UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF TEXAS
GALVESTON DIVISION

ASSOCIATION FOR MOLECULAR PATHOLOGY, and MICHAEL LAPOSATA, M.D., PH.D., Plaintiffs, v. UNITED STATES FOOD AND DRUG ADMINISTRATION, ROBERT M. CALIFF, M.D., in his official capacity as Commissioner of Food and Drugs, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, and XAVIER BECERRA, in his official capacity as Secretary of Health and Human Services, Defendants.	Case No. 3:24-cv-00241

COMPLAINT

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Plaintiffs Association for Molecular Pathology ("AMP") and Michael Laposata, M.D., Ph.D. bring this Complaint against Defendants United States Food and Drug Administration ("FDA" or "the Agency"); Robert M. Califf, M.D., in his official capacity as Commissioner of Food and Drugs; the United States Department of Health and Human Services ("HHS"); and Xavier Becerra, in his official capacity as Secretary of HHS. In support thereof, Plaintiffs state the following:

NATURE OF THE ACTION

1. This case challenges a historically unprecedented power grab that will jeopardize the health of hundreds of millions of Americans and, by Defendant FDA's own admission, impose tens of billions of dollars in new regulatory mandates on thousands of laboratories and laboratory professionals by subjecting their customized analytical processes (called "laboratory developed testing procedures" or "LDTs") to burdensome, duplicative, and unnecessary FDA regulation for the first time in American history.

2. Unless this Court acts, each of these highly trained professionals—including world-renowned pathologist Michael Laposata, M.D., Ph.D. and the thousands of other doctors and doctoral scientists who are members of AMP—now faces the risk of arrest, prosecution, and jail time for helping to diagnose and treat patients using the same kinds of robustly validated laboratory procedures that lawfully have been developed and used in their laboratories for decades. Indeed, FDA has declared their practice of medicine "illegal" and asserted that it not only can "pursue enforcement action … at any time" but "intends to do so." FDA, Medical Devices; Laboratory Developed Tests—Final Rule (the "Final Rule"), 89 Fed. Reg. 37,286, 37,295 (May 6, 2024).

3. That calculated threat will have precisely the chilling effect FDA intended, with disastrous results for both Plaintiffs and their patients. Many laboratories and laboratory professionals will be forced to stop providing vulnerable patients with cutting-edge medical care

and will abandon ongoing efforts to develop additional LDTs that could timely diagnose fast-moving diseases (*e.g.*, cancers) and mitigate emerging public-health threats (*e.g.*, the next pandemic). Others will risk, and many will have to declare, bankruptcy trying to comply with FDA's new mandates—leading to significant job losses in the pathology profession, driving future doctors into other fields, reducing training opportunities, and further exacerbating the ongoing shortage of pathologists in the United States. Many smaller laboratories aiming to survive FDA's regulatory overreach—especially those serving isolated, rural, or disadvantaged communities—will be forced to sell themselves to the few national laboratory conglomerates or private equity firms that can afford the extraordinary cost of FDA compliance. Competition among laboratories, and the innovation it spurs, will grind to a halt. And patients ultimately will pay the price, not only because recouping the Final Rule's massive compliance costs is likely to require significant price increases for every procedure a laboratory performs, but because many patients will face prolonged suffering—and some will die—from diseases or conditions that could have been prevented, diagnosed, and/or treated far sooner if new LDTs were developed and available. It is imperative that this Court act to prevent the catastrophic consequences that FDA's Final Rule will unleash.

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4. For nearly 50 years, Congress has drawn a sharp distinction between (1) mass-produced, tangible medical devices that are commercially distributed for third-party use outside the manufacturer's control (*e.g.*, implantable devices, surgical implements, and advanced imaging machines) and (2) highly customized LDTs which are developed and performed exclusively by highly trained healthcare professionals working within a federally licensed or accredited laboratory (*e.g.*, the specific sequence of individual processes used to examine bodily specimens in order to detect a disease-associated biomarker).

5. Tangible goods which are intended for medical use and do not act through chemical action on the body generally are subject to FDA's authority to regulate medical "devices" under the federal Food, Drug, and Cosmetic Act ("FDCA"), which Congress augmented in 1976 after reports of widespread pacemaker failures in 1972-1973 and the 1974-1975 Dalkon Shield Crisis in which thousands of women were seriously injured by an implantable intrauterine contraceptive. To help prevent such products from causing similar harms, the 1976 Medical Device Amendments ("MDA") to the FDCA generally subject each such device to FDA's prior (or "premarket") review before its manufacturer can "begin [its] introduction or delivery for introduction into interstate commerce for commercial distribution," 21 U.S.C. § 360(k), and to various postmarket controls that apply after the product's introduction. *See infra* ¶¶ 27-40. Not surprisingly, the FDCA's post-1976 device requirements are strict, inflexible, and designed to regulate mass-manufactured commodities that are distributed by the thousands or millions. These regulatory requirements also are costly to fulfill, heavily bureaucratized, and often plagued by delays.

6. In 1988, by contrast, Congress made clear that intangible laboratory procedures, like the well-validated LDTs Plaintiffs and their members develop and perform within their laboratories, are subject to a distinct regulatory framework. At that time, no one—not even FDA—had imagined that analytical procedures developed and performed within a single laboratory were subject to the then-decade-old MDA's pre- and postmarketing requirements for mass-produced medical devices that are commercially distributed across the country. But Congress recognized that "[s]ince many clinical decisions rest on the outcome of laboratory tests, the need for accuracy and reliability of test results is obvious," and it found that the then "present system for regulating the vast clinical laboratory industry … offers a patchwork of inconsistent and overlapping

standards that leaves some laboratories trying to comply with multiple layers of regulation … while others are free of any regulatory oversight." S. Rep. 100-561, at 3 (Sept. 29, 1988).

7. Needless to say, this assertion would have been nonsensical in 1988 if Congress already had subjected LDTs to FDA regulation when it passed the MDA in 1976. Yet even as Congress acknowledged that the then-current framework for regulating LDTs "cannot begin to provide the necessary assurances of quality," *id*.—a statement that likewise would have made no sense if Congress already had subjected LDTs to the MDA in order to provide the necessary quality assurances—Congress chose ***not*** to subject LDTs to FDA regulation under the FDCA.

8. Instead, Congress passed the Clinical Laboratory Improvement Amendments of 1988 ("CLIA"). Building on a 1967 predecessor statute that principally had been administered by what is now the Centers for Medicare & Medicaid Services ("CMS")—***not FDA***—CLIA amended provisions of the Public Health Service Act ("PHSA")—***not the FDCA***—by directing HHS to establish a uniform system of federal licensure and regulation for every "laboratory or clinical laboratory" that performs any "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).

9. In particular, CLIA augmented CMS's 1967 regulatory authority by directing the development of new federal "standards to assure consistent performance by laboratories … of valid and reliable laboratory examinations and other procedures." *Id*. § 263a(f)(1). It further ordered CMS to require that all clinical laboratories implement "a quality assurance and quality control program [that is] adequate and appropriate for [ensuring] the validity and reliability of the laboratory examinations and other procedures of the laboratory," *id*. § 263a(f)(1)(A); require such laboratories to "maintain records, equipment, and facilities necessary for the proper and effective

operation of the laboratory," *id*. § 263a(f)(1)(B); ensure that any laboratory personnel "performing and carrying out … laboratory examinations and other procedures" hold "qualifications … appropriate" to do so, *id*. § 263a(f)(1)(C); order these laboratories to participate in a rigorous and routine "proficiency testing program" that federal regulators have determined to be capable of ensuring "acceptable performance … for all examinations and procedures" conducted in the laboratory, *id*. §§ 263a(f)(1)(D)-(f)(3)(B); and to require compliance with any and all "such other requirements as [CMS] determines necessary to assure consistent performance by such laboratories of accurate and reliable laboratory examinations and procedures." *Id*. § 263a(f)(1)(E). Finally, in sharp contrast to the rigid requirements FDA applies to medical devices under the post-1976 FDCA, CLIA expressly called for CMS to use "flexibility … [i]n developing the standards to be issued" pursuant to the foregoing authorities. *Id*. § 263a(f)(2).

10. Some 40 years after Congress chose to subject LDTs to CMS's carefully tailored regulations under CLIA—and not the FDA's burdensome MDA-based requirements for tangible medical devices that are commercially distributed across the United States—FDA's unelected bureaucrats now claim that Congress made the wrong choice. And after nearly 20 years of trying and failing to convince Congress to vest FDA with regulatory authority over LDTs, *see infra* at ¶¶ 78-89, the Agency now has seized that authority for itself by issuing a Final Rule that will subject LDTs to costly, duplicative, and highly intrusive FDA regulation for the first time ever. *See* 89 Fed. Reg. at 37,286.

11. Though the Final Rule grudgingly acknowledges that CLIA vested CMS with authority to regulate laboratory procedures, FDA's Final Rule relies heavily on evidence that it admits is unverified and "largely anecdotal," 89 Fed. Reg. at 37,321, to assert that "CLIA does not provide sufficient assurances of safety and effectiveness for … LDTs." *Id*. at 37,416. Even though

Congress called for CMS-administered "proficiency testing" to ensure "acceptable performance … for all examinations and procedures" performed by laboratories, *id*. §§ 263a(f)(1)(D)-(f)(3)(B), the Final Rule declares that congressionally mandated "proficiency testing data, as standalone or comparative results, do not support [LDT] validation and performance expectations." 89 Fed. Reg. at 37,323. And despite conceding that "under CLIA, laboratories should already have some processes in place for detecting problems with their [LDTs]," *id*. at 37,307—*i.e*., the very "quality assurance and quality control program[s]" CLIA ordered CMS to implement for that purpose, 42 U.S.C. § 263a(f)(1)(A)—the Final Rule assails the adequacy of those programs simply because CMS's LDT requirements don't precisely mirror FDA's parallel requirements for mass-distributed medical devices. 89 Fed. Reg. at 37,309 (admitting that "compliance with CLIA requirements provides some quality assurances" but complaining that CMS's "CLIA regulations do not provide relevant assurances for certain [of FDA's] Q[uality] S[ystem] requirements").

12. FDA's explicit rejection of Congress's policy choices is neither appropriate nor lawful. Under our Constitution, Congress writes legislation, the President signs it, and the administrative state is bound by these laws unless and until they are amended. "After all, agencies have only those powers given to them by Congress and enabling legislation is generally not an open book to which the agency may add pages and change the plot line." *Career Colls. & Sch. of Tex. v. U.S. Dept. of Educ*., 98 F.4th 220, 243 (5th Cir. 2024) (quotations omitted); *see also Judge Rotenberg Educ. Ctr., Inc. v. FDA*, 3 F.4th 390, 399 (D.C. Cir. 2021) ("Federal agencies are creatures of statute. They possess only those powers that Congress confers upon them.").

13. Indeed, these principles carry added force when federal agencies seek to subject whole industries to vast new regulatory mandates by belatedly asserting power derived from decades-old legislation—especially when, as here, Congress in the interim repeatedly has

considered, but declined to grant, the asserted powers. *See, e.g.*, *West Virginia v. EPA*, 597 U.S. 697, 724-25 (2022) (citing *inter alia Util. Air Regulatory Group v. EPA*, 573 U.S. 302, 324 (2014) ("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.") (quotations and citations omitted); *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 159-60 (2000) (rejecting FDA's assertion of authority over tobacco products because "Congress, for better or for worse, has created a distinct regulatory scheme for tobacco products, squarely rejected proposals to give the FDA jurisdiction over tobacco, and repeatedly acted to preclude any agency from exercising significant policymaking authority in the area.")).

14. FDA's failure to adhere to these principles cannot stand. Like everyone else, the Agency is free to express its disagreement with Congress's policy choices and continue lobbying our elected representatives to grant FDA the regulatory authority it desires. But the Agency cannot lawfully seize power by the stroke of its own pen, and its violation of these fundamental precepts of administrative law cries out for judicial intervention. The Final Rule should be vacated and Defendants promptly enjoined from taking any action to enforce it.

PARTIES

15. Plaintiff AMP is a 501(c)(3) non-profit professional society dedicated to advancing the field of molecular pathology—a medical specialty that bridges the gap between clinical practice and laboratory science by examining the molecular composition of organ, tissue, or bodily fluid samples and interpreting results in order to make appropriate diagnoses and classify diseases, assist with treatment decisions, and provide essential medical care to patients. Together with its approximately 3000 members—including medical doctors and doctoral-scientist laboratory directors, basic and translational scientists, and technologists who work in academic and

community medical centers, government, and industry in all 50 States—AMP aims to improve the quality of healthcare in the United States by advancing clinical practice, science, and excellence in molecular pathology. AMP is nonstock corporation organized under Maryland law and maintains its headquarters and principal place of business in Rockville, MD.

16. As detailed in his accompanying Declaration, *see* Decl. of Michael Laposata, M.D., Ph.D. ("Laposata Decl.," attached as Ex. 1) (Aug. 15, 2024), Plaintiff Michael Laposata, M.D., Ph.D. is a world-renowned medical doctor and clinical pathologist who resides in Galveston, Texas and currently serves as Chairman of the Department of Pathology at the University of Texas Medical Branch-Galveston ("UTMB"). Dr. Laposata earned his M.D. and Ph.D. at Johns Hopkins University School of Medicine, and has taught at Harvard Medical School (where he was a tenured full Professor of Pathology and directed several clinical laboratories while in Boston) and Vanderbilt University School of Medicine (where he was the Edward and Nancy Fody Professor of Pathology and Medicine and served as the Pathologist-in-Chief at Vanderbilt University Hospital and its Director of Clinical Laboratories). Dr. Laposata's clinical expertise is in blood coagulation, with a special expertise in identifying diagnostic errors and mechanisms to prevent them. He has published over 180 peer-reviewed articles and authored or edited 9 books, including the leading pathology textbook LABORATORY MEDICINE: THE DIAGNOSIS OF DISEASE IN THE CLINICAL LABORATORY, which recently was renamed LAPOSATA'S LABORATORY MEDICINE in recognition of Dr. Laposata's contributions to the field. In its inaugural peer survey, THE PATHOLOGIST identified Dr. Laposata as the single most influential pathologist in the United States and the third most influential pathologist in the world, and he has received more than a dozen prestigious teaching and research awards, including the American Association for Clinical Chemistry's Award for Outstanding Contributions in Education and the American Society for

Clinical Pathology's H.P. Smith Award for Distinguished Pathology Educator. Though Dr. Laposata is an employee of the State of Texas, he brings this lawsuit in his personal capacity as a practicing medical doctor and clinical pathologist, and the views and opinions expressed herein are solely his own and not necessarily those of the State of Texas or any of its agencies and instrumentalities.[1]

17. Defendant FDA is an agency within Defendant HHS, 21 U.S.C. § 393(a), and maintains its principal place of business at 10903 New Hampshire Ave., Silver Spring, MD 20993. FDA is charged with overseeing and implementing, *inter alia*, the FDCA's medical device provisions under authority delegated to it by Congress and HHS, and it promulgated the Final Rule complained of in this action.

18. Defendant HHS has authority over FDA and maintains its principal place of business at 200 Independence Ave., S.W., Washington, DC 20204. Its Secretary, Defendant Becerra, is the official charged by law with administering the FDCA and bears ultimate responsibility for all actions undertaken by HHS and its constituent agencies, including FDA. Secretary Becerra is sued in his official capacity and maintains his office within HHS's headquarters at 200 Independence Ave., S.W., Washington, DC 20204.

19. Defendant Robert M. Califf, M.D., is the Commissioner of Food and Drugs and has the delegated authority to administer the FDCA. Commissioner Califf is responsible for all actions undertaken by FDA, including the Final Rule complained of in this action. Commissioner Califf

[1] Before filing this Complaint, Dr. Laposata notified the Attorney General of Texas of his intention to sue. The Attorney General has expressed no objection, and Plaintiffs understand that the State of Texas is considering potential future involvement in this litigation given its interest in maintaining the affordability, quality, and accessibility of healthcare services for Texans.

is sued in his official capacity, and maintains offices within FDA's headquarters at 10903 New Hampshire Ave., Silver Spring, MD 20993.

20. HHS and FDA are each an "agency" of the U.S. government within the meaning of the Administrative Procedure Act ("APA"). 5 U.S.C. § 701(b)(1).

JURISDICTION AND VENUE

21. This Court has subject matter jurisdiction under 28 U.S.C. § 1331 because this action arises under the FDCA, 21 U.S.C. §§ 301 *et seq*.; CLIA, 42 U.S.C. § 263a; the APA, 5 U.S.C. §§ 555, 702, and 706; and the Declaratory Judgment Act, 28 U.S.C. §§ 2201-02.

22. Plaintiffs have standing to sue because they and their members develop and perform thousands of LDTs that the Final Rule now declares to be "illegal" medical devices and because they plan to develop and use thousands of future LDTs—conduct that the Final Rule likewise declares "illegal" and for which Defendants repeatedly have threatened "to pursue enforcement action." 89 Fed. Reg. at 37,295. Indeed, the Final Rule's compliance burdens and repeated threats of criminal prosecution already have caused Plaintiffs and their members to curtail ongoing LDT development, including with respect to both new and modified LDTs that were under development when the Final Rule took effect. Decl. of Dr. Karen Kaul ("Kaul Decl.," attached as Ex. 2), at ¶¶ 16-17 (Aug. 16, 2024); Decl. of Dr. Eric Konnick ("Konnick Decl.," attached as Ex. 3), at ¶ 13 (Aug. 16, 2024); Laposata Decl. ¶ 13. There accordingly is a concrete, tangible, legally cognizable, and justiciable Article III case or controversy between the parties regarding whether the Final Rule is consistent with the the APA, CLIA, and the FDCA.

23. Venue is proper in this Court under 28 U.S.C. § 1391(e)(1)(C), because Defendants are agencies and officers of the United States, Plaintiff Dr. Laposata is a natural person who resides in Galveston, Texas, and no real property is involved in this action.

24. The Final Rule is a final agency action subject to judicial review under the APA.

STATUTORY AND REGULATORY BACKGROUND

A. The FDCA's Regulatory Framework for Medical Devices

1. Overview of the 1938 Act and 1976 Medical Device Amendments

25. Congress first authorized FDA to regulate medical "device[s]" when it passed the FDCA of 1938 (the "1938 Act"). Pub. L. No. 75-717, 52 Stat. 1040. The 1938 Act defined these products as tangible "instruments, apparatus[es], and contrivances, including their components, parts, and accessories, intended (1) for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man … or (2) to affect the structure or any function of the body." *Id.* § 201(h), 52 Stat. at 1041. Unlike its companion provisions for drugs, however, the 1938 Act did not authorize FDA to conduct premarket review of medical devices, much less require prior FDA clearance or approval before their release—only to inspect device manufacturing facilities, *id.* § 704, and to bring after-the-fact enforcement actions against entities who introduce or deliver adulterated or misbranded devices into interstate commerce. *Id.* §§ 301-304; *cf. id.* § 505(a), 52 Stat. at 1052 (barring the "introduction into interstate commerce any new drug, unless an application filed pursuant to subsection (b) is effective with respect to such drug.").

26. In 1972, however, FDA unilaterally claimed authority to regulate *in vitro* diagnostic ("IVD") products under the FDCA—not as devices but, surprisingly, as drugs that would be subject to premarket review under the 1938 Act's drug provisions. FDA, *In Vitro Diagnostic Products for Human Use—Proposed Rule*, 37 Fed. Reg. 16,613 (Aug. 17, 1972). FDA defined these IVDs as "reagents, instruments, and systems, intended for use in the diagnosis of disease, or in the determination of the state of health, in order to cure, mitigate, treat, or prevent disease." *Id.* at 16,614. But its rulemaking cited no textual basis in the FDCA for regulating these products as drugs. Instead, it declared there was no need to do so and asserted that until Congress granted it

premarket review authority over devices, it would exercise its "inherent … authority" under the FDCA to "protect the public health" by any means the Agency deemed "necessary." *See* FDA, *In Vitro Diagnostic Products for Human Use—Final Rule*, 38 Fed. Reg. 7,096, 7,096 (Mar. 15, 1973) ("[U]ntil new device legislation is enacted and where the authority inherent in section 505 of the Federal Food, Drug, and Cosmetic Act is necessary to protect the public health, [IVD] products will be regarded and classified as drugs under the Act. The FDA believes it is not in the public interest to spend time determining which [IVDs] are drugs and which are devices.").

27. However dubious that approach, it soon was overtaken by events. Following the pacemaker and Dalkon Shield crises, Congress granted FDA new authority to subject medical devices to premarket review and postmarket controls by passing the MDA. Pub. L. No. 94-295, 90 Stat. 539. Yet even as the MDA broadened the 1938 Act's "device" definition to include ***a subset*** of the IVDs that FDA previously claimed authority to regulate, it continued to make clear that only tangible goods qualified: It defined a "device" as "an instrument, apparatus, implement, machine, contrivance, implant, ***in vitro reagent***, or other similar or related article, including any component, part, or accessory, which is … intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals ... and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes." 21 U.S.C. § 321(h)(1) (emphasis added; enumerations omitted). As detailed *infra*, the MDA then required ***certain of these devices*** to undergo premarket review, with the form of review being dependent on FDA's assessment of its level of risk.

2. Premarket Requirements for Commercially Distributed Devices

a. The MDA's Risk-Classification Framework

28. The post-MDA statute now provides that before any new medical device can be "introduc[ed] or deliver[ed] for introduction into interstate commerce ***for commercial distribution***," FDA must grant one of three types of premarket authorization—(1) a substantial equivalence clearance (often called a "510(k) clearance" after its FDCA subsection), (2) a de novo classification, or (3) a premarket approval ("PMA")—unless FDA by regulation has exempted that type of device from such review. *See* 21 U.S.C. § 360(k) (emphasis added); *id*. § 360c(c)(2)(C)(ii) (classification status dependent on whether a given device was "introduced or delivered for introduction into interstate commerce ***for commercial distribution*** before May 28, 1976, or is within a type of device which was so introduced or delivered before such date") (emphasis added; internal enumeration omitted); *id*. § 360c(f)(1) (virtually identical); *id*. § 360e(b)(1) (same).

29. Both the particular form of premarket review required and the postmarket controls FDA requires "to provide a reasonable assurance of safety and effectiveness" depend on the device's risk classification. 21 U.S.C. § 360c(a)(1). Class I devices are deemed to be low risk and are subject to only the "general" controls that apply to all devices. 21 U.S.C. § 360c(a)(1)(A). Class II devices are moderate risk and can be subject to additional "special" controls. 21 U.S.C. § 360c(a)(1)(B). Devices that pose the highest risk are placed in class III and require PMA approval, which provides for the most stringent postmarket controls. 21 U.S.C. § 360c(a)(1)(C).

30. FDA regulations exempt most class I devices and a minority of class II devices from premarket review. *See* 21 U.S.C. § 360(l)-(m) (authorizing FDA to exempt class I and II devices in certain circumstances). Conversely, most class II devices and a minority of class I devices require 510(k) clearance. Any novel device is placed in class III by default, but it may be

eligible to be placed in class I or class II *via* the de novo classification process if it can be shown to pose only low to moderate risk with the use of appropriate controls. *See* 21 U.S.C. § 360c(f).

b. The MDA's Premarket Review Pathways

31. To obtain 510(k) clearance for a new medical device, applicants must first submit a premarket notification to FDA establishing that the proposed device is substantially equivalent to a legally marketed predicate device—*i.e*., that the proposed device and its predicate have the same intended use and either (1) share the same technological characteristics or (2) have different technological characteristics that do not raise additional safety and effectiveness concerns. 21 U.S.C. § 360c(i). The type and quantity of information needed to establish such equivalence depends on the extent of any differences between the proposed device and its predicate, and FDA almost invariably requires studies for that purpose. *See* 21 U.S.C. § 360c(a)(1)(B); *see also* 21 C.F.R. § 807.87(f)-(g). If FDA determines the subject device is "not substantially equivalent" to its predicate, the device will be designated in class III and the applicant must seek either reclassification through the de novo pathway or full PMA approval. *See* 21 U.S.C. § 360c(f).

32. Applicants also can seek de novo classification for a low- or moderate-risk device that FDA has not previously classified without first seeking 510(k) clearance. *Id*. § 360c(f)(2). These submissions are considerably more onerous than 510(k)s. They almost always require data from preclinical studies (such as laboratory or animal testing) and/or human clinical studies and, unlike 510(k) submissions, must also include an analysis of the expected benefits of the device, its known and potential risks, and an explanation of why the proposed device's benefits outweigh its risks. *See id*. § 360c(a)(2). If FDA denies a de novo classification request, the device remains in class III and PMA approval often is required before the device may be distributed. *Id.* § 360c(f).

33. PMA applications are the most burdensome premarket pathway—typically requiring both preclinical and clinical trial data and detailed information regarding the design of the device and each of its components, its manufacturing process, and its proposed labeling. *See id*. § 360e(c)(1). A benefit-risk analysis is also required. *Id*. § 360c(a)(2). In addition, FDA frequently conducts a preapproval inspection of the manufacturing facility and clinical study sites before it will approve a PMA. *See* 21 C.F.R. § 814.44(e)(1)(iii).

34. Regardless of pathway, significant investments of time and money are required to conduct the required studies, analyze the resulting data, and then prepare these submissions. FDA itself estimates that preparing and submitting a single submission costs up to $530,410 for a comparatively simple 510(k) or de novo application and $9.29 million for a PMA application (though these self-serving estimates substantially underestimate their true cost). FDA, Laboratory Developed Tests Final Rule: Final Regulatory Impact Analysis ("FRIA," attached as Exh. 4), at 115-123; *but see* J. Makower *et al*., *FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies*, at 7 (Nov. 2010) ("[S]urvey data also showed that the average total cost for participants to bring a low- to moderate-risk 510(k) product from concept to clearance was approximately $31 million, with $24 million spent on FDA dependent and/or related activities. For a higher-risk PMA product, the average total cost from concept to approval was approximately $94 million, with $75 million spent on stages linked to the FDA.").

35. Applicants must also pay FDA a separate "user fee" for each submission. These fees increase annually. In 2024, the standard user fees for a 510(k), de novo classification, and PMA are $21,760, $145,068, and $483,560, respectively. FDA, Medical Device User Fee Rates for Fiscal Year 2024—Notice, 88 Fed. Reg. 48,870, 48,873 (July 28, 2023). In 2025, these user

fees will increase to $24,335, $162,235, and $540,783, respectively. FDA, Medical Device User Fee Rates for Fiscal Year 2025—Notice, 89 Fed. Reg. 61,433, 61,437 (July 31, 2024).

36. The total cost of subjecting LDTs to these premarket review requirements thus will be extraordinary: Once the Final Rule takes full effect, FDA under-estimates that compliance with the MDA's premarket requirements alone will be as much as ***$4.21 billion per year***. *See* FRIA at 124 (derived from Table 36). In reality, the true cost will be far higher—as the Agency conceded when it first proposed the rule. *See* FDA, Laboratory Developed Tests Proposed Rule: Preliminary Regulatory Impact Analysis ("PRIA," attached as Exh. 5), at 85 (derived from Table 31) (estimating that subjecting LDTs to FDA's premarket investigational use, 510(k), de novo, and premarket approval requirements would cost up to ***$12.29 billion per year***, which itself underestimated the true regulatory costs).

37. Finally, while there are aspirational "goal dates" for reviewing submissions, FDA's "review clock" is paused whenever it requests more information or identifies a major deficiency—which happens in the vast majority of cases. *See* FDA, *Report on Performance Goals for 2nd Quarter FY 2024* (the "Q2 MDUFA Report") (May 31, 2024). That means it typically takes FDA far longer to complete review of a new device application than the goal dates suggest: In 2023, FDA took up to ***451 days, 437 days, and 458 days*** to review 510(k), de novo, and PMA applications, respectively. *See* Q2 MDUFA Report at 32, 124, 169. In the interim, these long delays deprive undiagnosed patients of access to life-saving targeted therapies while serious diseases—*e.g.*, a fast-moving cancer—progress. And given the rapid pace of scientific and technological progress, they ensure that many diagnostic tests are obsolete before FDA acts.

3. Postmarketing Requirements for Commercially Distributed Devices

a. Restrictions on Changes to Cleared or Approved Devices

38. Securing FDA marketing authorization for a new device is only the start. Once 510(k) clearance or de novo classification is granted, any "change or modification in the device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process" or that would constitute "a major change or modification in the intended use of the device" requires submission of a new 510(k) or de novo application. 21 C.F.R. § 807.81(a)(3). A vast array of post-approval changes, including many that commonly are made in the laboratory context, can trigger these requirements: changing detection reagents; altering calibration or quality control materials; altering substrates; changing specimen types; changing how specimens are processed; changing incubation times and temperatures; altering a user interface; or otherwise any device component or accessory. FDA, *Guidance for Industry: Deciding When to Submit a 510(k) for a Change to an Existing Device*, at 38 (Oct. 25, 2017); *see also* 89 Fed. Reg. at 37,305 & n.36 (stating that these principles generally could apply to LDTs).

39. Once FDA has approved a PMA, its sponsor must submit a PMA supplement for FDA review and approval before making "any change … that affects safety or effectiveness" regardless of its significance, including any change to the device's indication(s) for use, labeling, manufacturing procedures or facilities, or its performance or design specifications. 21 U.S.C. § 360e(d)(5); 21 C.F.R. § 814.39(a). Even when a given change will not affect device safety or effectiveness, the change must be disclosed in an annual report PMA holders submit to FDA. 21 C.F.R. §§ 814.39(a) & 814.84(b). And an entirely new PMA may be required if a change to a device results in a design so different from the original version of the device that the previously

submitted preclinical and clinical data do not in FDA's view provide a reasonable assurance of safety and effectiveness for the modified device. *See* 21 U.S.C. § 360e(d)(5)(B)(i).

b. Postmarketing Controls

40. Beyond substantially limiting the sponsor's ability to modify a device after its clearance or approval, FDA subjects most devices to stringent postmarketing controls regardless of their classification. As previously noted, there are two categories of controls: "general" and "special." The former includes FDA's device registration and listing requirements; medical device reporting ("MDR") requirements; correction and removal requirements; recall requirements; requirements under FDA's quality system regulation ("QSR"); labeling requirements; and Unique Device Identification requirements. *See* 21 C.F.R. Parts 801, 803, 806, 807, 820. "Special controls" are tailored to the specific type of device and can include performance standards, postmarketing surveillance, the maintenance of patient registries, labeling requirements, data requirements, and other guidelines. Compliance with these postmarketing requirements will entail extraordinary expense: FDA originally estimated that subjecting LDTs these requirements would require up to ***$450 million in one-time costs*** and ***$2.025 billion in annual recurring costs***, PRIA at 85 (derived from Table 31), though—through the sleight of hand we detail *infra* at ¶¶ 99-102, 156-58—it later reduced those estimates to up to ***$85 million in one-time costs*** and ***$327 million in annual recurring costs***. *See* FRIA at 123-24 (derived from Table 36).

4. The Practice-of-Medicine Exemption

41. Finally, while the FDCA authorizes FDA to regulate the manufacturing of commercially distributed medical devices, it makes clear that FDA may not "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; *see also Judge Rotenberg Educ. Ctr., Inc. v. FDA*, 3 F.4th 390, 395 (D.C. Cir. 2021) ("Section 396 constrains the FDA's authority by prohibiting it from regulating the practice of medicine."). Consistent with this broad "practice-of-medicine exemption," the MDA specifically exempts certain persons from the statute's core device-related requirements—including any "practitioner who is licensed by law to prescribe or administer devices intended for use in humans and who manufactures or imports devices solely for use in the course of his professional practice." 21 U.S.C. § 360(g)(2). These exemptions include the statute's registration, device listing, recordkeeping and reporting (*i.e.*, MDR, device tracking, and correction and removal requirements), 510(k) premarket notification, record-inspection requirements, and, by extension, the statute's de novo and PMA requirements. *See id.* §§ 360(g)(2), 360i(c)(1) & 374(a)(2)(B).

B. CLIA's Regulatory Framework for LDTs

42. As we detail *infra*, LDTs—which are neither tangible goods nor commercially distributed for third-party use, but instead are multi-step, protocol-based procedures that are developed and performed by highly trained professionals inside a federally licensed or accredited laboratory and further subject to mandatory proficiency testing by a federally approved external provider—are and always have been subject to a distinct regulatory regime: CLIA (rather than the FDCA), which is administered by CMS (rather than FDA), and under which Congress expressly provided for the regulatory "flexibility" clinical laboratories need in order to meet and adapt to urgent and/or unique patient needs. 42 U.S.C. § 263a(f)(2).

1. The 1967 Clinical Laboratories Improvement Act ("1967 CLIA")

43. Though FDA had been regulating "devices" since the 1938 Act was enacted, Congress did not authorize federal regulation of laboratory-based processes and procedures until

it passed the original CLIA in 1967, Pub. L. No. 90-174 § 5(a), 81 Stat. 536—nearly a decade before the MDA. As enacted, the 1967 CLIA defined the term "laboratory" as "a facility for the biological, microbiological, serological, chemical, immuno-hematological, hematological, biophysical, cytological, pathological, or other 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, man." 81 Stat. at 536.

44. Like its modern counterpart, the 1967 CLIA operated as a federal licensing regime: It barred anyone from "solicit[ing] or accept[ing] in interstate commerce,[2] directly or indirectly, any specimen for laboratory examination or other laboratory procedures, unless there is in effect a license for such laboratory issued by the Secretary [of HHS]." *Id*. To "assure consistent performance by the laboratories of accurate laboratory procedures and services," *id*. at 536-37, the 1967 statute (1) barred HHS from issuing any such license unless it first "determine[d] that such laboratory will be operated in accordance with standards found necessary by the Secretary to carry out the purposes of this section," *id*. at 536, and (2) required the Secretary to promulgate standards sufficient to "assure—(i) maintenance of a quality control program adequate and appropriate for accuracy of the laboratory procedures and services; (ii) maintenance of records, equipment, and facilities necessary to proper and effective operation of the laboratory; (iii) qualifications of the director of the laboratory and other supervisory professional personnel necessary for adequate and effective professional supervision of the operation of the laboratory (which shall include criteria

[2] The statute defined "interstate commerce" in its traditional sense: as "trade, traffic, commerce, transportation, transmission, or communication ***between any State*** or possession of the United States, the Commonwealth of Puerto Rico, or the District of Columbia, ***and any place outside thereof***, or within the District of Columbia." 81 Stat. at 536 (emphasis added).

relating to the extent to which training and experience shall be substituted for education); and (iv) participation in a proficiency testing program established by the Secretary." *Id*. at 537.

45. Alongside CLIA, the Social Security Act further barred any laboratory from receiving federal payment under Medicare/Medicaid unless they are certified by HHS as meeting appropriate quality standards. *See* 42 U.S.C. § 1395x(s)(17) (current). To reduce duplication under these two regulatory systems—CLIA licensure and Medicare certification—HHS delegated authority over both regimes to CMS (then called the Health Care Financing Administration).

2. The 1988 CLIA Amendments

46. By 1988, Congress had determined that the 1967 CLIA was failing to provide adequate federal oversight of clinical laboratories. Though it noted that more than 12,000 laboratories had been licensed and/or certified by CMS and literally billions of diagnostic tests were being performed each year, Congress found that "the present system for regulating the vast clinical laboratory industry cannot begin to provide the necessary assurances of quality. There are no uniform guidelines for all laboratories doing similar types of work. Instead, the current system offers a patchwork of inconsistent and overlapping standards that leaves some laboratories trying to comply with multiple layers of regulation … while others are free of any regulatory oversight." S. Rep. 100-561 at 3.

47. It further observed that these deficiencies and inefficiencies were compounded by the fact that "improvements in medical technology ha[d] changed the nature of the testing" after enactment of the 1967 CLIA. H.R. Rep. 100-899 at 11; *see also id*. at 11 ("Refinements in laboratory technology has led to automated batch processing of tests which were once performed by hand [and] lower dependence on highly skilled technical personnel."); S. Rep. 100-561 at 3 ("Advances in medical technology have given physicians more ways to examine specimens of

body tissues and fluids to gain information important to proper diagnosis and therapy."). Given these changes and the fact that so "many clinical decisions rest on the outcome of laboratory tests," Congress concluded that "the need for accuracy and reliability of test results is obvious." S. Rep. 100-561 at 3.

48. Yet rather than subject laboratory procedures to FDA regulation under the FDCA, Congress instead strengthened CMS's authority under CLIA. The 1988 CLIA amendments did so in several ways. ***First***, while the 1967 CLIA applied only to laboratories that "solicit[ed] or accept[ed samples] in interstate commerce" as that term was defined in its traditional sense, Pub. L. No. 90-174 § 5(a), 81 Stat. at 536; *see also supra* at n.2, the 1988 CLIA broadened CMS's authority to the full extent of Congress's Commerce Clause authority: It provided simply that "[n]o person may solicit or accept materials derived from the human body for laboratory examination or other procedure unless there is in effect for the laboratory a certificate issued by the Secretary under this section [for the relevant] examination or procedure." Pub. L. No. 100-578, § 2, 102 Stat. 2903 (1988) (codified at 42 U.S.C. § 263a(b)).

49. ***Second***, while the 1967 CLIA required only that CMS promulgate regulatory standards "to assure consistent performance by the laboratories of ***accurate*** laboratory procedures and services," 81 Stat. at 536-37 (emphasis added), the 1988 CLIA broadened CMS's mandate by requiring it to "assure consistent performance by laboratories issued a certificate under this section of ***valid and reliable*** laboratory examinations and other procedures." 42 U.S.C. § 263a(f)(1) (emphasis added). Consistent with that modification, the 1988 statute substantially expanded CMS's responsibility for promulgating laboratory quality standards: It altered the agency's 1967 mandate to require implementation of "a quality assurance and quality control program adequate

and appropriate ***for the validity and reliability*** of the laboratory examinations and other procedures of the laboratory." *Id*. § 263a(f)(1)(A) (emphasis added).

50. ***Third***, the 1988 CLIA substantially enhanced CMS's other responsibilities. It ordered CMS to impose personnel qualifications based on "the type of examinations and procedures being performed … and the risks and consequences of erroneous results." *Id*. § 263a(f)(1)(C). Rather than merely requiring "participation in a proficiency testing program," 81 Stat. at 537, the 1988 CLIA detailed both how to perform such proficiency testing and the applicable standards, including a requirement that there be "a system for grading proficiency testing performance to determine whether a laboratory has performed acceptably." 42 U.S.C. § 263a(f)(3). And the 1988 CLIA gave CMS a new, catch-all grant of authority to require compliance with any and all "other requirements as [CMS] determines necessary to assure consistent performance by such laboratories of accurate and reliable laboratory examinations and procedures." *Id*. § 263a(f)(1)(E).

51. ***Finally***, in recognition of the varying complexity of modern LDTs and the need for laboratories to rapidly adapt to changing circumstances, the 1988 CLIA directed CMS to exercise "flexibility … in developing the standards to be issued" and ordered it to "take into consideration—(A) the examinations and procedures performed and the methodologies employed, (B) the degree of independent judgment involved, (C) the amount of interpretation involved, (D) the difficulty of the calculations involved, (E) the calibration and quality control requirements of the instruments used, (F) the type of training required to operate the instruments used in the methodology, and (G) such other factors as the Secretary considers relevant." *Id*. § 263a(f)(2).

3. CMS's Implementation of the 1988 CLIA

52. CMS's post-1988 CLIA regulations divide laboratory procedures into three categories—waived (*i.e.*, low complexity), moderate complexity, and high complexity—and a procedure's categorization in turn determines the requirements laboratories must follow before it can be performed. *See* 42 C.F.R. § 493.25. Because LDTs generally are deemed high complexity,[3] the following sections focus on the requirements for high-complexity laboratories.

a. Registration and Certification of Laboratories Performing High-Complexity LDTs

53. Clinical laboratories seeking to develop and/or perform any high-complexity LDT must first apply to either CMS or an HHS-approved accreditation program and be granted a "certificate" allowing them to operate. 42 C.F.R. § 493.25(a); *id.* § 493.45(a)(1).[4] The application must fully "[d]escribe the characteristics of the laboratory operation and the examinations and other test procedures performed," including "[t]he name and total number of test procedures and examinations performed," the "methodologies for each laboratory test procedure or examination performed," and "[t]he qualifications … of the personnel directing and supervising the laboratory and performing the examinations and test procedures." *Id.* § 493.43(c)(3). The laboratory must also "make [all] records available and submit reports to HHS," *id.* § 493.43(d), and every

[3] Indeed, the Final Rule effectively defines LDTs as high-complexity procedures. *See, e.g.*, 89 Fed. Reg. 37,289 ("FDA has generally considered an LDT to be an IVD that is intended for clinical use and that is designed, manufactured, and used within a single laboratory that is certified under [CLIA] and meets the regulatory requirements under CLIA to perform high complexity testing.").

[4] Because the standards for HHS-approved accreditation must meet or exceed those for CMS certification—and generally do exceed the CMS standards—we focus only the latter here, which establishes a proverbial "floor." *See* 42 C.F.R. § 493.551(a) (requiring that "the requirements of the accreditation organization or State licensure program [be] equal to, or more stringent than, the CLIA condition-level requirements specified in this part, and the laboratory would meet the condition-level requirements if it were inspected against these requirements").

laboratory that receives an initial registration certificate must then "[b]e inspected" in order to "determine program compliance" with CMS's CLIA regulations before the certificate expires. *Id*. §§ 493.45(c)(2)-(e)(1). The extensive requirements for which compliance must be demonstrated are set forth in subparts H, J, K, M, and Q of CMS's CLIA regulations, *id*. § 493.45(c)(3), and partially described *infra* at ¶¶ 57-72.

54. If the laboratory successfully completes the required inspection, CMS issues it a "certificate of compliance" which authorizes the laboratory to lawfully perform the high-complexity LDTs and other laboratory processes reviewed in connection with the registration certificate. *Id*. § 493.49(a). That triggers several further requirements.

55. ***First***, certified laboratories must comply with strict notification requirements, *id*. § 493.49(b)(1), including that they "[n]otify HHS no later than 6 months after any deletions or changes in test methodologies for any test or examination … for which the laboratory has been issued a certificate of compliance." *Id*. § 493.51(c). ***Second***, such laboratories "[m]ust permit announced or unannounced inspections" in order to "determine compliance with the applicable requirements," "evaluate complaints," address concerns "that tests are being performed, or the laboratory is being operated in a manner[,] that constitutes an imminent and serious risk to human health," and "[t]o collect information regarding the appropriateness of tests … categorized as … high complexity." *Id*. § 493.49(b)(2)(i)-(iv). Noncompliance with these requirements can lead to the revocation of the laboratory's certificate and denial of eligibility to receive payment under Medicare and Medicaid. *Id*. § 493.49(c). ***Third***, these certificates are valid for a maximum of two years, *id*. § 493.49(d), and the laboratory must seek renewal at least nine months before expiration by submitting a renewal application that includes the same types of information required during the initial application process. *Id*. § 493.49(g).

56. Together, these requirements thus mandate that, across a certification/accreditation cycle, CMS and/or the HHS-approved accrediting organization: (1) evaluates and certifies every high-complexity LDT that is developed and performed by a given laboratory (including its specific methodology), any changes that have been made to any previously certified methodology for a previously certified LDT, and any new LDTs that have been developed and are being performed since the initial certificate was issued; (2) has unfettered access to all records relating all LDTs that have been developed or modified and are being performed; and (3) regularly inspects every laboratory that performs LDTs for general compliance and can do so at any other time, including when concerns arise about the quality of the laboratory's overall operations and/or the accuracy, reliability, or validity of any specific LDT(s). As noted previously, *supra* n.4, these are minimum requirements; HHS-approved accrediting organizations typically engage in more stringent laboratory oversight than the minimum standards set forth in CMS's regulations.

b. Quality Assurance and Quality Control Requirements for High-Complexity LDTs

57. CMS's regulations also establish strict requirements to ensure the quality, validity, reliability, and accuracy of every laboratory procedure performed in a certified or accredited laboratory, including for every individual LDT. *See* 42 C.F.R. Subpart K (42 C.F.R. §§ 493.1200-1299). These quality requirements obligate every certified laboratory to "establish and maintain written policies and procedures that implement and monitor a quality system for all phases of the total testing process … as well as general laboratory systems," *id*. § 493.1200(a), and to implement "a quality assessment component that ensures ***continuous improvement of the laboratory's performance and services*** through ongoing monitoring that identifies, evaluates and resolves problems." *Id*. § 493.1200(b) (emphasis added). In contrast to FDA's quality requirements—which are designed to keep devices static and then monitor them for adverse events after launch—

CLIA's regulations thereby seek to ensure not only the initial quality of in-house laboratory procedures but that laboratories continually improve these in-house procedures over time.

58. To do so, CMS's quality regulations ***first*** ensure that the processes and methodologies for every LDT (whether new or modified) are fully documented and that the laboratory follows them at all times. *Id*. § 493.1251(a) ("A written procedure manual for all tests, assays, and examinations performed by the laboratory must be available to, and followed by, laboratory personnel."). These protocols must specify each LDT's requirements for "patient preparation; specimen collection, labeling, storage, preservation, transportation, processing, and referral; and criteria for specimen acceptability and rejection," as well as the "[s]tep-by-step performance of the procedure, including test calculations and interpretation of results," the "[p]reparation of slides, solutions, calibrators, controls, reagents, stains, and other materials used in testing," the "[c]alibration and calibration verification procedures," "[t]he reportable range for test results for the test system," the "[c]ontrol procedures," the "[c]orrective action to take when calibration or control results fail to meet the laboratory's criteria for acceptability," the "[l]imitations in the test methodology, including interfering substances," its established "[r]eference intervals (normal values)" and the standards for identifying "[i]mminently life-threatening test results, or panic or alert values," "[p]ertinent literature references" to support the LDT, and a "system for entering results in the patient record and reporting patient results including … the protocol for reporting imminently life-threatening results, or panic, or alert values." *Id*. § 493.1251(b). Any "changes in procedures must be approved, signed, and dated by the current laboratory director before use," *id*. § 493.1251(d), and "[t]he laboratory must maintain a copy of each procedure with the dates of initial use and discontinuance." *Id*. § 493.1251(e).

59. ***Second***, CMS's regulations expressly authorize laboratories to (1) develop and perform LDTs that ***have not been cleared or approved by FDA*** and (2) ***to modify IVDs that previously were cleared or approved by FDA***—provisos that would make no sense if LDTs were (and since 1976 have been) subject to mandatory FDA premarket review under the FDCA. *Id.* § 493.1253. In particular, CMS's regulations require that "[e]ach laboratory that ***modifies an FDA-cleared or approved test system***,[5] or ***introduces a test system not subject to FDA clearance or approval (including methods developed in-house [i.e., an LDT]***…) … must, before reporting patient test results, establish [its] performance specifications." *Id.* § 493.1253(b)(2) (emphases added). Not surprisingly, any equipment used to develop, improve, validate, perform, and interpret such LDTs must be properly maintained, calibrated, and controlled. *Id.* §§ 493.1254-56.

60. ***Finally***, CMS's quality regulations provide detailed quality standards for particular types of procedures, *id.* §§ 493.1261-78, and establish protocols for identifying and correcting errors. These provisions require laboratories to "ensure[] continuous improvement of the laboratory's performance and services," *id.* § 493.1200, including by: documenting and investigating "all complaints and problems," *id.* § 493.1233; maintaining "an ongoing mechanism to monitor, assess, and, when indicated, correct problems" and taking all steps "necessary to prevent recurrence of problems," *id.* § 493.1239; and following "corrective action policies and procedures … in a manner that ensures accurate and reliable patient test results," including where the laboratory learns of any problems with its test systems, controls, or calibration materials, *id.* § 493.1282, its analytic systems, *id.* § 493.1289, or with respect to reporting results, *see id.*

[5] A "test system" includes "the instructions and all of the instrumentation, equipment, reagents, and supplies needed to perform an assay or examination and generate test results." 42 C.F.R. § 493.2.

§ 493.1291(k) & 493.1299. Again, these provisions not only contemplate but require the prompt implementation of corrective actions by the laboratory—including modifications to established processes and procedures—not just the reporting of issues to regulatory authorities.

c. Proficiency Testing Requirements

61. Consistent with CLIA's directive that all laboratory processes be subject to regular "proficiency testing" in order to ensure they are and remain "valid and reliable," 42 U.S.C. §§ 263a(f)(1), (f)(1)(D) & (f)(3), CMS's regulations further require that any laboratory performing high-complexity processes and procedures (including LDTs) "must successfully participate in a proficiency testing program approved by CMS … for each specialty, subspecialty, and analyte or test in which the laboratory is certified under CLIA." 42 C.F.R. § 493.803(a); *see also id*. Subparts H and I (detailing these standards). Notably, this regular and frequent postmarket assessment process is unique to procedures regulated under CLIA; ***there is no parallel process requiring routine external quality testing for commercially distributed devices under the FDCA***.

62. At its most basic, CLIA-mandated proficiency testing entails rigorous and regular evaluation of laboratory performance by an HHS-approved provider, with the frequency of such testing being dependent on the particular LDT or procedure at issue. 42 U.S.C. § 263a(f)(3)(A) ("The testing shall be conducted on a quarterly basis, except where the Secretary determines for technical and scientific reasons that a particular examination or procedure may be tested less frequently (but not less often than twice per year)."). Applicable standards and performance criteria in turn are determined by CMS and/or accrediting organization requirements. *Id*. § 263a(f)(3)(B) ("The standards established … shall include uniform criteria for acceptable performance under a proficiency testing program, based on the available technology and the clinical relevance of the laboratory examination…. The standards shall also include a system for grading proficiency testing

performance to determine whether a laboratory has performed acceptably for a particular quarter and acceptably for a particular examination or procedure or category of examination or procedure over a period of successive quarters.").

63. More specifically, CMS's CLIA regulations require that the proficiency testing provider—"a private nonprofit organization or a Federal or State agency, or entity acting as a designated agent for the State" which has received prior HHS approval to perform proficiency testing, 42 C.F.R. § 493.901—must regularly provide each CLIA-certified laboratory with challenge samples that "mimic actual patient specimens" and have been prepared "for each specialty, subspecialty, and analyte or test for which [the receiving laboratory] provides testing." *Id*. § 493.901(c)(1)(ii). The receiving laboratory then "must examine or test, as applicable, the proficiency testing samples it receives … in the same manner as it tests patient specimens," *id*. § 493.801(b), using the same "personnel who routinely perform the testing in the laboratory, using the laboratory's routine methods." *Id*. § 493.801(b)(1). They must also "document the handling, preparation, processing, examination, and each step in the testing and reporting of results for all proficiency testing samples," *id*. § 493.801(b)(6), and then report their results to the HHS-approved proficiency testing provider with "an attestation statement that proficiency testing samples were tested in the same manner as patient specimens with a signature block … completed by the individual performing the test as well as by the laboratory director." *Id*. § 493.901(c)(5).

64. Once the HHS-approved proficiency testing provider receives the laboratory's proficiency testing report, it must "appropriately evaluate and score the testing results, and identify performance problems," *id*. § 493.901(b), using "[a] scientifically defensible process for determining the correct result for each challenge offered by the program." *Id*. § 493.901(c)(2). It then must "[p]rovide HHS or its designees and participating laboratories with … reports of

proficiency testing results and all scores for each laboratory's performance … for each CLIA-certified specialty, subspecialty, and analyte or test," *id*. § 493.901(a)(1), and must also "[f]urnish to HHS cumulative reports on an individual laboratory's performance." *Id*. § 493.901(b). Finally, CMS's CLIA regulations establish detailed standards for determining acceptable performance for each category of tests performed by a given laboratory. *See generally id*. Subparts H & I.

65. Failing to successfully complete proficiency testing results in severe consequences: CMS not only can bar the laboratory from performing a particular LDT or type of LDT, but can suspend, limit, or revoke the laboratory's certification; bar the laboratory from receiving Medicare/Medicaid payments; impose civil monetary penalties; and initiate civil or criminal actions to enjoin and/or punish violations. *See* 42 C.F.R. § 493.803 (requiring that each laboratory successfully complete proficiency testing); 42 C.F.R. §§ 493.1800-50 (detailing the various sanctions CMS can seek for violations). Again, ***there is no comparable regulatory mandate for ongoing performance testing of FDA-cleared or FDA-approved devices***. Only CLIA-certified laboratory procedures are subject to routine, federally mandated postmarket validation that is backed by a rigorous enforcement regime.

d. Personnel Requirements

66. CLIA's regulatory framework differs from the FDCA's in another important aspect. While literally anyone—even a child or amateur hobbyist—can develop a medical device for third-party use outside the developer's control and without routine confirmatory testing, CLIA imposes strict qualifications for all personnel performing procedures in high-complexity laboratories. 42 U.S.C. § 263a(f)(1)(C) (requiring that laboratories "use only personnel meeting such qualifications as the Secretary may establish for the direction, supervision, and performance of examinations and procedures within the laboratory"). Laboratories performing high-complexity

testing—which by definition include any laboratory that develops and performs LDTs, *supra* at n.3—are subject to the strictest personnel qualifications.

67. ***First***, each such laboratory must have a "laboratory director" who not only "must possess a current license as a laboratory director issued by the State in which the laboratory is located, if such licensing is required," 42 C.F.R. § 493.1443(a), but must also be (1) a doctor who is licensed to practice medicine and holds an appropriate Board certification or its equivalent; (2) a doctor who is licensed to practice medicine and has extensive laboratory training or experience overseeing high complexity testing; or (3) a chemical, physical, biological, or clinical laboratory doctoral scientist who is certified by an HHS-approved Board. *Id*. § 493.1443(b)(1)-(3).

68. These highly qualified doctors and Board-certified doctoral scientists in turn are charged with both legal and practical responsibility for everything that happens within the laboratory. That includes ensuring that all "testing systems developed and used for each of the tests performed in the laboratory provide quality laboratory services," *id*. § 493.1445(e)(1); "that the test methodologies selected have the capability of providing the quality of results required for patient care; [that the v]erification procedures used are adequate to determine the accuracy, precision, and other pertinent performance characteristics of the method; and [that l]aboratory personnel are performing the test methods as required for accurate and reliable results," *id*. § 493.1445(e)(3), and "that consultation is available to the laboratory's clients [*e.g.*, the physician who ordered a given LDT] on matters relating to the quality of the test results reported and their interpretation concerning specific patient conditions." *Id*. § 493.1445(e)(9).

69. ***Second***, laboratories that develop and perform LDTs must also employ a "technical supervisor" charged with "[s]election of the test methodology that is appropriate for the clinical use of the test results" and "[v]erification of the test procedures performed and establishment of

the laboratory's test performance characteristics, including the precision and accuracy of each test and test system." *Id*. § 493.1451(b)(1)-(2). They also are responsible for "[r]esolving technical problems and ensuring that remedial actions are taken," *id*. § 493.1451(b)(5), "assuring that each individual performing tests receives regular in-service training and education appropriate for the type and complexity of the laboratory services performed," *id*. § 493.1451(b)(7), and "[e]valuating the competency of all testing personnel and assuring that the staff maintain their competency." *Id*. § 493.1451(b)(8). These individuals must also hold a state license if required in their State, and—depending on the particular specialties and subspecialties of services performed in the laboratory—hold either an M.D. or Ph.D. and be Board-certified or otherwise have completed at least one year of laboratory experience or training in the specialties or subspecialities performed within the laboratory, or have a relevant Master's or Bachelor's degree and multiple years of experience and training in the laboratory's specialties or subspecialities. *See id*. § 493.1449.

70. ***Third***, laboratories performing LDTs must have a "clinical consultant" who is "qualified to consult with and render opinions to the laboratory's clients concerning the diagnosis, treatment and management of patient care," including by "provid[ing] consultation to the laboratory's clients," "assist[ing] the laboratory's clients in ensuring that appropriate tests are ordered to meet the clinical expectations," "ensur[ing] that reports of test results include pertinent information required for specific patient interpretation," and "communicat[ing] to the laboratory's clients on matters related to the quality of … test results … and their interpretation concerning specific patient conditions." *Id*. § 493.1457(a)-(d). Not surprisingly, the clinical consultant must be "a doctor … licensed to practice … in the State in which the laboratory is located" and further be qualified to serve as a laboratory director even if that is not their position. *Id*. § 493.1455.

71. ***Finally***, all testing personnel and technologists carrying out procedures in a high complexity laboratory must satisfy a combination of licensing, educational, training, competency, and/or experience-based requirements. *Id*. § 493.1489-1495.

72. These personnel requirements distinguish the development and/or improvement, validation, execution, and interpretation of LDT procedures performed within a CLIA-licensed high-complexity laboratory from the manufacturing of medical devices that are commercially distributed for use outside the sponsor's control and direction. CLIA ensures that every aspect of the LDT—from its initial design to the interpretation of its results—remains under the supervision of highly credentialed, expertly trained healthcare professionals engaged in the practice of medicine, whereas mass-produced medical devices that are commercially distributed can be developed, manufactured, and distributed by anyone, for use by individuals (including lay users) who need not meet such rigorous educational, training, or experience-based requirements.

C. FDA's Belated Assertion of Authority Over LDTs

73. For decades following the MDA's 1976 enactment, FDA did not formally express any belief that LDTs were subject to its FDCA-derived device authorities. It took no action against high-complexity laboratories performing LDTs under CLIA, and even as Congress recognized in 1988 that literally billions of individual laboratory procedures were being performed each year, *see, e.g.*, H.R. Rep. No. 100-899 at 12—all of them under a "system for regulating the vast clinical laboratory industry [that] cannot begin to provide the necessary assurances of quality," S. Rep. No. 100-561 at 3—neither the House nor Senate reports accompanying the MDA even intimated that FDA since 1976 had been responsible for (or that it even had expressed an opinion to Congress about its potential role) in regulating LDTs. *See, e.g.*, H.R. Rep. No. 100-899, at 11 (1988) ("The Federal government regulates laboratories under two programs. [CLIA] requires that all

laboratories which send specimens in interstate commerce be subject to regulation by the Federal government. Title XVIII of the Social Security Act requires that laboratories serving as providers in the Medicare program be subject to quality standards established by the Secretary."); *see also* S. Rep. No. 100-561 at 3 (substantially similar). Needless to say, Congress's failure in 1988 to identify FDA as an existing (or even a potential) regulator of LDTs would have been a puzzling omission if the MDA in 1976 already had charged FDA with responsibility for regulating LDTs.

74. Indeed, the Agency admits that it did not formally assert that it might have authority to regulate LDTs as medical devices until it issued a tangentially related final rule in November 1997—21 years after the MDA's passage; nine years after the 1988 CLIA; and without first having solicited public comment on that question. *See* FDA, Medical Devices; Laboratory Developed Tests—Proposed Rule (the "Proposed Rule"), 88 Fed. Reg. 68,006, 68,015 (Oct. 3, 2023) (citing FDA, Medical Devices; Classification/Reclassification; Restricted Devices; Analyte Specific Reagents—Final Rule (the "ASR Rule"), 62 Fed. Reg. 62,243 (Nov. 21, 1997)). Yet even then, the ASR Rule's passing assertion of possible regulatory authority over LDTs was both unsupported by any statutory analysis and directly at odds with the position the Final Rule asserts.

75. The sole stated purpose of that rulemaking had been to determine the risk classification for analyte specific reagents ("ASRs")—commercially distributed chemicals or antibodies which can be purchased from third parties and then used "as components of tests that have been cleared or approved by FDA and also by clinical laboratories that use the ASR's to develop in-house tests used exclusively by that laboratory [*i.e.*, LDTs]." *Id*. at 62,244. During that proceeding, no commenter appears to have disputed that individual ASRs were classifiable devices under the MDA. But FDA did receive a single comment proposing that most ASRs should be designated as class II or class III medical devices precisely because they can be used in connection

with the performance of LDTs, which the comment noted are "not … reviewed independently [by FDA] for safety and effectiveness" and, the comment falsely claimed, developed in laboratories that allegedly "do not have expertise in developing in vitro diagnostic tests." *Id*. at 62,249.

76. You would never know it from reading the Final Rule, but FDA flatly ***rejected*** the commenter's position with respect to LDTs. Though it passingly asserted—without a single reference to the FDCA or its device definition—the Agency's "belie[f] that clinical laboratories that develop such tests are acting as manufacturers of medical devices and are subject to FDA jurisdiction," *id*., it concluded "that CLIA regulated laboratories qualified to perform high complexity testing have demonstrated expertise and ability to use ASR's in test procedures and analyses" and found both "that the use of in-house developed tests [*i.e*., LDTs] has contributed to enhanced standards of medical care in many circumstances and that significant regulatory changes in this area could have negative effects on the public health." *Id*. It also distinguished the ***commercially distributed ASRs*** at issue from ***the LDTs*** in connection with which they can be used, noting that FDA's regulatory authority was focused on "the classification and regulation of ASR's ***that move in commerce***, not tests developed ***in-house*** by clinical laboratories … and ***used exclusively by that laboratory***." *Id*. (emphases added).

77. But dubious assertions of authority often lead regulators down a slippery slope. And despite its modest beginnings and embedded limitations, FDA's bald assertion that LDTs might be subject to FDA regulation—and not just the commercially distributed ASRs used as part of an LDT's performance in the laboratory—quickly assumed a life of its own. Within a year of the ASR Rule, FDA declared that "[a]ny [LDT] produced ***using an ASR*** falls within the definition of device … ***even when only [the ASR] is transported interstate***" and regardless of "whether the [LDT itself] is in interstate commerce ***for commercial distribution***" beyond the laboratory performing

it. *See* Citizen Petition Resp., FDA Docket No. FDA-1992-P-0047, at 7-8 (Aug. 12, 1998) (emphases added). Indeed, FDA even told laboratories they needed to "look at the transportation of the ***ingredients of the ASR*** as well as the ASR itself" to determine whether LDTs using a given ASR would themselves be deemed FDA-regulated medical devices. *Id*. at 8 (emphasis added).

D. Congress's Refusals to Grant FDA Regulatory Authority Over LDTs

78. Had that claim been taken seriously, it would have forced clinical laboratories into an impossible dilemma. ASR producers have no obligation to disclose the ingredients in their ASRs, let alone their origins and transportation histories; those are trade secrets. *See* 18 U.S.C. § 1839(3). But there is a stark contrast between saying something and doing it. And despite FDA's newly asserted position, the Agency took no action to enforce its increasingly aggressive pronouncements regarding LDTs for nearly another decade.

79. That changed in 2005 and 2006—some three decades after the 1976 MDA enactment and nearly two decades after the 1988 CLIA—when FDA informed certain laboratories "that their in-house tests were medical devices and that they must comply with the [FDCA] or stop offering their tests." Citizen Petition, Docket No. FDA-2006-P-0149, at 3 (Sept. 28, 2006). Many of the LDTs targeted in this first enforcement wave involved processes for assessing patients' genetic information—which of course has come to play an increasingly important role in modern medicine ever since the Human Genome Project was completed in 2003.

80. FDA's attempts to intimidate clinical laboratories working on the cutting edge of science, technology, and precision medicine immediately got Congress's attention. And in the nearly two decades that have followed this sea change in FDA's approach, Congress repeatedly has considered—and emphatically rejected—scores of bills that would do precisely what neither 1967 or 1988 versions of CLIA nor the 1938 or 1976 versions of the FDCA did: create a premarket

review process for LDTs, including by granting FDA legal authority to regulate LDTs under its FDCA medical-device authorities. Despite decades of intense lobbying by the Agency, Congress has refused to pass a single one of these bills, and indeed, repeatedly has condemned FDA's attempts to assert authority over LDTs.

81. The first legislative effort to authorize FDA to exercise at least partial authority over LDTs was the Genomics and Personalized Medicine Act of 2006. *See* S. 3822, 109th Cong. (2006). That legislation, which was introduced by then-Senator Obama, notably began by recognizing that FDA lacked authority to regulate LDTs under the FDCA—only certain third-party ASRs which can be used to help perform LDTs that otherwise are subject to CMS's authority under CLIA. *See id*. § 3 (defining "laboratory-developed genetic test" as "a molecular genetic test that is designed, validated, conducted, and offered as a service by a clinical laboratory subject to [CLIA] using either commercially available analyte specific reagents (***FDA-regulated***) or reagents prepared by the laboratory (***not FDA-regulated***), or some combination thereof.") (emphases added). But in light of FDA's manifest interest in regulating these LDTs, and recognizing that subjecting LDTs to dual regulation by both CMS and FDA would be unnecessarily duplicative and unduly burdensome, the draft legislation would have required HHS both to determine how genetic LDTs should be classified and whether CMS or FDA should be the agency to review them. *Id*. § 7. But Congress failed to pass this legislation in either its original form or when it was reintroduced, largely in the same form, in 2007 and in 2008. *See* Genomics and Personalized Medicine Act of 2007, S. 976, 110th Cong. (2007); Genomics and Personalized Medicine Act of 2008, H.R. 6498, 110th Cong. (2008).

82. In 2007, separate legislation was introduced that effectively would have centralized all regulatory authority over LDTs in FDA. *See* Laboratory Test Improvement Act of 2007, S. 736,

110th Cong. (2007). Indeed, this proposed legislation would have done by statute precisely what the Final Rule now tries to do by FDA's own hand: It would have amended the FDCA to expressly provide that "[a]ny laboratory-developed test shall be deemed to be a device under section 201(h)." *Id*. § 3. It then would have subjected LDTs to all FDCA requirements—not only compelling FDA premarket review and clearance/approval, but ordering non-compliant LDTs off the market—except for the Agency's current good manufacturing practice requirements, which it indicated could be satisfied by complying with CMS's CLIA regulations. *Id*. §§ 5-7. Congress, however, once again refused to grant FDA the authority its Final Rule now seizes by administrative fiat.

83. In 2011, Congress considered yet another approach to these issues in the Modernizing Laboratory Test Standards for Patients Act of 2011, H.R. 3207, 112th Cong. (2011). Unlike earlier efforts, this proposed legislation would have required premarket review of most LDTs but would have charged CMS with that responsibility by specifically excluding these products from the FDCA's device definition. *Id*. §§ 2-3. It too failed to pass, but in its place Congress sought to rein in the Agency by passing the Food and Drug Administration Safety and Innovation Act of 2012 ("FDASIA"). *See* Pub. L. No. 112-144, 126 Stat. 993.

84. FDASIA effectively barred FDA from taking any action on LDTs without prior Congressional oversight by precluding FDA from issuing even a non-binding draft guidance document regarding its possible regulation of LDTs "without, at least 60 days prior to such issuance—(1) notifying the [House and Senate] of the Administration's intent to take such action; and (2) including in such notification the anticipated details of such action." *Id*. § 1143 (codified at 21 U.S.C. § 371 (note) (2012)); *see also* 158 Cong. Rec. H3825, H3863 (daily ed. June 20, 2012) (statement of Rep. Burgess) ("[FDA] is now required to notify Congress before issuing guidance regarding the regulation of laboratory-developed tests. I still believe we should strengthen and

improve CLIA's oversight of laboratory-developed tests, instead of even contemplating any type of duplicative regulation.").

85. In July 2014, FDA submitted to Congress and then publicly released Draft Guidances soliciting public comment on an FDCA-based framework for potentially regulating LDTs. FDA, Framework for Regulatory Oversight of [LDTs], 79 Fed. Reg. 59,776, 59,777 (Oct. 3, 2014); FDA, Notification and Medical Device Reporting for [LDTs], 79 Fed. Reg. 59,779 (Oct. 3, 2014). Those Draft Guidances were poorly received: In 2016, the House Appropriations Committee declared that FDA's approach would represent "a significant shift in the way LDTs are regulated," "circumvents the normal rulemaking process[,] and changes expectations for patients, doctors, and laboratories for the first time since [CLIA] was passed in 1988." H.R. Rep. No. 114-531, at 72 (Apr. 19. 2016). It therefore explicitly "direct[ed] the FDA to suspend further efforts to finalize the LDT guidance and [to] continue working with Congress to pass legislation that addresses a new pathway for regulation of LDTs." *Id*. at 72-73. In January 2017, FDA formally abandoned the Draft Guidances in order "to give our congressional authorizing committees the opportunity to develop a legislative solution." FDA, Discussion Paper on [LDTs], https://www.fda.gov/media/102367/download (Jan. 13, 2017).

86. In March 2017, Representatives Larry Bucshon, M.D. and Diana DeGette publicly circulated a 215-page, bipartisan discussion draft of yet another legislative attempt to reform the regulation of LDTs. *See* Press Release, Dr. Bucshon, DeGette Release Draft of the Diagnostic Accuracy and Innovation Act, available at https://tinyurl.com/DAIA-PR (Mar. 21, 2017). Their Diagnostic Accuracy and Innovation Act ("DAIA") would have created an entirely new regulatory category called "in vitro clinical tests" (or "IVCTs")—separate from the statute's existing categories for drugs, biological products, and medical devices—that encompassed both LDTs and

traditional IVDs (*e.g.*, reagent kits and instruments). DAIA Discussion Draft § 2, at https://tinyurl.com/DAIA-PDF (2017). It then would have subjected most such IVCTs to FDA review and regulation under a brand-new FDCA-based regulatory framework, *id*. § 3, while effectively limiting CMS's oversight to laboratories' operating performance and execution of FDA-authorized IVCTs. *See id*. § 5.

87. Consistent with the prior appropriations order directing FDA to "work[] with Congress," the Agency was asked to provide Technical Assistance on the DAIA discussion draft. Yet rather than provide the requested Technical Assistance, FDA responded by submitting an alternative legislative package that would have granted the Agency even greater regulatory authority over LDTs than DAIA had proposed. FDA, FDA's Views on the Diagnostic Accuracy and Innovation Act (DAIA), at https://thefdalawblog.com/wp-content/uploads/2018/08/FDA-LDT-Draft-Leg.pdf (Aug. 3, 2018). That draft legislation served as the basis of the Verifying Accurate Leading-Edge IVCT Development ("VALID") Act of 2020 described in the following paragraphs, and DAIA itself was never formally introduced in Congress.

88. Instead, two alternative pieces of legislation were introduced in 2020—FDA's preferred VALID Act of 2020 and the Verified Innovative Testing in American Laboratories ("VITAL") Act of 2020. *Compare* VALID Act of 2020, H.R. 6102, 116th Cong. (2020) *with* VITAL Act of 2020, S. 3512, 116th Cong. (2020). These bills proposed two diametrically opposed approaches to LDTs. Like the DAIA discussion draft, VALID would have created a new regulatory framework for IVCTs under the FDCA, though it continued to provide for dual oversight by both FDA and CMS. *Id*. VITAL, by contrast, expressly deemed laboratory services to be "professional health care activity" that would be regulated under CLIA; indeed, it expressly excluded LDTs from the FDCA. *Id*. VITAL further called for CMS to hold a public meeting on possible amendments

to CLIA and instructed CMS to report its findings and recommendations to Congress. *Id*. Yet neither VALID Act nor VITAL were passed, and versions of both bills have been introduced in subsequent Congresses—likewise without success. *See* Verifying Accurate Leading-Edge IVCT Development Act of 2021, H.R. 4128, 117th Cong. (2021); Verified Innovative Testing in American Laboratories Act of 2021, S. 1666, 117th Cong. (2021); Food and Drug Administration Safety and Landmark Advancements Act of 2022, S. 4348, 117th Cong. (2022); Verifying Accurate Leading-Edge IVCT Development Act of 2023, H.R. 2369, 118th Cong. (2023).

89. All told then, Congress has considered at least a dozen different pieces of legislation during the past two decades that would have directly addressed FDA's authority to regulate LDTs. Yet every one of these proposals has prompted intense political debate, and the only successful legislative efforts—FDASIA's ban against FDA unilaterally issuing even a non-binding guidance document and the subsequent appropriations order "direct[ing] FDA to suspend further efforts to finalize the LDT guidance and continue working with Congress to pass legislation," *see supra* ¶¶ 83-85—unambiguously condemned the Agency's attempt to remove these issues from the political process by seizing authority to regulate LDTs for itself.

E. Defendants' Continued Defiance

1. HHS's Condemnation of FDA's Overreach During the Pandemic and Its Post-Election Reversal

90. The Agency's increasingly strident approach to LDT regulation not only has faced resistance in Congress; even HHS previously condemned FDA's overreach. In 2020—with the COVID-19 pandemic intensifying and thousands of Americans dying every day—FDA made the surprising decision to publicly threaten laboratories that had been performing COVID-related LDTs in the wake of FDA's ill-fated decision to authorize a flawed COVID test kit that had been developed by the Centers for Disease Control and Prevention ("CDC"). *See* Memo. from R.

Charrow (HHS) to S. Hahn (FDA) re Federal Authority to Regulate LDTs (the "Charrow Memo," attached as Exh. 6), at 1-2 (June 22, 2020) (quoting FDA's warnings to laboratories performing COVID-related LDTs, which now have been removed from the Agency's website).[6] Those threats prompted "many state university laboratories [to] complain[] that [FDA's] policy hindered their ability to develop and use LDTs to detect the virus that causes COVID-19," *id*. at 2, and HHS's General Counsel then was "asked by departmental leadership to review the legal bases—both substantive and procedural—for FDA's regulation of [LDTs]." *Id*. at 1.

91. In a lengthy legal memorandum, HHS's General Counsel concluded that while ***in vitro reagents*** qualify as medical devices, that proposition "does not necessarily lead to the conclusion that ***LDTs*** fall within FDA's jurisdiction." *Id*. at 6 (emphasis added). To the contrary, it found that "even assuming that LDTs are medical devices" and that this dubious interpretation might be upheld under the now-overruled doctrine of "*Chevron* deference," *id*., LDTs do not meet the additional preconditions to the FDCA's application, *id*. at 8-13, and courts might in any case "take the position that Congress has addressed the federal regulation of laboratory testing in

[6] After a years-long investigation into CDC's development of this flawed-but-FDA-authorized test kit, HHS's Office of Inspector General ("OIG") concluded that the kit's failure resulted largely from the fact that CDC failed to comply with the most basic CLIA-based policies and procedures that high complexity laboratories follow. HHS OIG, *CDC's Internal Control Weaknesses Led to Its Initial COVID-19 Test Kit Failure, But CDC Ultimately Created a Working Test Kit*, at 15-20 (Oct. 2023) (finding that CDC: lacked the "assigned roles and responsibilities that … laboratories require"; "used different document control systems that were not compatible with each other," which led to staff "using conflicting versions of documents and procedures at the same time [and] being unable to distinguish between draft, obsolete, and current versions of laboratory procedures"; "did not have an adequate system in place to control all the process changes … which then allowed for incorrectly performed quality testing procedures to occur"; and suffered from "a lack of oversight of quality processes" because "having established standardized laboratory quality measures in place was not a priority" for CDC). Despite these shocking failures, it bears reiterating that FDA reviewed and granted an Emergency Use Authorization for the CDC's failed COVID-19 test kit on February 4, 2020; it took only days for CLIA-certified public health laboratories to recognize that the CDC's FDA-authorized test kit was completely invalid.

CLIA." *Id*. at 17. It further recognized that developing LDTs is part of the practice of medicine, *id*. at 10, and concluded that "FDA's determination that LDTs are devices, none of which was published for notice and comment rulemaking, are inconsistent with [CMS's] CLIA rule and the legislative history surrounding the 1988 amendments" and therefore could not be enforced regardless of any arguable merit they might have. *Id*.

92. On August 19, 2020, HHS implemented the Charrow Memo by declaring "that [FDA] will not require premarket review of [LDTs] absent notice-and-comment rulemaking." HHS, Rescission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests, *available at* https://tinyurl.com/HHS-LDT-Rescission (Aug. 19, 2020). Freed from FDA's shackles, laboratories resumed developing COVID-related LDTs—especially to help identify new variants of the COVID-causing virus that had not (and could not have) been targeted by earlier tests. These efforts saved thousands of lives, if not far more.

93. The apparent resolution of this issue did not last long. In a transparently political decision, Defendant Becerra revoked both the Charrow Memo and HHS's implementation notice on November 15, 2021—pointedly emphasizing that they reflected "a policy established during the previous administration." HHS, Statement by HHS Secretary Xavier Becerra on Withdrawal of HHS Policy on Laboratory-Developed Tests (the "Becerra Statement"), at https://tinyurl.com/Becerra-Withdrawal-Notice. The same day, FDA announced that it was restoring its prior position on LDTs. FDA, Press Release: FDA Updates Test Policies to Help to Ensure Accuracy and Reliability of Tests and Increase Access to At-Home Tests, *available at* https://tinyurl.com/FDA-Reversion-Notice (Nov. 15, 2021).

2. The Proposed Rule

94. On October 3, 2023, FDA published a Proposed Rule announcing its intent to begin regulating LDTs as medical devices. 88 Fed. Reg. at 68,006. To do so, FDA proposed amending its current definition of IVDs to include all "reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions … ***including when the manufacturer of these products is a laboratory***." *Id*. at 68,031 (proposed amendment to 21 C.F.R. § 809.3(a) emphasized). The accompanying preamble explained that this new proviso was designed to "reflect FDA's longstanding view that LDTs are devices [because] the device definition in the [FDCA] does not differentiate between entities manufacturing the device. In other words, whether an IVD is a device does not depend on where or by whom the IVD is manufactured." *Id*. at 68,017. The Proposed Rule further asserted that developing and performing an LDT is tantamount to "manufacturing" a new device and made clear that FDA intended to subject LDT-related activities to the FDCA's full panoply of pre- and postmarketing requirements. *Id*. at 68,018-19.

95. The Proposed Rule sought to justify this radical new enforcement wave by asserting that FDA's concerns with LDTs "have grown in recent years" and claiming "the situation is getting worse." *Id*. at 68,010. But to support those dire claims, the Proposed Rule relied principally on anecdotal evidence, including unverified news reports; litigation "complaints, adverse event reports, and other allegations identifying problems with [LDTs]" which the Agency conceded it "ha[d] not confirmed," *id*. at 68,010-11 & n.10; a handful of small-scale studies purporting to show "high variability in performance" among certain LDTs—including one from which several of its original co-authors withdrew because of its flawed methodology and data misrepresentation, and others that the Agency flatly mischaracterized; and an undisclosed number of additional

submissions for COVID-19 emergency use authorizations from laboratories whose cardinal sin was allegedly omitting their validation data in the original submissions they sent to FDA. *See id*.

96. Despite this wafer-thin "evidence" of flawed LDTs, the accompanying PRIA made clear that the Agency's plan to regulate every LDT in America would have a staggering economic impact. It estimated that the Proposed Rule would apply to ***as many as 160,800 currently performed LDTs*** and that ***up to 15,552 additional LDTs per year*** would become subject to FDA's regulatory mandates, at an estimated cost of ***up to $113.86 billion in one-time compliance costs*** and ***up to $14.31 billion in annual recurring costs***. PRIA at 75-76 (Table 24), 85 (Table 31) (emphases added). The PRIA further conceded that roughly half of the affected LDTs are performed by "small businesses," *id*. at 110, and that these entities "are more likely to reduce operations or exit the market than large laboratories," with the ultimate effect of "driving production concentration to a few large laboratories," "increas[ing] the risk of supply chain contractions, risking shortages for certain [LDTs] and therefore affecting prices and access." *Id*. at 88-89.

3. The Final Rule

97. FDA received thousands of comments regarding the Proposed Rule, including more than 150 separate comments filed by AMP itself, individual AMP members, and by groups, entities, and organizations to which AMP or its individual members belong (collectively, the "AMP Comments"). The AMP Comments comprehensively challenged the legal analysis and policy rationales set forth by the Proposed Rule, including by contending: that LDTs are not medical devices within the meaning of the FDCA; that clinical laboratories and their respective medical professionals do not manufacture medical devices but instead perform professional healthcare services to treat patients; that the Proposed Rule would unlawfully interfere with the practice of medicine; that the FDCA's substantive provisions would not apply to LDTs even if they were medical devices because, *inter alia*, LDTs are not commercially distributed; that FDA's

effort to regulate LDTs conflicts with CLIA, its implementing regulations and with Congress's repeated refusals to pass legislation authorizing FDA to regulate LDTs; that the Proposed Rule would force clinical laboratories to stop providing essential medical care to their patients, delay diagnoses and treatment initiation for vulnerable patients, and prevent laboratories and laboratory professionals from leveraging scientific, technological, and medical breakthroughs; that FDA had seriously underestimated both the Proposed Rule's compliance costs and the number of LDTs it would affect; that the exorbitant costs of compliance would force the closure of numerous small laboratories, stifle innovation, and impose particularly severe harms on disadvantaged communities and patients with rare diseases; that FDA lacks the resources and personnel needed to implement the Proposed Rule, which not only would jeopardize the provision of LDT-based services but the Agency's ability to review devices that it can and does lawfully regulate; and that the factual claims proffered in support of the Proposed Rule relied on anecdotal and otherwise unreliable evidence that FDA itself admitted were unverified, systematically exaggerated the risks associated with LDTs, and ignored evidence that ran counter to FDA's narrative, including evidence that LDTs frequently outperform FDA-cleared or FDA-approved alternatives. Numerous other comments echoed these same points.

98. FDA was not swayed. Despite the overwhelmingly negative response to its Proposed Rule, FDA published its Final Rule in the *Federal Register* on May 6, 2024, *see* 89 Fed. Reg. at 37,286—shortly before the deadline to avoid triggering the Congressional Review Act. *See* 5 U.S.C. § 801(d). Its operative provisions made no changes to the Proposed Rule's amendment to FDA's definition of IVDs, which now includes the proviso declaring that this category includes "reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions … ***including when the manufacturer of these products is a laboratory***." 89 Fed. Reg. at 37,312

(emphasis added). The Preamble then proceeded to reject the myriad challenges that AMP and its members had raised. *See generally id*. at 37,311-433.

99. The Preamble did, however, announce major changes to FDA's implementation plan. Conceding that actually subjecting every LDT to the FDCA would "lead to the loss of access to safe and effective" LDTs "on which patients currently rely," *id*. at 37,293—a concession that fatally undermines the Final Rule's whole justification—the Preamble outlines an array of "enforcement discretion policies" that at least superficially would exempt certain LDTs from certain provisions of the FDCA. *See id*. at 37,294-95. Most notably, the Preamble indicates that FDA will "generally not enforce premarket review and [quality system] requirements (except for [recordkeeping] requirements) for currently marketed … LDTs that were first marketed prior to the date of issuance of this rule and that are not modified, or that are modified [only] in certain limited ways." *Id*. at 37,295. It also outlines several other "enforcement discretion" categories, including for LDTs: "manufactured and performed within the Veterans Health Administration (VHA) or the Department of Defense (DoD)"; approved by the New York's Clinical Laboratory Evaluation Program; "manufactured and performed by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within the same healthcare system"; certain LDTs associated with blood transfusions and Human Leukocyte Antigens; ones that in FDA's view resemble the types of LDTs performed in 1976; or those conducted "solely for forensic (law enforcement) purposes." *Id*. at 37,294-95.

100. Even so, the Preamble goes on to stress that FDA considers itself free to modify or revoke these policies at any time. *Id*. at 37,390 ("As with any enforcement discretion policy, this policy is subject to change."). And indeed, the Preamble repeatedly threatens to take enforcement action against laboratories and laboratory professionals who develop and perform even those LDTs

which fall squarely within these non-binding enforcement discretion policies. *Id*. at 37,295 ("[I]t is illegal to offer [LDTs] without complying with applicable requirements. Regardless of the … enforcement discretion policies for certain [LDTs] discussed below, FDA retains discretion to pursue enforcement action for violations of the FD&C Act at any time, and intends to do so when appropriate."); *id*. at 37,301 ("[R]egardless of this or any other enforcement discretion policy, FDA retains discretion to pursue enforcement action at any time against violative [LDTs]."); *id*. at 37,304 (identical); *id*. at 37,307 (identical); *see also id*. at 37,297 ("These policies do not in any way alter the fact that it is illegal to market an [LDT] that lacks required premarket authorization or is otherwise in violation of the FD&C Act, the PHS Act, or FDA regulations.").

101. Finally, the Preamble discloses a phased, four-year implementation plan for applying the FDCA's device requirements to LDTs that fall outside these non-binding enforcement discretion policies—culminating with application of the FDCA's complete panoply of regulatory requirements for new LDTs no later than May 6, 2028. *See* 89 Fed. Reg. at 37,294.

102. Coincident with the Final Rule's release—and principally as a result of the ill-defined and illusory enforcement discretion policies set forth in the Final Rule's non-binding Preamble—the Agency released a revised financial impact projection that reduces the estimated price tag of compliance to ***up to $85 million in one-time regulatory costs*** (from the ***up to $113.86 billion*** estimated in the PRIA) and ***up to $4.54 billion in annual recurring costs*** (from the ***up to $14.31 billion*** estimated in the PRIA). *See* FRIA at 123-24.

103. On July 12, 2024, the House Committee on Appropriations responded to the Final Rule by declaring that it "puts forth a proposed regulatory framework that is a significant shift in the way LDTs are regulated and changes expectations for patients, doctors, and laboratories for the first time since the Clinical Laboratory Improvement Amendments Act was passed in 1988 at

the risk of greatly altering the United States' laboratory testing infrastructure and reducing patient access to information that informs their healthcare decision making. The Committee directs the FDA to suspend its efforts to implement the rule and continue working with Congress to modernize the regulatory approach for LDTs." H.R. Rep. 118-583, at 88 (July 12, 2024).

FACTUAL BACKGROUND

104. It would be hard to overstate the importance of professionally trained molecular pathologists—who hold an M.D. or Ph.D. and often both—to the practice of modern medicine. These highly trained experts develop, refine, perform, and/or interpret the essential laboratory processes and procedures used to help screen and diagnose patients, select an appropriate course of treatment, monitor disease progression, and offer individualized risk assessments. *See* Kaul Decl. ¶¶ 6-9; Konnick Decl. ¶¶ 5-9; Laposata Decl. ¶ 6-8. Through sophisticated scientific techniques, rigorous procedures, strict quality control measures, and the application of their extensive scientific and medical training, these laboratory professionals ensure that each patient's unique conditions and characteristics are accurately assessed and understood by the patient's care team so that those healthcare professionals can make critical medical decisions that will affect patients for the rest of their lives. Kaul Decl. ¶¶ 6-9; Konnick Decl. ¶¶ 5-9; Laposata Decl. ¶ 6-7.

105. While certain laboratory processes are well-established, standardized, and supported by ample market demand—such that a previously developed, mass-produced, and commercially distributed reagent or test kit (*i.e.*, an IVD) has been made available—science and medicine are constantly evolving and commercially distributed IVDs often rely on outdated information or are not appropriate, available, affordable, or applicable to a given patient's needs and their physician's diagnostic hypothesis or treatment plan. Kaul Decl. ¶ 6; Konnick Decl. ¶ 7; Laposata Decl. ¶ 7-8. So, for example, there may not be a commercialized IVD for a new disease

or condition, a rare disease or condition, or a particular variant of a common disease or condition; an existing IVD may not have been validated for a particular patient population (*e.g.*, children) or specimen type; or the necessary IVD may not be readily available in the marketplace at the particular time it is needed, covered by the patient's insurance carrier, or otherwise be affordable.

106. To reiterate the obvious example noted earlier, no IVD test kits were available to assess the presence or absence of the virus that causes COVID-19 before the COVID-19 pandemic. And the extraordinary failure of CDC's original IVD—which, to reiterate, FDA reviewed and authorized ***despite CDC's CLIA-noncompliant processes and procedures***, *see supra* n.6—came to light only because they were identified by the CLIA-compliant laboratories and laboratory professionals FDA now claims it needs to regulate. Laposata Decl. ¶ 8. So, rather than being designed under FDA's burdensome, duplicative, and far-from-flawless oversight, the first valid procedures for distinguishing the SARS-COV-2 virus from more benign respiratory illnesses were developed as LDTs in clinical laboratories—including by Dr. Laposata and his colleagues—and saved innumerable lives before any reliable IVD test kit was available in the market. *Id.* at ¶¶ 8-9.

107. Needless to say, these gaps put patients at risk—particularly those who live in rural, isolated, and/or disadvantaged communities, where patients tend to suffer from greater background risks (*e.g.*, preexisting conditions) and diminished access to affordable medical care that make delays in diagnosis and the initiation of treatment especially dangerous. To help solve this problem and provide high-quality care to patients, clinical laboratories and their professionals—like Dr. Laposata and the roughly 3000 members of AMP—have been developing and performing highly individualized LDTs for decades. *Id.* at ¶ 7; Konnick Decl. ¶ 8; Kaul Decl. ¶ 6.

108. For AMP members—many of whom, like Dr. Laposata and Dr. Konnick, work in academic or university medical centers—developing a new LDT typically begins after a patient's

attending physician and/or laboratory leadership (*e.g.*., the CLIA laboratory director or technical supervisor) identifies a local clinical need for assessing whether patients present a given biomarker (or "analyte"). Some biomarkers are the subject of commercially available IVD kits. Konnick Decl. ¶ 7. But given the rapid pace of developments in modern medicine, science, and technology, new and clinically relevant biomarkers are being identified every day in peer-reviewed academic, medical, and scientific literature and through government-supported clinical research—the majority of which lack an established, economical, and commercialized option, even for many years after their clinical relevance has been recognized. Kaul Decl. ¶ 13; Konnick Decl. ¶ 7; Laposata Decl. ¶¶ 8-9, 13-14. Without LDTs, these gaps can compromise both the development of new therapies and their utility. Kaul Decl. ¶ 13; Konnick Decl. ¶ 7; Laposata Decl. ¶ 14-15.

109. A significant, early example of this phenomenon involves the cancer drug erlotinib (Tarceva®)—a targeted cancer therapy that prevents the epidermal growth factor receptor protein ("EGFR") from being active. In 2010, the National Comprehensive Cancer Network guidelines recommended that erlotinib be administered as a first-line treatment for patients with stage IV non-small cell lung cancer ("NSCLC") harboring EGFR mutations, and in 2011 the American Society of Clinical Oncologists recommended that EGFR mutation testing be conducted for all patients with advanced NSCLC (then the leading cause of cancer-related deaths in both the U.S. and the world). These recommendations were based on a transformative clinical study demonstrating that patients whose tumors harbor an EGFR mutation not only benefit from first-line treatment with erlotinib but are harmed by standard chemotherapy. *See* R. Rosell *et al*., *Screening for Epidermal Growth Factor Receptor Mutations in Lung Cancer*, 361 NEW ENG. J. MED. 958-967 (Sept. 3, 2009). Although erlotinib already was FDA-approved and available in the United States, FDA did not approve the first IVD for EGFR mutation testing until 2013—leaving a multiyear gap where,

in the absence of the LDTs used to determine eligibility for this transformative use of erlotinib, many NSCLC patients would have been denied access to a targeted therapy that could have saved innumerable lives.

110. A more recent example involves the drug Keytruda® (pembrolizumab), a critically important therapy that harnesses the power of the body's immune system to fight more than a dozen different types of cancer. It functions as an "immune checkpoint inhibitor," which is a type of immunotherapy known to be particularly effective in tumors with mismatch repair deficiency ("dMMR tumors")—a condition where increased mutations develop in cancer cells due to their impaired ability to repair errors made when DNA is copied during cell division. FDA first approved Keytruda® to treat any dMMR tumor in May 2017, but there was no FDA-approved IVD for diagnosing dMMR tumors at that time. As a result, and as FDA itself has acknowledged, the clinical trials supporting Keytruda's broad indication for treating any dMMR tumor enrolled patients based entirely on results from LDTs (the vast majority of which were performed in local laboratories). *See* FDA, *Press Release: FDA grants accelerated approval to pembrolizumab for first tissue/site agnostic indication*, https://tinyurl.com/PembroPR (May 30, 2017) ("The identification of MSI-H or dMMR tumor status for the majority of patients (135/149) was prospectively ***determined using local laboratory-developed, investigational polymerase chain reaction (PCR) tests for MSI-H status or immunohistochemistry (IHC) tests for dMMR***. For 14 of the 149 patients, MSI-H status was determined in a retrospective assessment of 415 patients' tumor samples using a central ***laboratory developed PCR test***.") (emphases added).

111. Without those LDTs, Keytruda could not have been approved for use in any dMMR tumor when FDA did so. And without such dMMR LDTs, it would have taken years for doctors to be able to prescribe Keytruda® for this vital indication even after FDA approved it. That is so

because when FDA approved Keytruda® for treating any dMMR tumor, it neither approved a companion IVD nor recommended a specific method for determining treatment eligibility. Indeed, FDA did not approve the first IVD specifically labeled for determining patient eligibility for pembrolizumab or other immune checkpoint inhibitors until April 2021, nearly 4 years after Keytruda®'s approval to treat all dMMR tumors. Since approximately 3% of all cancerous tumors exhibit dMMR, *see* Y. Kang *et al*., *A scoping review and meta-analysis on the prevalence of pan-tumour biomarkers (dMMR, MSI, high TMB) in different solid tumours*, 12 SCI. REPORTS 20495, at 5-6 & Table 1 (2022), hundreds of thousands of cancer patients would have been denied life-extending and potentially life-saving therapy if not for the LDTs that ***first*** enabled Keytruda®'s approval for the treatment of any dMMR tumor and ***then*** empowered doctors to begin prescribing Keytruda® immediately for patients that might not otherwise be eligible to benefit from this therapy. There are countless other examples where LDTs have enabled life-saving medical interventions. K. Kaul *et al*., *The Case for Laboratory Developed Procedures: Quality and Positive Impact on Patient Care*, 4 ACADEMIC PATHOLOGY 1-21 (2017).

112. These gaps are where clinical pathologists and their fellow laboratory professionals shine. Once a particular biomarker or set of biomarkers has been identified (*e.g*., EGFR mutations or dMMR), the pathologist and his or her team begin researching and identifying the appropriate set of methods and materials needed to create and perform an LDT for that biomarker. Kaul Decl. ¶ 7; Konnick Decl. ¶ 8. For molecular pathology, these LDTs are developed exclusively within a clinical laboratory certified or accredited under CLIA and whose operations therefore must be controlled by a doctor (either an M.D. or a Ph.D., and often both). Kaul Decl. ¶ 9; Laposata Decl. ¶ 6; *see also supra* at ¶¶ 66-68.

113. These high complexity laboratories typically have the instrumentation and other machinery needed to perform an array of distinct analytical methods, including polymerase chain reaction ("PCR"), fluorescence *in situ* hybridization ("FISH"), chromosomal microarray analysis, Sanger sequencing by capillary electrophoresis ("CE"), and Next Generation Sequencing ("NGS"). *See* Konnick Decl. ¶ 8. Each of these techniques is a well-established scientific method for performing genetic and molecular analysis; far from being novel or exotic clinical laboratory creations, these techniques are standard across an array of scientific settings—including academia, research sponsored and conducted by the National Institutes of Health, other branches of medicine, and non-medical scientific research in fields as diverse as agriculture (*e.g.*, animal husbandry, botany, and horticulture), archaeology and anthropology (*e.g.*, to identify the diet, health, and other characteristics of ancient hominids), biology and ecology (*e.g.*, to study living organisms and their ecosystems), criminology and forensics (*e.g.*, to analyze crime-scene evidence), and epidemiology (*e.g.*, to trace the evolution of an emerging disease).

114. Each of these methods has advantages and disadvantages. So the first step for a molecular pathologist is to determine which of these methods is best-suited for detecting the genetic or molecular variant(s) of interest given the clinical context. Konnick Decl. ¶ 8. This decision, along with all the others that a molecular pathologist and his or her team make while developing an LDT, is based on their extensive scientific and medical training, clinical research, review of the literature and clinical practice guidelines, experience, and expertise. Kaul Decl. ¶ 7.

115. Once a given method has been selected, the molecular pathologist can begin identifying the reagents, probes, primers, and/or other materials needed to execute that method. In the case of genetic testing, for example, these materials are necessary to prepare and analyze the patient sample (*e.g.*, a tissue biopsy) by extracting the sample's genetic material (*i.e.*, DNA and/or

RNA) and then performing a series of controlled processes to evaluate that material using commercially available machinery and accessories (*e.g.*, a sequencing platform manufactured by Illumina, Roche, Thermo Fisher Scientific, or any number of other well-known manufacturers of sequencing or other analytic laboratory equipment). Konnick Decl. ¶¶ 8-9; Kaul Decl. ¶ 7.

116. Though these processes are highly technical, they—just like the overall technique selected and the commercially available machinery and accessories used to perform it—are not remotely unique to the pathology laboratory. Konnick Decl. at ¶ 8; Kaul Decl. at ¶ 7. As in the myriad other disciplines that rely in whole or part on such technology, the materials used in a molecular pathology laboratory are manufactured by third parties and purchased commercially, and the same kinds of design processes are used in a virtually infinite array of useful settings. In short, molecular pathologists who develop and perform LDTs do not ***manufacture*** new machines or implements or ***formulate*** their own reagents and accessories. Konnick Decl. ¶ 8. Instead, these highly trained medical professionals ***develop and execute a well-validated process*** by leveraging well-established, pre-existing technologies. Kaul Decl. ¶ 7.

117. The final step in LDT development is to enable the analysis of results. In the sequencing context, for instance, this step requires the development and use of algorithms that align the sequence reads from a given sample with a reference genome for comparative purposes—*i.e.*, to identify the presence or absence of an analyte. Konnick Decl. ¶¶ 8-9. This process entails the identification and memorialization of detailed protocols relating to the LDT's tolerance limits, sensitivities, and other performance measures. Kaul Dec. ¶ 9. Needless to say, every LDT and its precise specifications must be robustly validated prior to use, as required by CLIA, HHS-approved laboratory accrediting agencies (*e.g.*, the College of American Pathologists ("CAP")), and applicable state regulatory regimes. Konnick Decl. ¶ 9; Kaul Decl. ¶ 8. Full validation reports and

records are produced and maintained by the clinical laboratory, where they remain available for regulatory inspection pursuant to CLIA at any time. Kaul Decl. ¶ 8.

118. The development of a validated LDT ultimately culminates with the production of a written protocol detailing each material used to perform the LDT and the precise sequence of steps and processes for performing the LDT and reporting results. *Id.* at ¶ 9. This protocol is maintained and must be followed by all laboratory professionals involved in performing the LDT. *Id.* Thus, in contrast to the tangible, mass-produced, and commercially distributed products that FDA regulates as devices under the FDCA, the embodiment of an LDT is a written protocol—including all of its supporting materials—that is designed to be performed entirely within the developing laboratory by highly trained professionals working with and under the supervision of a doctor, not a tangible good that is distributed beyond the developing laboratory for use by third parties (including lay users) acting outside the developer's direct supervision and control. *Id.*

119. Once executed, the output of a validated LDT is a report delivered to the healthcare provider who ordered the analysis. *Id.* at ¶ 5. Each report includes the patient's identifying details, the type of specimen analyzed, and the specific LDT performed. It also includes details regarding both the LDT methodology (including its limitations and validated performance criteria) and its results, *id.*, *e.g.*, whether any genetic or molecular variants were found; their potential clinical significance, supported by citations to sources and authorities that the physician can consult for reference; the level of scientific certainty as it pertains to the clinical significance of any variants identified, and the limitations of both the LDT and its methodology. These reports require extensive scientific and medical knowledge, experience, and training both to produce and interpret—which is one reason why CLIA requires every high complexity laboratory to employ a clinical consultant, *supra* at ¶ 70—and it is not uncommon for molecular pathologists to spend

considerable time discussing the report, the underlying LDT, and its particular characteristics and limitations with the patient's care team before they make a formal diagnosis and select a therapeutic course. Kaul Decl. ¶ 5; Laposata Decl. ¶¶ 6, 11. Once again, this typically does not and cannot happen with third-party-manufactured, commercially distributed IVD kits—for which only limited information is available because of the product's opaque and proprietary characteristics, and because there otherwise is no relationship between the kit's producer and the healthcare professionals using it.

120. As CLIA expressly authorizes, molecular pathologists also work continually to improve and optimize their LDTs based on ongoing research and clinical feedback, new scientific discoveries, clinical needs, and technological advances. Kaul Decl. ¶ 10; Laposata Decl. ¶ 10. This innovation, flexibility, and customization—which to reiterate is both allowed and encouraged by CMS's regulations, *see supra* at ¶ 55-59—is essential for addressing the complex and evolving landscape of science and medicine. Kaul Decl. ¶ 10. Of course, no substantial change can be made to an LDT without the LDT being revalidated and its protocol updated to reflect and document the change. *Id.* ¶ 9.

121. Once an LDT has been developed and is available for use in a clinical laboratory, molecular pathologists and their colleagues work closely with treating physicians both to identify the right LDT for a particular patient's medical needs and to interpret the clinical significance of its results for that patient. *Id.* at ¶ 5; Laposata Decl. ¶ 11. Before ordering an LDT, treating physicians commonly contact the laboratory's clinical director, technical supervisor, or clinical consultant to better understand which (if any) LDT might be appropriate for analyzing a given patient specimen. Kaul Decl. ¶ 5. And after an LDT is performed according to its validated protocol, the laboratory frequently integrates these results into the patient's broader clinical report.

Id. If the treating physician seeks to obtain additional information about the LDT, the report, or the associated laboratory methods, limitations, and results, the physician can (and often does) contact the clinical director, technical supervisor, or clinical consultant to better understand how interpret the LDT's results within the patient's clinical context. *Id.*

CLAIMS FOR RELIEF

COUNT ONE: UNLAWFUL AGENCY ACTION

122. Plaintiffs incorporate each of the preceding paragraphs by reference.

123. The APA prohibits federal agencies from taking any action that is "not in accordance with the law," 5 U.S.C. § 706(2)(A), "contrary to constitutional right, power, privilege, or immunity," *id*. § 706(2)(B), or otherwise "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right." *Id*. § 706(2)(C). In reviewing federal agency action for compliance with these restrictions, "the reviewing court shall decide all relevant questions of law" and "interpret all constitutional and statutory provisions." *Id*. § 706. That means courts must "exercise their independent judgment in deciding whether an agency has acted within its statutory authority" and "may not defer to an agency interpretation of the law simply because a statute is ambiguous." *Loper Bright Enters. v. Raimondo*, 603 U.S. ___, slip op. at 35 (2024).

124. Despite the broad scope of this Court's interpretive authority, the statutory question in this case is narrow: This Court needs to determine only whether the FDCA ***clearly and unambiguously*** authorizes FDA to regulate LDTs under the FDCA. That is so because this case falls squarely within the "major questions doctrine," under which "courts 'expect Congress to speak clearly if it wishes to assign to an agency decisions of vast economic and political significance.'" *West Virginia*, 597 U.S. at 716 (indirectly quoting *Utility Air*, 573 U.S. at 324); *see also Alabama Ass'n of Realtors v. HHS*, 594 U.S. 758, 764 (2021) ("We expect Congress to speak

clearly when authorizing an agency to exercise powers of vast economic and political significance."). "Like many parallel clear-statement rules in our law, this one operates to protect foundational constitutional guarantees," *id*. at 735 (Gorsuch, J., concurring), including "to protect the Constitution's separation of powers." *Id*. at 737 (citing *id*. at 723 (majority op.)).

125. In major-question cases, even interpretations that have "textual plausibility" must yield when the acting agency belatedly claims authority to subject whole industries—here, tens of thousands of clinical laboratories and laboratory professionals—to vast new regulatory mandates to which they "had never before been subject." *West Virginia*, 597 U.S. at 722 (quoting *Brown & Williamson Tobacco Corp.*, 529 U.S. at 133 and citing *Utility Air*, 573 U.S. at 310, 324). After all, such "[e]xtraordinary grants of regulatory authority are rarely accomplished through 'modest words,' 'vague terms,' or 'subtle devices,'" *id*. at 723 (quoting *Whitman v. Am. Trucking Ass'n*, 531 U.S. 457, 468 (2001)), and courts generally "presume that 'Congress intends to make major policy decisions itself, not leave those decisions to agencies.'" *Id*. (quoting *U.S. Telecom Ass'n v. FCC*, 855 F. 3d 381, 419 (D.C. Cir. 2017) (Kavanaugh, J., dissenting from denial of rehearing en banc)). For these reasons, agency actions implicating a major question require "more than a merely plausible textual basis…. The agency instead must point to 'clear congressional authorization' for the power it claims." *Id*. at 723 (quoting *Utility Air*, 573 U. S. at 324).

126. At least three distinct (if often-coinciding) types of agency actions trigger this clear-statement rule: (1) actions where "an agency claims to discover in a long-extant statute an unheralded power to regulate 'a significant portion of the American economy,'" *Utility Air*, 573 U.S. at 324 (quoting *Brown & Williamson*, 529 U.S. at 159); (2) actions where Congress previously has considered but declined to grant the regulatory authority claimed by the agency, *West Virginia*, 597 U.S. at 731 (citing *Brown & Williamson*, 529 U.S. at 144; *Alabama Ass'n*, 594 U.S. at 760;

FTC v. Bunte Bros., Inc., 312 U.S. 349, 352 (1941)); *see also id*. at 743 (Gorsuch, J., concurring) ("[T]his Court found it telling when Congress has considered and rejected bills authorizing something akin to the agency's proposed course of action. That too may be a sign that an agency is attempting to work around the legislative process to resolve for itself a question of great political significance.") (internal quotations and citations omitted); and (3) actions imposing federal mandates that would require "billions of dollars in spending each year" by the newly regulated parties. *King v. Burwell*, 576 U.S. 473, 485 (2015).

127. This case doesn't check just one of these boxes: It checks them all. The Final Rule relies on a 1976 statute that FDA (1) did not first formally say empowered it to regulate LDTs until 1997, and then only in passing, and (2) took no concrete steps to enforce until 2005—at which point Congress promptly, and since then repeatedly, intervened. *Supra* ¶¶ 73-89. Yet FDA now claims to hold unprecedented regulatory power over laboratory processes that are a "ubiquitous" and "growing sector of" the healthcare system, 88 Fed. Reg. at 68,010 (estimating that "70 percent of medical decisions are based on laboratory test results"), and which Congress since 1967 has subjected to a distinct federal regulatory regime that is specifically designed to ensure the quality of laboratory procedures. *Supra* ¶¶ 42-72 (discussing CLIA); *see also Brown & Williamson*, 529 U.S. at 144 (rejecting FDA's assertion of regulatory authority over tobacco in part because "Congress has created a distinct regulatory scheme to address the problem of tobacco and health").

128. The economic significance of the statutory interpretation on which the Final Rule is based hardly can be overstated. FDA itself estimates that enforcing its interpretation would affect an estimated ***1.65 billion LDT-based medical procedures per year*** by subjecting ***up to 160,800 currently used LDTs*** and up to ***another 15,550 new LDTs per year*** to FDA regulation at a cost of ***up to $114 billion in one-time expenditures*** and another ***$14.31 billion in annually recurring***

costs—nearly all of which then would be passed onto the ***hundreds of millions of Americans*** who benefit from these ***billion-plus laboratory procedures each year***. *See* PRIA at 27-28, 85-86. That seriously underestimates the actual compliance costs, but even if accurate would represent a dramatic and historically unprecedented expansion of the Agency's regulatory activity. In 2023, for instance, FDA authorized only about ***5,800*** total device submissions (including supplements to already-approved submissions), S. Fitzgerald, *The US FDA CDRH 2023 Annual Report*, *available at* https://tinyurl.com/Emergo-CDRH-2023RecordsReview (Jan. 25, 2024), at a tiny fraction of the cost the Final Rule will impose on our Nation's healthcare system and the American people.[7]

129. The vast economic significance of FDA's late-breaking interpretation in turn explains why Congress has devoted so much political capital to these issues during the past two decades. As detailed *supra*, Congress now has considered a dozen different pieces of legislation directly addressing the regulatory status of LDTs since 2006, and time and again has refused to authorize precisely what FDA now says the FDCA empowered it to do some 50 years ago: regulate LDTs as medical devices. *Supra* ¶¶ 78-89 (detailing the many pieces of legislation Congress has considered and rejected). Indeed, to the extent Congress has taken affirmative action on this

[7] For purposes of the major questions doctrine, it is irrelevant that the Final Rule now claims FDA does not necessarily intend to apply its interpretation of the FDCA to all LDTs (while nonetheless reserving the power to do so whenever it pleases). *See supra* ¶¶ 99-102 (detailing the Final Rule's stated enforcement discretion policies); *but see* 89 Fed. Reg. at 37,301 ("[R]egardless of this or any other enforcement discretion policy, FDA retains discretion to pursue enforcement action at any time."). The purpose of the economic-significance inquiry is to determine "whether Congress in fact meant to confer … such a sweeping and consequential authority," *West Virginia*, 597 U.S. at 721, and that logic applies without respect to whether an agency says it intends to defy what it claims Congress commanded. In any event, even the Final Rule's dialed-back approach is burdensome enough to trigger the major questions doctrine: FDA estimates that even its Final Rule will impose ***more than $4.5 billion per year in annual recurring costs*** on the laboratory professionals it now seeks to regulate. FRIA at 123-24 (Table 36); *see also King*, 576 U.S. at 485 (holding that the major questions doctrine applied to an HHS interpretation "involving billions of dollars in spending each year and affecting the price of health insurance for millions of people").

subject, it unequivocally has rejected the Agency's efforts to seize authority over LDTs—first barring FDA from issuing even a non-binding guidance document concerning potential regulation of LDTs without first subjecting it to prior Congressional oversight, 21 U.S.C. § 371 (note) (2012), and then explicitly "direct[ing] the FDA to suspend further efforts to finalize the LDT guidance and [to] continue working with Congress to pass legislation that addresses a new pathway for regulation of LDTs in a transparent manner." H.R. Rep. No. 114-531, at 72-73. Indeed, we note that Congress has just done so again: "The Committee directs the FDA to suspend its efforts to implement the [Final Rule] and continue working with Congress to modernize the regulatory approach for LDTs." H.R. Rep. 118-583, at 88. And if this long history of Congressional deliberation and action weren't a sure "sign that [FDA] is attempting to work around the legislative process to resolve for itself a question of great political significance," *West Virginia*, 597 U.S. at 743 (Gorsuch, J., concurring), the fact that Defendant Becerra chose to revoke HHS's pandemic-era actions regarding LDTs in part because they were "established during the previous administration" leaves no doubt about the Final Rule's enduring political significance. *Supra* ¶ 93 (quoting the Becerra Statement).

130. The Final Rule thus embodies precisely the kind of agency action of "vast economic and political significance" that triggers the major questions doctrine, *West Virginia*, 597 U.S. at 716, and as detailed *infra*, the FDCA does not remotely grant FDA the required "'clear congressional authorization' for the power[s] it claims." *Id.* at 723 (quoting *Utility Air*, 573 U.S. at 324). Indeed, FDA's interpretation would not reflect the statute's "single, best reading" even if this weren't a classic major questions case (which it is). *See Loper Bright*, 603 U.S. __, slip op. at 22; *see also id*. at 23 ("In the business of statutory interpretation, if it is not the best, it is not permissible.") (internal quotations and citation omitted).

131. The Final Rule necessarily hinges on the proposition that LDTs are "devices" under 21 U.S.C. § 321(h)(1) because the substantive FDCA provisions FDA now says it intends to apply to LDTs apply only to "devices." 21 U.S.C. § 360(k) (requiring premarket review prior to "the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use"). But the Final Rule itself admits there is a "lack of language in the [FDCA] specifically mentioning … LDTs," 89 Fed. Reg. at 37,349, and LDTs otherwise fall outside the statutory definition's enumerated categories—which include only tangible goods, not intangible procedures. 21 U.S.C. § 321(h)(1) (defining "device" only as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article"); *see also Dubin v. United States*, 599 U.S. 110, 124 (2023) ("Under the familiar interpretive canon *noscitur a sociis*, a word is known by the company it keeps.") (internal quotations omitted).

132. Many of the statute's surrounding provisions reinforce the conclusion that only tangible goods fall within that definition—not intangible medical services or procedures. For example, the statute requires registration by most persons who "repackage[e] or otherwise chang[e] the container, wrapper, or labeling of any … device package in furtherance of the distribution of the … device from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer or user." 21 U.S.C. § 360(a)(1). That proviso makes perfect sense in the context of tangible goods that move from one place to another—*i.e.*, the mass-produced, commercially distributed objects on which Congress was focused after the pacemaker and Dalkon Shield crises. But it makes no sense in the context of LDTs, which FDA admits are both designed and used within a single laboratory and by their very nature cannot be packaged, repackaged, wrapped, contained, or transferred. *See, e.g.*, 89 Fed. Reg. at 37,289.

133. To cite another illustrative example, the same is true of the MDA provisions relating to device recalls—which allow FDA to order a manufacturer to "replace the device with a like or equivalent device" and "refund the purchase price of the device (less a reasonable allowance for use if such device has been in the possession of the device user for one year or more…)." 21 U.S.C. § 360h(b)(2). Again, these authorities make perfect sense in the context of tangible goods that are delivered from one person or place to another, but have no plausible application in the context of an LDT procedure that never leaves the laboratory.

134. The MDA's device definition and related statutory provisions are notable not only for what they include but also for what they exclude. As set forth *supra* at ¶ 26, FDA initially claimed "inherent" authority to regulate IVDs in 1973, and at that time defined this category to include "reagents, instruments, ***and systems*** intended for use in the diagnosis of disease." 21 U.S.C. § 167.1(a) (1973) (emphasis added). But when the MDA amended the "device" definition in 1976, it added only "in vitro ***reagent***" to the list—not the broader category of *in vitro* "***systems***" from the regulation. *See* 21 U.S.C. § 321(h)(1) (emphasis added). There hardly could be a clearer sign that Congress meant ***only*** to subject ***reagents***—which are tangible goods, like everything else in the definition—to the FDCA, not the performance of intangible LDT procedures that FDA now says count as a "test system." *See* 89 Fed. Reg. at 37,331 (quoting the statutory definition—which does not include the words "test system"—and then claiming "FDA does not agree that [the FDCA] definition is limited by its plain language to physical objects or material things, but even if it were, ***a test system*** is a physical object and a material thing") (emphasis added).

135. Any broader interpretation would lead to patently absurd results. In many respects, developing and performing an LDT in a CLIA-certified laboratory is indistinguishable from designing and performing a surgical procedure that is comprised of many distinct steps, some of

which use medical devices that themselves are FDA-regulated. If, as the Final Rule expressly claims, *see* 89 Fed. Reg. at 37,331, the mere selection and sequenced deployment of individual devices as part of an overall process—for instance, a surgeon's selection and use of scalpels, scissors, forceps, needles, and sutures during an operation to repair a muscle tear—constitutes the manufacturing of a brand-new medical device just because one or more individually regulated devices are used in conjunction, then literally every surgery that has been performed in the United States since 1976 has been a felony proceeding. That is not—and cannot be—the law.

136. Finally, we note that even if the device definition were broad enough to conceivably encompass LDTs—and it is not—FDA's choice to construe it as covering LDTs runs headlong into CLIA. Since 1967, Congress has maintained and enhanced CLIA for the specific purpose of regulating laboratory procedures—including through licensing, registration, clearance, quality, inspection, testing, and personnel requirements that are specifically tailored to the laboratory context. *Supra* ¶¶ 42-72. And when Congress decided the original CLIA was falling short in 1988, it not only strengthened CMS's oversight of LDTs in lieu of empowering FDA but failed even to suggest that FDA might have a role to play in regulating laboratory procedures. *Supra* ¶¶ 46-47, 73. That is a sure sign that Congress never understood LDTs to be subject to the FDCA nor intended FDA to regulate LDTs—which in turn is why CMS's post-1988 CLIA regulations expressly authorize CLIA-certified laboratories both to "modif[y] an FDA-cleared or approved test system" and to "introduce[] a test system ***not subject to FDA clearance or approval (including methods developed in-house…)***." 42 C.F.R. § 493.1253(b)(2) (emphasis added).

137. The Final Rule thus not only needlessly duplicates CLIA by subjecting laboratories to overlapping standards administered by different federal agencies; it directly conflicts with it, as the Charrow Memo expressly recognized. *See* Charrow Memo at 16 (citing both CMS's CLIA

regulations and the 1988 CLIA amendments' legislative history). Indeed, much of the Final Rule takes direct aim at CLIA—for instance, by challenging the adequacy of proficiency testing. *See, e.g.*, 89 Fed. Reg. at 37,323 (claiming that "proficiency testing data, as standalone or comparative results, do not support test validation and performance expectations" because it is "highly contrived" and "insufficiently challenging"). Those criticisms are meritless on their own terms, but the key point here is that ***proficiency testing is the method Congress chose*** to ensure "acceptable performance … for all examinations and procedures" performed by clinical laboratories, under standards and criteria that ***Congress charged CMS*** with establishing. 42 U.S.C. §§ 263a(f)(1)(D) & 263a(f)(3). If FDA now believes that such proficiency testing is inadequate or that CMS's standards are not sufficiently rigorous, it can either ask Congress to amend CLIA or request that CMS modify the standards, methods, and criteria for proficiency testing. But in our system of government, federal agencies do not get to defy Congress just because they disagree with its choices. *See, e.g.*, *NRDC, Inc. v. EPA*, 902 F.2d 962, 977 (D.C. Cir. 1990) ("It hardly bears noting that [agency] discretion cannot include the power to rewrite a statute and reshape a policy Congress itself has made.") (internal quotation and original alteration omitted), *partially vac'd in irrelevant aspects* 921 F.2d 326 (D.C. Cir. 1991); *Quarles v. St. Clair*, 711 F.2d 691, 708 n.60 (5th Cir. 1983) ("The role of the agencies remains basically to execute legislative policy; they are not more authorized than are the courts to rewrite acts of Congress.") (internal quotation omitted).

138. In any event, when distinct statutory regimes conceivably could be applied to a single object, the usual rule is that the more specific law governs even in the absence of a conflict. *See, e.g.*, *D. Ginsberg & Sons, Inc. v. Popkin*, 285 U.S. 204, 208 (1932) ("Specific terms prevail over the general in the same or another statute which otherwise might be controlling."). Indeed, the Supreme Court made this very point in its seminal major-questions case, when it rejected

FDA's attempt to regulate tobacco products as "combination products" comprised of both a "drug" (*i.e.*, pharmacologically active nicotine) and a delivery "device" (*i.e.*, the cigarette or other product that delivers that drug). *See Brown & Williamson*, 529 U.S. at 131. As the Court explained, "the implications of a statute may be altered by the implications of a later statute. This is particularly so where the scope of the earlier statute is broad but the subsequent statutes more specifically address the topic at hand." *Id*. at 143 (citing *United States v. Estate of Romani*, 523 U.S. at 530-531 ("[A] specific policy embodied in a later federal statute should control our construction of the earlier statute, even though it has not been expressly amended.")). After recounting Congress's repeated efforts to regulate tobacco outside the FDCA, it concluded that "Congress has created a distinct regulatory scheme to address the problem of tobacco and health, and that scheme, as presently constructed, precludes any role for the FDA." *Id*. at 144; *see also Train v. Colorado Public Interest Research Group Inc.*, 426 U.S. 1, 23-25 (1976) (rejecting claims that EPA could regulate nuclear materials even though they plainly qualified as "radioactive materials" under the Clean Water Act because such materials were specifically regulated by the Atomic Energy Act).

139. FDA may not recall the lesson it was taught thirty years ago, but *Brown & Williamson*'s logic applies with equal force to the Agency's assertion of regulatory authority over LDTs. Again, Congress was well aware in 1988 of the need to ensure the quality and validity of LDTs, and it chose to do so by strengthening CMS's oversight under CLIA—not by empowering FDA (let alone assuming that FDA already had the power) to impose burdensome, duplicative, costly, and ill-suited FDCA-based regulations on laboratories and their professionals.

140. The fact that LDTs do not clearly and unambiguously fall within the FDCA's "device" definition—and if anything, fall clearly and unambiguously outside it—is alone sufficient to require vacatur of the Final Rule. Again, the validity of the entire Final Rule hinges on this issue,

because the operative statutory provisions to which FDA seeks to subject LDTs apply only to "devices." But that is hardly the only reason why the Final Rule is invalid. Even if LDTs clearly and unambiguously were devices, a statutory definition alone cannot supply the clear statement required in major-question cases. *See, e.g.*, *Utility Air*, 573 U.S. at 315-16, 319-21 (rejecting claims that Congress clearly authorized EPA to regulate greenhouse gases simply because they fall within the statutory definition of "air pollutant"); *Solid Waste Agency v. U.S. Army Corps of Engineers*, 531 U.S. 159, 172-73 (2001) (rejecting claims that Congress granted the Army Corps of Engineers regulatory authority over isolated wetlands simply because they fall within the statutory definition of "waters of the United States"). In the Fourth Circuit's words, "an expansive, vaguely worded definition is not akin to clear congressional authorization. So, in a major-questions case, more is required before holding that the agency has been granted the asserted power." *N.C. Coastal Fisheries Reform Grp. v. Capt. Gaston LLC*, 76 F.3d 291, 302 (4th Cir. 2023).

141. That makes sense. Statutory definitions generally are not operative on their own; they merely supply meaning to terms used in a statute's substantive clauses—the ones establishing actual legal duties and rights. That is so here. The device definition itself establishes no duties, prohibitions, jurisdiction, or powers; it is merely a dictionary entry "[f]or the purposes of this chapter," 21 U.S.C. § 321, and thus lacks any legal force outside of Title 21's operative provisions. The Final Rule unwittingly concedes this principle. *See* 89 Fed. Reg. at 37,334 ("Whether a particular provision of the FD&C Act requires a connection to interstate commerce goes to the reach of ***that specific provision***, ***not of the device definition***.") (emphasis in original). And when it comes to the operative provisions of the FDCA, they not only fail to supply the requisite "'clear congressional authorization' for the power [FDA] claims," *West Virginia*, 597 U.S. at 723 (quoting *Utility Air*, 573 U. S. at 324), but foreclose the Final Rule's application to Plaintiffs.

142. Without limiting the breadth or scope of Plaintiffs' challenge to the Final Rule under 5 U.S.C. § 706(2), two examples help to underscore just how far afield the Final Rule strays from the FDCA's operative provisions: ***First***, it eviscerates the FDCA's practice-of-medicine exemption, and ***second***, it defies the MDA's commercial-distribution requirement.

143. With respect to the former, the Supreme Court long has recognized that "the FDCA expressly disclaims any intent to directly regulate the practice of medicine." *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 350-51 (2001) (citing 21 U.S.C. § 396); *see also Apter v. HHS*, 80 F.4th 579, 592 (5th Cir. 2023) ("[T]he [FDCA] expressly shields [d]octors from certain kinds of FDA meddling."). Most relevant here, the statute expressly exempts licensed healthcare providers (including Dr. Laposata and AMP's licensed providers) from the device registration, recordkeeping, reporting, full inspection, and listing requirements. 21 U.S.C. § 360(g)(2) ("The foregoing subsections … shall not apply to … practitioners licensed by law to prescribe or administer … devices and who manufacture, prepare, propagate, compound, or process … devices solely for use in the course of their professional practice."); 21 U.S.C. § 360i(c)(1) (establishing a similar exemption from the MDA's recordkeeping and reporting requirements). By extension, the MDA exempts these professionals from its 510(k) requirements, which apply only to a "person who is required to register under this section," 21 U.S.C. § 360(k), and, by further extension, from the de novo classification and PMA requirements—which are defined by cross-reference back to section 510(k); to the statute's reporting, recordkeeping, and inspection requirements; or to both. 21 U.S.C. §§ 360c(f)(2)(A)(i)-(ii), (f)(4), (f)(6)(C), (i)(E)(i)-(iii); *id*. § 360e(e)(1)(D).

144. The Final Rule defies these critically important exceptions. Even though the FDCA defines the de novo classification and PMA requirements by reference back to section 510(k) and/or the reporting, recordkeeping, and inspection requirements from which licensed

professionals are exempt, the Final Rule declares that otherwise exempted healthcare professionals are fully subject to the de novo and PMA pathways. 89 Fed. Reg. at 37,347. Not content to stop there, it then effectively eliminates these professionals' antecedent exemption from the MDA's 510(k), registration, recordkeeping, reporting, full inspection, and listing requirements. *Id*.

145. The Final Rule does so in three ways. ***First***, it asserts that ***the institutions and entities*** with which these otherwise-exempt individuals are affiliated can be held liable for these individuals' LDT-related activities even though Congress granted ***the individuals themselves*** immunity. *Id*. Indeed, the Final Rule goes so far as to make clear that FDA could "impose liability on a solo practitioner's personal service corporation" even if the practitioner herself cannot be held personally liable simply because the statute uses "the possessive terms 'their' and 'his'" in establishing the practice-of-medicine exemption. *Id*. That proposition is preposterous, and FDA's absurdist reading of the practice-of-medicine exemption inevitably will cause many institutions to bar licensed professionals from providing essential patient-care services that Congress expressly exempted from regulation precisely because they are performed by licensed professionals. *Id*.

146. ***Second***, the Final Rule declares that the practice-of-medicine exemption does not apply when an otherwise-exempt professional works on an LDT in concert with anyone who is not themselves exempt. *See* 89 Fed. Reg. at 37,347 ("[T]o the extent that comments are arguing that the exemptions apply" where "one individual is licensed to administer the device and others manufacture the device, FDA disagrees.") (internal parenthesis mark omitted). Leaving aside the fact that professional laboratorians developing and performing an LDT are not "manufacturing" anything, that assertion conflicts with CLIA's intentional allocation of distinct responsibilities to distinct laboratory professionals holding distinct qualifications precisely because high-quality laboratory work requires collective effort by many different people—not the work of a single

woman or man acting alone. *See supra* ¶¶ 66-72. Indeed, if FDA's position were correct and applied, for instance, to the surgical context, then FDA could target the scrub nurses, medical technicians, and other individuals who assist a surgeon simply because they are not themselves licensed to prescribe the devices used during an operation. Again, this cannot be the law; it would make it impossible to practice medicine in America, which is precisely what the practice-of-medicine exemption is designed to avoid.

147. ***Finally***, the Final Rule declares that the practice-of-medicine exemption does not in any event apply to anything involving "commercial activity." *Id*. (internal quotation omitted). The Final Rule does not define that term, but it presumably would be triggered whenever an otherwise-exempt professional ultimately seeks payment for providing laboratory services—which of course is the case for virtually every medical procedure performed in the United States, whether in a laboratory or an operating room. Together, these remarkable claims lay bare the breathtaking scope of the Final Rule's assertion of regulatory authority, which would thoroughly undermine a crucial statutory exemption that has shielded the practice of medicine from FDA interference for decades and thereby violate FDA's duty "to give effect, if possible, to every clause and word of a statute, rather than to emasculate an entire section." *United States v. Menasche*, 348 U.S. 528, 538-39 (1955) (internal quotation and citation omitted).

148. The Final Rule not only guts the practice-of-medicine exemption; it writes the FDCA's commercial distribution requirement out of the statute. As emphasized, the FDCA does not empower FDA to regulate devices in the abstract, but instead subjects devices to such regulation only if certain other conditions are satisfied. One of those conditions is the statute's commercial distribution requirement: Rather than subject every medical device to the premarket 510(k), de novo, or PMA requirements, the MDA only applies those requirements to devices that

are or will be "introduc[ed] or deliver[ed] … into interstate commerce ***for commercial distribution***." 21 U.S.C. § 360(k) (emphasis added); *see also id*. § 360c(c)(2)(C)(ii) (classification dependent on whether a given device was "introduced or delivered for introduction into interstate commerce ***for commercial distribution*** before May 28, 1976, or is within a type of device which was so introduced or delivered before such date") (emphases added; internal enumeration omitted); *id*. § 360c(f)(1) (virtually identical); *id*. § 360e(b)(1) (same); *id*. § 360e(i)(1) (same).

149. The statute does not define "commercial distribution," so courts must "look to the [phrase's] ordinary definition." *CSX Transp., Inc. v. Ala. Dep't of Revenue*, 562 U.S. 277, 284 (2011). That meaning is not hard to find: "Commerce" refers to "the exchange or buying and selling of ***commodities especially on a large scale and involving transportation from place to place***." Webster's Third New International Dictionary of the English Language, Unabridged, Merriam-Webster (2002) (emphasis added). And in its most common and contextually appropriate sense, "distribution" refers to the "delivery" or "conveyance" of a good "from a main source" to another location. *Id*. Put those two concepts together—as the statute does through its repeated reference to "commercial distribution"—and these mutually reinforcing definitions make clear than the statute's premarket submission requirements apply only where a tangible commodity good is the subject of an exchange from one person or entity to another and from one place to another.

150. That understanding makes perfect sense in the context of mass-produced tangible devices. For example, when a manufacturer seeks to produce a new syringe, the resulting commodity good will be transferred by the thousands from the manufacturer to its customers, from one place to others, as part of an ordinary business transaction. LDTs, by contrast, bear no resemblance to this archetype. They are not commodities, but medical procedures that are designed within a laboratory, for use by that laboratory, and never leave that laboratory or its control (or

that of its affiliates, which FDA's own regulations expressly exempt from the MDA, *see* 21 C.F.R. § 807.3(b)); Kaul Decl. ¶ 9. There is no transfer of title. And neither the clinician nor the patient receives the LDT—only information from a process-based service performed by and within the laboratory. Kaul Decl. ¶ 9. Indeed, this is precisely the distinction FDA itself drew in the ASR Rule—when it expressly distinguished "ASR's ***that move in commerce***" from "tests developed ***in-house*** … and ***used exclusively by that laboratory***." 62 Fed. Reg. at 62,249 (emphases added).

151. The Final Rule makes no credible effort to refute this analysis. Instead, it relies principally on the legislative history of the FDCA to claim that "the phrase 'commercial distribution' means 'on the market.'" 89 Fed. Reg. 37,338 (quoting H.R. Rep. No. 94-853, at 36 (Feb. 29, 1976)). But even if legislative history could override the plain and contextually obvious meaning of "commercial distribution," *but see Ratzlaf v. United States*, 510 U.S. 135, 147-148 (1994) ("[We] do not resort to legislative history to cloud a statutory text that is clear."), FDA's invocation of words that do not appear anywhere in the statute only begs the question of what "on the market" means. The dictionary is no help to FDA: The "market" is "a sphere within which price-making forces operate ***and in which exchanges in title tend to be followed by actual movement of goods***," and placing a product "on the market" typically means to put an item "up for sale" or to make it "available for purchase" ***within that sphere***. Webster's Third New International Dictionary of the English Language, Unabridged, Merriam-Webster (2002). But again, title to an LDT is never transferred from the laboratory to anyone else, and the LDT itself never moves. It remains within the laboratory, for use exclusively by the laboratory, at the request of a licensed healthcare provider, and, in accordance with CLIA, under supervision and direction of a licensed professional. Kaul Decl. ¶ 9. Regardless of how FDA prefers to rewrite the statute, it provides no authority for the Agency's imposition of vast new regulatory mandates.

152. We need go no further for now. As we repeatedly have stressed, this is a major-questions case—where the Agency itself admits that billions of dollars, billions of procedures, and the health of hundreds of millions of Americans are at stake—and that means FDA's Final Rule can only be upheld if the statute clearly and unambiguously supports the Agency's assertion of power to regulate LDTs as medical devices. *West Virginia*, 597 U.S. at 723 ("The agency instead must point to 'clear congressional authorization' for the power it claims."). FDA has not met its burden—and it cannot do so. Instead, its interpretation time and again runs directly counter to both the FDCA's text and structure and CLIA. The Final Rule must be vacated.

COUNT TWO: ARBITRARY, CAPRICIOUS, AND ABUSIVE AGENCY ACTION

153. Plaintiffs incorporate each of the preceding paragraphs by reference.

154. The APA prohibits FDA from acting in a way that is "arbitrary, capricious, [or] an abuse of discretion." 5 U.S.C. § 706(2)(A). That requires agencies to "examine the relevant data and articulate a satisfactory explanation for its action including a rational connection between the facts found and the choice made. In reviewing that explanation, [courts] must consider whether the decision is based on a consideration of the relevant factors and whether there has been a clear error of judgment." *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (internal quotations and citations omitted). Agency actions are by definition arbitrary and capricious if the Agency "failed to consider an important aspect of the problem" or "offered an explanation for its decision that runs counter to the evidence before the agency." *Id*.

155. Despite the sweeping nature of the authority FDA claims, it all but admits that subjecting LDTs to the FDCA's regulatory requirements cannot rationally be justified by the poor-quality, mischaracterized, and admittedly "largely anecdotal" reports the Final Rule invokes. *See* 89 Fed. Reg. at 37,321. Even taking that "evidence" at face value (and for the many reasons

detailed in the AMP Comments, it cannot be), FDA at most claims that in any given year, less than a handful of the tens of thousands of LDTs currently in use raise "concerns": Since 2008, FDA says it has identified just 52 total "concerns" with LDTs—or about 3 "concerns" per year—among the up to 160,800 LDTs it estimates are currently in use. ***That is a "concern" rate of just 0.03%***. 89 Fed. Reg. at 37,322 n.52 ("Four concerns were identified between 2008 and 2011, 10 concerns between 2012 and 2015, 15 concerns between 2016 and 2019, and 23 concerns between 2020 and 2023."); *but see* PRIA at 23-24 (admitting that FDA does not know "the number of … LDTs currently on the market" but estimating there could be 160,800 currently in use with an additional 15,552 new LDTs introduced each year). And for all the Agency's rhetoric about the supposedly "growing"—yet still infinitesimal—number of allegedly "problematic LDTs," the Final Rule ultimately asserts only that FDA has "uncertainty," 89 Fed. Reg. at 37,303, 37,311, 37,320, 37,322, 37,375, 37,377, 37,410—even as it concedes that applying the FDCA to LDTs "could lead to the ***loss of access to safe and effective IVDs on which patients currently rely***," *id*. at 37,293 (emphasis added), and will at a minimum impose ***billions of dollars per year*** in new regulatory mandates. FRIA at 124; *see also supra* ¶ 34 (noting that FDA's final cost projections are based on estimated expenditures that are far lower than real-world survey data reveal); *id*. ¶ 96 (noting that FDA's PRIA estimated ***tens of billions of dollars*** in annualized compliance costs, irrespective of any dispute over the estimated costs for any of the inputs used in that calculation).

156. That is why the Final Rule's non-binding and legally irrelevant Preamble ultimately announces an array of supposed "enforcement discretion policies" that—if they even could be taken seriously in the face of FDA's repeated threats to take enforcement action despite those policies, *see* 89 Fed. Reg. at 37,295, 37,297, 37,301, 37,304, 37,307, 37,390—would exempt tens

of thousands of LDTs from the requirements FDA otherwise insists are necessary to protect the public. *See id*. at 37,294-95 (summarizing these non-binding policies).

157. Make no mistake: Plaintiffs believe that many of these enforcement discretion policies—and still others—are essential.[8] As the AMP Comments repeatedly explained and the Final Rule and its FRIA effectively concede, fully subjecting LDTs to burdensome and duplicative FDA regulation will drive laboratories out of business and cause significant job losses in the pathology profession; stifle the development of new LDTs; subject those LDTs which are developed to lengthy delays while FDA struggles under a crush of new applications and inspections; thwart innovation and otherwise drive LDTs offline by barring the kinds of changes CLIA expressly allows; increase healthcare costs by forcing laboratories to raise prices in order to recoup their massive new compliance costs; and, most important, prevent patients from accessing tens of thousands of admittedly "safe and effective" LDTs, which ultimately will delay patient diagnoses or lead to misdiagnoses, prevent the timely initiation of treatment, and force millions of Americans to suffer from prolonged and advancing diseases, extended and ever-more-invasive medical treatments, and far worse clinical outcomes—including untold thousands of deaths. *See* Laposata Decl. at ¶¶ 10-15; Kaul Decl. at ¶¶ 14-22; Konnick Decl. at ¶¶ 11-17.

158. Yet far from redeeming its decisions, FDA's admission that actually applying the FDCA to LDTs would wreak such havoc in our healthcare system serves only to condemn the Final Rule. A rational agency facing these consequences would thoroughly reconsider whether the

[8] That said, FDA's categories are arbitrarily under- and over-inclusive. For example, in a classic case of "rules for thee but not for me," it exempts the federal government's largest healthcare providers from regulation. 89 Fed. Reg. at 37,294 ("FDA intends to exercise enforcement discretion and generally not enforce requirements for LDTs manufactured and performed within the Veterans Health Administration (VHA) or the Department of Defense (DoD).").

statute sensibly could or should be interpreted in a way that would unleash those results—not manufacture a series of *ad hoc* exemptions that defy what the agency claims Congress compelled. And in the end, FDA's enforcement-discretion dodge is doomed to fail anyway. The Final Rule will impose ***all of these harms*** because no rational provider can rely on an "enforcement discretion policy" that is outlined only in a non-binding Preamble, remains "subject to change as circumstances warrant," *id*. at 37,390, and not only is accompanied by repeated threats "to pursue enforcement action at any time" but a stark warning that FDA "intends to do so." *Id*. at 37,295. And these flimsy assurances will provide ***none of the benefits*** FDA intended them to generate on paper—namely the tens of billions of dollars in supposed cost savings that FDA derives from offering these phantom guarantees. *See supra* ¶ 102 (showing that these policies reduced the rule's cost estimate from up to $113.86 billion in one-time costs and $14.31 billion in annual recurring costs to "just" $85 million in one-time costs and $4.54 billion in recurring costs).

159. Without belaboring the point, this is not the stuff of reasoned agency decision-making—let alone a justification sufficient to warrant the imposition of what FDA concedes still will be billions of dollars per year in new regulatory compliance costs even if its legally inoperative and expressly self-defeating regulatory Preamble could be taken seriously. Whether or not FDA has the authority to regulate LDTs under the FDCA (and it does not, for the reasons outlined previously), its Final Rule represents the height of arbitrary, capricious, and abusive agency action. It must be vacated.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that this Court enter judgment in their favor and against Defendants, and grant the following relief:

A. **DECLARE** that the Final Rule is contrary to law, in excess of statutory jurisdiction, authority, or limitations, short of statutory right, arbitrary, capricious, and an abuse of discretion and **VACATE AND SET IT ASIDE**;

B. **ENJOIN** Defendants from taking any action in furtherance of the enforcement of the Final Rule;

C. **AWARD** Plaintiffs their costs and attorneys' fees; and

D. **AWARD** Plaintiffs such other relief as the Court may deem just and proper.

Dated: August 19, 2023

Respectfully submitted,

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