed to assure due deliberation,” *Smiley v. Citibank (South Dakota), N.A.*, 517 U.S. 735, 741 (1996), which in turn is essential to “informed administrative decisionmaking.” *Chrysler Corp. v. Brown*, 441 U.S. 281, 316 (1979). A mandate that an agency be *required* to consider comments is critical, “because the concern is that an agency is not likely to be receptive to suggested changes once the agency puts its credibility on the line” *Advocates for Highway & Auto Safety v. Federal Highway Admin.*, 28 F.3d 1288, 1292 (D.C. Cir. 1994).

Closely related to the requirement that the agency *consider* comments is the rule that it meaningfully *respond* to relevant and significant ones. Thus, “[t]he requirement that agency action not be arbitrary or capricious includes a requirement that the agency adequately explain its result and respond to relevant and significant public comments.” *Pub. Citizen, Inc. v. FAA*, 988 F.2d 186, 197 (D.C. Cir. 1993) ; see also *Home Box Office, Inc. v. FCC*, 567 F.2d 9, 35-36 (D.C. Cir.), *cert. denied*, 434 U.S. 829 (1977) (“[T]here must be an exchange of views, information, and criticism between interested persons and the agency. . . . Moreover, a dialogue is a two-way street: the opportunity to comment is meaningless unless the agency responds to significant points raised by the public.”).

These requirements have real teeth. Numerous courts have set aside actions by agencies for failing to adequately consider or respond to comments.¹¹ FDA rulemakings often result in changes to proposed rules. And numerous studies have shown that a significant proportion of proposed rules—approaching 40%—are “withdrawn in whole or in part because of the receipt of some significant adverse comment.” Noah, 93 NEB. L. REV. at 96.

FDA’s Guidance bypasses the APA’s well-established notice-and-comment procedures. Instead, it was issued consistent with FDA’s so-called “good guidance practices” regulation. See 21 C.F.R. §10.115; 79 Fed. Reg. at 59778 (Oct. 3, 2014). Although FDA is nominally accepting

¹¹ E.g., *Cape Cod Hosp. v. Sebelius*, 630 F.3d 203, 211 (D.C. Cir. 2011) (vacating challenged rules because agency failed to provide a reasoned response to the hospitals’ comments); *Louisiana Federal Land Bank Ass’n, FLCA v. Farm Credit Admin.*, 336 F.3d 1075, 1080-81 (D.C. Cir. 2002) (remanding challenged rule because of agency’s failure to respond to comment); *Fox Television Stations, Inc. v. FCC*, 280 F.3d 1027, 1050-51 (D.C. Cir. 2002) (holding that FCC’s failure to consider and respond to three arguments raised by commenter required that regulations be vacated), *modified on reh’g*, 293 F.3d 537 (D.C. Cir. 2002); *Nehemiah Corp. of America v. Jackson*, 546 F.Supp.2d 830, 842-43 (E.D. Cal. 2008) (holding that agency failed to respond to two categories of comments and setting aside challenged rule).

public comments on the Guidance documents, there is an important distinction between “good guidance practices” and APA rulemakings: the guidance regulation provides merely that FDA will *review* comments received and prepare a final version that “incorporates suggested changes, when appropriate.” 2 C.F.R. §10.115(g)(1)(iv). FDA is thus left to decide on its own what is “appropriate,” and it is not required to *respond* to significant comments. K.M. Lewis, *Informal Guidance and the FDA*, 66 Food & Drug L.J. 507, 522 (2011). The absence of a *mandate* to consider comments makes a critical difference. In the rulemaking context, it is firmly established that “[c]onsideration of comments as a matter of grace is not enough.” *McLouth Steel Products Corp. v. Thomas*, 838 F.2d 1317, 1323 (D.C. Cir. 1988). That is all FDA offers here, and experience shows that it is inadequate. “[E]ven though FDA accepts comments from the public [with respect to a guidance document] ... it is very unusual for FDA to actually change its position or incorporate any of the feedback into the guidance.” K.M. Lewis, *Informal Guidance and the FDA*, 66 Food & Drug L.J. 507, 522 n.142 (2011).

2. FDA May Not Use “Guidance” Documents To Avoid Considering the Enormous Economic Impact of its Proposal.

In addition, APA rulemakings are subject to Executive Orders mandating that federal regulations be cost-effective, evidence-based, and compatible with economic growth, innovation, job creation, and competitiveness.¹² However, the FDA Guidance documents in this proceeding do not consider the cost and economic impact of the proposed extension of FDA jurisdiction over clinical laboratories. Further, the extent to which the Office of Management and Budget (OMB) reviews guidance documents is “unclear” at best, and even in the relatively rare instances where that review does occur, there is a “significant question . . . whether the use of guidance documents might allow agencies to avoid [the] disciplining requirements,” such as cost-benefit analysis, “that would otherwise have applied through the regulatory review process.”¹³ This process is an important way of ensuring agency accountability. See Elena Kagan, *Presidential Administration*, 114 HARV. L. REV. 2245, 2286-87 (2001).

The absence of an economic impact analysis is a particularly glaring omission given the sweeping practical effects of FDA’s radical change in policy. As noted, FDA’s assertion of jurisdiction will significantly burden clinical laboratories, superimposing a duplicative bureaucratic regime on a vibrant and constantly evolving laboratory testing industry that is already closely regulated under CLIA, and that FDA has no prior experience in regulating. FDA, moreover, has failed to explain how the current CMS regulations and FDA’s proposed framework would work together in practice, raising numerous open questions that would be best resolved through a full airing of comments. For example, how would inspections and quality control procedures operate, if FDA and CMS have different rules and requirements? What is the “label” on an LDT, since no physical item is actually being distributed to which a label could be applied? How would FDA’s existing “adverse event” and “device malfunction” reporting requirements apply to laboratory-developed testing services? What does it mean to say that a test “malfunctioned”? Are laboratory-developed testing services subject to the medical device tax

¹² See Regulatory Planning and Review, Exec. Ord. No. 12866, 58 Fed. Reg. 51735 (Sept. 30, 1993); Improving Regulation and Review, Exec. Ord. No. 13563, 76 Fed. Reg. 3821 (Jan. 18, 2011).

¹³ Nina A. Mendelson & Jonathan B. Wiener, *Responding to Agency Avoidance of OIRA*, 37 HARV. J.L. & PUB. POL’Y 447, 487, 489 (2014); see also *id.* at 485-89; Nina A. Mendelson, *Regulatory Beneficiaries and Informal Agency Policymaking*, 92 CORNELL L. REV. 397, 411 & n. 80 (2007); Lars Noah, *Governance by the Backdoor: Administrative Law(lessness?) at the FDA*, 93 NEB. L. REV. 89, 111-12 (2014) (noting that OMB review of guidance documents is uncertain).

under the Affordable Care Act? Would laboratory consultations be considered “off-label promotion”? The practical implications of FDA’s proposal are left largely unexplored.

Economic impact analysis is essential here, moreover, where the regulatory burdens on FDA will be daunting. There are more than 11,000 laboratories currently permitted to use and develop laboratory-developed testing services, and there may be more than 100,000 laboratory-developed testing services. Under the Guidance, every laboratory developing and performing LDTs will be required to “notify” FDA that it is performing a laboratory-developed test and provide extensive information about each laboratory-developed test being offered by that laboratory within 6 months of the issuance of the final guidance. By comparison, last year, FDA approved 21 Pre-Market Submissions for all medical devices, only 4 of which were for *in-vitro* diagnostic test kits. And FDA is proposing this enormous expansion of its regulatory responsibilities at a time when it is facing severe resource constraints—a reality that FDA implicitly recognizes by giving itself nearly *a decade* to implement its new regulatory scheme. This is hardly the time for FDA to take on a vast new regulatory task at all, much less one that is has not thoroughly explored through full examination.

Meanwhile, the Guidance presupposes that, after FDA notification, FDA will proceed to determine which of the tests are “high risk” and therefore require submission of an application for Pre-Market Approval. And FDA’s guidance for identifying “high risk” laboratory-developed testing services will not even be issued for two years. Thus, a meaningful economic impact analysis cannot be performed, and there is simply no basis on which FDA could conclude that its jurisdictional expansion will be cost-effective.

More broadly, the Guidance threatens to pose a serious obstacle to innovation and chill investment in medical testing advancements by disrupting the familiar regulatory landscape that has rationally governed clinical laboratories for decades. FDA’s approach is inconsistent at its core with the way new laboratory-developed testing services have developed, with rapid identification of genes and biomarkers, and with reliance on cutting-edge research that is not conducive to being frozen by the need for regulatory approvals. Laboratory tests are constantly evolving in response to rapid scientific advances. Given the threats of Ebola and other infectious diseases on the horizon, now is not the time to delay patient access to vital laboratory-developed testing services or to compromise America’s leadership in diagnostic discovery. FDA cannot impose radical transformations on matters of such great social and economic importance without conducting a full assessment of the broader impact.

In sum, FDA has taken a procedural shortcut to subject laboratory-developed testing services to a regulatory regime that it has no legal authority to require in the first place. That is simply not the way that FDA, or any other federal agency, should act.

CONCLUSION

FDA lacks legal authority to exercise jurisdiction over laboratory-developed testing services, and violates well-settled principles of administrative law in attempting to exercise such jurisdiction through guidance documents. The proposed Guidance should be withdrawn.