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A Common Legislative Framework: The Right Approach for In Vitro Clinical Tests

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INTRODUCTION

The COVID-19 pandemic has underscored the essential nature of accurate, accessible diagnostic tests for their critical roles in public health surveillance and clinical care. Access to accurate and reliable testing to identify individuals exposed to or infected with a rapid spreading disease is critical to an effective public health response. The lack of adequate COVID-19 testing at the outset of the pandemic foreclosed the country's opportunities to stop widespread community transmission of the disease, and exacerbated its consequences.[1] As a result of controversies over COVID-19 testing, the profile of *in vitro* clinical diagnostics tests has been dramatically elevated from the shadow of therapeutic products.

In response to this public health crisis, members of Congress introduced legislation with the aim of preventing a similar dearth of testing during future emergencies. On March 5, 2020, the Verifying Accurate Leading-edge IVCT Development (VALID) Act of 2020 was introduced by House Representatives Diana DeGette (D-CO) and Larry Bucshon, MD (R-IN),[2] with an identical bill introduced in the Senate by U.S. Senators Michael Bennet (D-CO) and Richard Burr (R-NC) [3]. The VALID Act is a comprehensive diagnostic reform bill, which creates a new class of product within the Food and Drug Administration (FDA) jurisdiction called *in vitro* clinical tests (IVCTs) to include both *in vitro* diagnostic products (IVDs)[4] manufactured by the conventional device manufacturers and those developed and used within a single clinical laboratory, i.e. laboratory-

[1] Michael Shear et al., *The Lost Month: How a Failure to Test Blinded the U.S. to Covid-19*, N.Y. Times (Mar. 28, 2020). https://www.nytimes.com/2020/03/28/us/testing-coronavirus-pandemic.html
[2] VALID Act of 2020, H.R. 6102, 116th Cong. (2020).
[3] VALID Act of 2020, S. 3404, 116th Cong. (2020).
[4] 21 C.F.R. § 809.3. IVD is defined as *in vitro* diagnostic products are reagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

developed tests (LDTs)[5]. To leverage the learning from the COVID-19 testing, the FDA also joined Congress's reform efforts on legislation beyond emergency rules and responses, calling for "a common legislative framework to ensure that all clinical tests are accurate and reliable."[6]

Also, in March and in response to the COVID testing challenges, Senator Rand Paul (R-KY) induced the Verified Innovative Testing in American Laboratories Act of 2020 (VITAL Act) that assigns the responsibility of overseeing the regulation of LDTs to the Centers for Medicare & Medicaid Services (CMS) instead of FDA, including during a declared emergency.[7]

To certain degree, these bills are the continuation of a long-standing (over twenty years) debate[8] over whether diagnostic tests are best regulated by a single agency (FDA) under the Food, Drug and Cosmetic Act (FDCA)[9], or by a dual system—LDTs developed at clinical laboratories are regulated by CMS under the Clinical Laboratory Improvement Amendments of 1988 (CLIA)[10] and IVDs developed by device manufacturers are regulated by FDA under FDCA. Proponents for the a common regulatory framework argue that the current dual system creates federal gaps in regulatory oversight because CLIA does not require clinical validity assessment of LDTs. They contended that "[m]odern LTDs are often complex, have a nationwide reach, and high-risk uses and without oversight could present risks for patients and healthcare professionals who rely on the

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[5] U.S. Food & Drug Admin., *Draft Guidance for Industry, Food and Drug Administration Staff, and Clinical Laboratories: Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)*, 5 (Oct. 3, 2014). https://www.fda.gov/media/89841/download

[6] Shuren, *infra* note 19.

[7] VITAL Act of 2020, S. 3512, 116th Cong. (2020).

[8] *See, e.g.,* Gail H. Javitt, *In Search of a Coherent Framework: Options for FDA Oversight of Genetic Tests,* 62 Food & Drug L.J. 617 (2007); Deborah G.B. Leonard, *The FDA is Coming! The FDA is Coming!* 6 Molecular Diagnosis 153 (2001) (editorial).

[9] 21 U.S.C. § 321(h).

[10] 42 U.S.C. § 263a; *see also* Laboratory Requirements, 42 C.F.R. § 493 (regulations implementing CLIA).

results of LDTs to make medical decisions."[11] In the COVID-19 context, they readily pointed to the poor quality of unregulated LDTs to support their view.[12] On the other hand, proponents for the dual regulatory system argue that FDA oversight is duplicative with CLIA regulations, and the inefficient FDA processes led to the delayed COVID-19 response.[13]

The COVID-19 pandemic may be the "final straw" that overcomes the legislative inertia to end this long-standing legislation debate once and for all. Unraveling this debate requires understanding the interaction between the current regulatory structure as well as the competing interests among all stakeholders. Section I of this paper recounts the lessons learned from the COVID-19 testing crisis. These lessons should guide policy and practice to ensure timely access to accurate, high-quality, and innovative testing. Section II identifies the gaps and inconsistencies in the current regulatory framework. Section III describes how the common legislative framework proposed by VALID Act would address the issues in the current system to ensure safety, effectiveness and timely access to a board range of diagnostic tests. Section V proposes further development and refinement of VALID Act to eliminate redundancy, build regulatory flexibility and agility, and strengthen postmarket enforcement powers.

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[11] *Examining the Regulation of Diagnostic Tests and Laboratory Operations*, Hearing Before the S. Comm. On Health, 144th Cong. (2015) (statement of Jeffery Shuren, M.D., J.D., Director, Center for Devices and Radiological Health, Food and Drug Administration, Department of Health and Human Services).
[12] Shuren, *supra* note 19.
[13] *See* Association for Molecular Pathology Commends Senator Rand Paul for Introducing the Verified Innovative Testing in American Laboratories (VITAL) Act of 2020 (Mar.18, 2020) https://www.amp.org/AMP/assets/File/pressreleases/2020/VITAL_2020_PR_AMP__3_18_2020.pdf?pass=67

I. Learning from the COVID-19 Diagnostic Testing Crisis

On January 31, 2020, the U.S. Secretary of Health and Human Services (HHS) declared a public health emergency due to a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak in the U.S.[14] On February 4, 2020, FDA received emergency authority to expedite public access to COVID-19 diagnostic tests under emergency use authorization (EUA).[15] On the same day, FDA granted an EUA to the first COVID-19 test developed by the Centers for Disease Control and Prevention (CDC).[16] The CDC test is a molecular test designed to identify the genetic material of SARS-CoV-2. FDA chose to limit the initial approval to the CDC test for the purpose of ensuring accurate surveillance testing by the state and local public health laboratories.[17] It was later discovered that the early batch of the CDC test that produced inclusive or invalid results was contaminated.[18] Pressured by the unmet need to rapidly expand testing capacities for COVID-19 screening and clinical care, on February 29, 2020, FDA issued a policy to allow qualified laboratories to perform patient testing provided they submitted the validation data in EUA requests within fifteen business days.[19] Although this approach resulted in earlier access to COVID-19 testing, the delayed FDA EUA review and the less-vigorous standards allowed the clinical use of

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[14] U.S. Dep't Health & Hum. Servs., Alex M. Azar II, *Determination that a Public Health Emergency Exists*, (Jan. 31, 2020). https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx

[15] 85 Fed. Reg. 7316 (Feb. 7, 2020).

[16] U.S. Food & Drug Admin., *Letter from RADM Denise M. Hinton, Chief Scientist, to Robert R. Redfield, Director, Centers for Disease Control and Prevention* (Mar. 2, 2020). https://www.fda.gov/media/135763/download

[17] Joshua M. Sharfstein et al., *Diagnostic Testing for the Novel Coronavirus* JAMA 323(15), 1437 (2020). Under the Project Bioshield Act of 204, the FDA has broad discretion about which laboratory test can be used for the response during declared emergencies.

[18] ABC News, *EXCLUSIVE: Internal HHS investigation finds CDC's early test kits were 'contaminated'* (Jun. 19, 2020). https://abc3340.com/news/nation-world/exclusive-internal-hhs-investigation-finds-cdcs-early-test-kits-were-contaminated

[19] Jeffery Shuren & Timothy Stenzel, *Covid-19 Molecular Diagnostic Testing—Lessons Learned*, N Engl J Med 383:17 (2020).

some tests with performance problems.[20] According to FDA, 82 out of 125 EUA requests from the laboratories were identified with design or validation problems, and several were denied authorization.[21] Recognizing the potential safety risks, FDA did not apply this relaxed "test-first and EUA-later" policy to the COVID-19 tests developed by commercial manufacturers, and the first commercial COVID-19 test did not receive EUAs until mid-March 2020 due to a large backlog of EUAs.[22]

Timely access to accurate and reliable COVID-19 testing has proven to be central to effective public health measures during the pandemic. Evidence suggests that containment of COVID-19 may depend on early case detection and contact tracing.[23] For example, Taiwan has been able to limit COVID-19 spread to only a few hundred confirmed cases among its 24 million population through proactive testing and contact tracing.[24] In contrast, a testing delay as short as three days has shown to make the most efficient contact tracing strategy for COVID-19 ineffective.[25] The one-month delay in rolling out reliable COVID-19 testing at the onset of the

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[20] *See e.g.*, Laurie McGinley, *Dozens of coronavirus antibody tests on the market were never vetted by the FDA, leading to accuracy concerns*, Wash. Post, (Apr. 19, 2020) https://www.washingtonpost.com/health/2020/04/19/fda-antibody-tests-coronavirus-review/; Zachary Brennan & David Lim, *FDA pushed through scores of inaccurate antibody tests without agency review*, Politico (Apr. 27, 2020); https://www.politico.com/news/2020/04/27/reliable-antibody-tests-coronavirus-207589 (accessed on March 19, 2021); Thomas Burton, *FDA Sets Standards for Coronavirus Antibody Tests in Crackdown on Fraud*, Wall Street J, (May 4, 2020).. https://www.wsj.com/articles/fda-sets-standards-for-coronavirus-antibody-tests-in-crackdown-on-fraud-11588605373

[21] Shuren, *infra* note 19.

[22] U.S. Food & Drug Admin., *In Vitro Diagnostics EUAs*. https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas#individual-molecular

[23] Joel Hellewell et al., *Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts*. Lancet Glob Health. 2020; S2214-109X (20)30074-7 (2020).

[24] C. Jason Wang et al., *Response to COVID-19 in Taiwan*. JAMA 323(14): 1341 (2020).

[25] Mirjam E Kretzschmar et. al., *Impact of delays on effectiveness of contact tracing strategies for COVID-19: a modelling study*, The Lancet Public Health 5: e452 (2020).

pandemic hampered the country's ability to contain the spread of this highly contagious virus in the communities,[26] not to mention the dangers that faulty diagnostic tests can pose to patient care.[27]

In response to the public criticism for the slow rollout of COVID-19 tests, FDA carried out a "*postmortem*" analysis on the initial test shortage.[28] The lessons learned include, among others, "a common legislative framework is needed to ensure that all clinical tests are accurate and reliable."[29]

[26] *See* Michael Shear et al., *The Lost Month: How a Failure to Test Blinded the U.S. to Covid-19*, N.Y. Times (Mar. 28, 2020); https://www.nytimes.com/2020/03/28/us/testing-coronavirus-pandemic.html; James Glanz & Campbell Robertson, *Lockdown Delays Cost at Least 36,000 Lives, Data Show*, N.Y. Times (May 20, 2020). https://www.nytimes.com/2020/05/20/us/coronavirus-distancing-deaths.html
[27] Steven Woloshin et al., *False Negative Tests for SARS-CoV-2 Infection —Challenges and Implications*, N Engl J Med 383:6 (2020).
[28] Shuren, *supra* note 19.
[29] *Id.*

II. Current Regulatory Framework for IVDs

A. Unique Aspects of IVDs

One of the paradoxes of IVD regulations is that IVDs simply do not fit well into the existing medical device regulatory structure. Although IVDs are "devices" under FDCA,[30] they are in many ways distinct from traditional medical devices in terms of their product characteristics and regulatory nuances. On many occasions, FDA needed to craft creative regulatory approaches to adhere to the general medical device regulatory framework while regulating IVDs effectively.

First, unlike other medical devices IVDs do not have direct contact with the patient, so they cannot affect the structure or function of the body. Rather, IVDs are non-invasive tests performed on blood or tissue samples outside the human body, i.e., *in vitro*. Both the benefits and the risks of IVDs derive from the diagnostic information that they provide. For example, FDA has adopted two IVD-specific standards to evaluate whether an IVD meets the "reasonable safety and effectiveness" premarket requirement: (1) analytical validity, referring to how accurately and precisely a diagnostic measures its intended analyte; and (2) clinical validity, describing how well a diagnostic can characterize or predict a patient's health status.[31] In the IVD context, it is critical to assess both analytical and clinical validity because erroneous information provided by a diagnostic test may lead to harmful clinical decisions.[32]

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[30] FDCA § 201(h)(2), 21 U.S.C. § 321(h)(2). The definition of device in the FDCA includes "an . . . in vitro reagent . . . intended for use in the diagnosis of disease or other conditions . . ."

[31] U.S. Dep't Health & Hum. Servs., *Report of the Secretary's Advisory Committee on Genetics, Health, and Society, U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services*, 96-98 (Apr. 2008). https://osp.od.nih.gov/wp-content/uploads/2013/11/SACGHS_oversight_report.pdf

[32] U.S. Food & Drug Admin., *Risk of False Results with the Curative SARS-Cov-2 Test for COVID-19: FDA Safety Communication* (Jan. 4, 2021). https://www.fda.gov/medical-devices/safety-communications/risk-false-results-curative-sars-cov-2-test-covid-19-fda-safety-communication

Second, IVDs are technologically distinct from other medical devices. Most IVDs include not only software-controlled electronic equipment, but also biochemical materials, such as reagents, controls, and calibrators.[33] The technical expertise required to review and regulate IVDs is therefore different from that for other types of medical devices. This is evident that while most scientific reviewers in the Center of Devices and Radiological Health (CDRH) have engineering background, the Office of Health Technology 7 (OHT7: In Vitro Diagnostics and Radiological Health—OIR) are predominantly staffed with laboratorians, biochemists, molecular biologists, and microbiologists.[34] Accordingly, what constitutes "valid scientific evidence" to OHT7 reviewers may sound foreign to the scientific reviewers from the rest of CDRH since different terminology is used to convey that a clinical test is safe and effective. Further, IVD review heavily relies on the recognized consensus standards for test validation, specifically those promulgated by the Clinical and Laboratory Standard Institute (CLSI).[35]

Third, IVDs do not fit well in FDA's predominant regulatory pathway to market—premarket notification, or 510(k).[36] FDA classifies all medical devices including IVDs into class I, II or III based on the level of control necessary to provide "reasonable assurance of safety and effectiveness."[37] The applicable regulatory pathway is primarily determined by the risk associated with an IVD, as established by its classification. Most class II and a minority of class I devices

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[33] 21 C.F.R. § 809.3.
[34] U.S. Food & Drug Admin., *CDRH Management Directory by Organization*. https://www.fda.gov/about-fda/cdrh-offices/cdrh-management-directory-organization
[35] U.S. Food & Drug Admin., *Recognized Consensus Standards* https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/search.cfm
[36] Institute of Medicine (IOM), *Medical Devices and the Public's Health: The FDA 510(k) Clearance Process at 35 Year,* 4 (2011). In fiscal year 2020, FDA issued 2,259 510(k) clearances and 38 PMA approvals. Agenda for Quarterly Meeting on MDUFA IV (FY 2018-2020) Performance, 36, 127, (Mar. 17, 2021). https://www.fda.gov/media/146795/download
[37] FDCA § 513(a)(1), 21 U.S.C. § 360c(a)(1).

require 510(k) clearance, which requires a finding of "substantial equivalence" to another legally marketed device—a predicate.[38] The 510(k) process involves a comparison of a new device to a predicate rather than an independent demonstration of the new device's safety and effectiveness, as required for a class III device premarket approval (PMA).[39] This comparative review approach is intended to ensure controlled technological evolution of a broad range of moderate risk devices, as the newly cleared devices become the baseline for future comparison.[40]

In contrast, the use of predicate in IVD 510(k) clearance is curtailed due to the unique performance requirements of IVDs. As mentioned previously, an IVD's performance is measured by its analytical and clinical validity. The results obtained from different IVDs to measure the same substance must be equivalent and within clinical meaningful limits, i.e., the maximal allowed variability without affecting patient care.[41] Ideally, IVD performance is established by comparing with the "truth," which is typically a reference method or a harmonized test traceable to a reference method or reference materials.[42]

As a result, "paper predicate" are commonly used in IVD 510(k)s. A paper predicate is a predicate that has the same intended use as the new device, but it is not used for head-to-head performance comparison with the new device to establish its substantial equivalence to the

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[38] 21 C.F.R § 807 Subpart E.
[39] 21 C.F.R § 814.
[40] Accordingly, more recent predicates are generally preferred because FDA has expressed some concern about the use of older predicates in 510(k) clearance. FDA statement, *Statement from FDA Commissioner Scott Gottlieb, M.D. and Jeff Shuren, M.D., Director of the Center for Devices and Radiological Health, on transformative new steps to modernize FDA's 510(k) program to advance the review of the safety and effectiveness of medical devices* (Nov. 26, 2018). https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-jeff-shuren-md-director-center-devices-and.
[41] Miller et al., *Roadmap for harmonization of clinical laboratory measurement procedures.* Clin Chem 2011. 57: 1118-1126.
[42] American Ass'n for Clinical Chemistry, *Harmonization of Clinical Laboratory Test Results*, https://www.aacc.org/advocacy-and-outreach/position-statements/2018/harmonization-of-clinical-laboratory-test-results-update

predicate. Rather, the performance of a new device is directly compared to a well-established reference method. This alternative regulatory approach adheres 510(k) requirements while meeting the unique IVD regulatory needs. FDA achieved this rule tweak by issuing discretionary "special controls" guidance for Class II devices. The special control guidance permits a variety of measures in FDA's discretion, including but not limited to, performance standards, reference method and clinical data requirements.[43] Further, unlike other medical device 510(k)s, of which only a minority need to submit clinical data, many IVD 510(k)s include clinical data from perspective studies or studies that use leftover clinical samples or "banked" samples.[44]

Finally, the classification regulation for IVDs depends on the intended use[45] of an IVD at the "test system" level. Although there is no general statutory or regulatory definition of test system, analyte-specific test systems are typically classified and defined with a specific clinical indication for use in the regulation. For example, *Hemoglobin A1c Test System* is classified as class II and indicated as "an aid in the diagnosis of diabetes mellitus and as an aid in the identification of patients at risk for developing diabetes mellitus" under 21 C.F.R. §862.1373. But the spectrophotometer designed to use with this hemoglobin A1c test is classified as class I, and exempted from premarket review.[46] This apparent "deregulation" of IVD instrument, however, does not create a regulatory gap, because the test system performance cannot be evaluated alone

[43] On May 7, 2021, a total of 127 draft and final guidance documents are listed as Class II Special Controls Documents. https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/class-ii-special-controls-documents.
[44] U.S. Food & Drug Admin., *Guidance for Sponsors, Institutional Review Boards, and Food and Drug Administration Staff: Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable* (Apr. 25, 2006). https://www.fda.gov/media/122648/download.
[45] 21 C.F.R § 864.4020.
[46] *See, e.g.*, 21 C.F.R. § 862. 2300 Colorimeter, Photometer, Spectrophotometer For Clinical Use.

without the associated instrument. In fact, most IVD instruments undergo rigorous FDA premarket review with the associated tests.

In short, fitting IVDs into the medical device regulations has always been like trying to fit a square peg into a round hole.

B. Fragmented LDT Oversight under CLIA

While FDA has managed to fit IVDs into the medical device regulatory framework with a few rule tweaks, the fragmented LDT oversight is more problematic because it creates regulatory gaps and inconsistencies among diagnostic tests developed by manufacturers and clinical laboratories. The fragmented LDT regulatory framework is in part due to the federal regulatory gaps within CLIA.

CLIA defines a clinical laboratory as a facility that "examines materials collected from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of disease or for health assessment."[47] CLIA is administered by CMS in partnership with the states. Under CLIA, a clinical laboratory must hold one of five types of certificates, depending on the "complexity" of the testing performed by the laboratory (i.e., the difficulty of and level of training needed to correctly perform the test).[48] The goal of CLIA is to ensure that the laboratory can produce accurate, reliable, and timely test results. The regulations address the qualifications and training of laboratory personnel, recordkeeping, quality control processes, and proficiency testing. The CLIA regulatory framework places significant responsibility on the laboratory director to ensure that all phases of testing are properly performed.[49] By controlling the quality of laboratory

[47] 42 U.S.C. § 263a.
[48] 42 C.F.R. § 493.1773.
[49] 42 C.F.R. § 493.1445.

practices, CLIA standards are designed to ensure the analytical validity of the tests.[50] Clinical laboratories that do not comply with the CLIA regulations may be subject to sanctions, civil money penalties, civil lawsuits, imprisonment, or a criminal fine.[51]

As a statute primarily designed to regulate laboratory practices rather than test development, CLIA does not include any independent assessment of the clinical validity of the tests offered by the laboratory.[52] Many state policymakers point to this gap within CLIA as one of the main reasons for placing additional safeguard to oversight LDTs. Two states, New York and Washington, have replaced the CLIA certification requirements with their own state licensing regulatory regime. Clinical laboratories in these states are CLIA-exempt because CMS has determined that the state requirements are equal to or more stringent than the CLIA requirements, but laboratories must obtain the appropriate state license.[53] Several other states require state laboratory licensure in additional to CLIA certification.[54]

In addition, state licensing requirements may apply if a laboratory receives samples from and/or reports results to that state. For example, New York requires that all clinical laboratories accepting samples from and reporting results to New York state residents must hold a New York state permit.[55] New York also requires laboratories to obtain approval for all tests performed by the laboratory on samples originating from New York. Depending on the type of test (e.g., FDA-

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[50] *See* What is CMS' authority regarding Laboratory Developed Tests (LDTs) and how does it differ from FDA's authority? (Oct. 22, 2013) https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/LDT-and-CLIA_FAQs.pdf

[51] 42 C.F.R. § 493.1806.

[52] *See supra* note 50.

[53] N.Y. Pub. Health Law § 574; Wash. Rev. Code Ann. § 70.42.020.

[54] *E.g.*, Alabama (Ala. Admin. Code § 420-5-8); California (Cal. Bus. & Prof. Code § 1256(a)(1)); Georgia (Ga. Code Ann. § 31-22-20; Kentucky (Ky. Rev. Stat. Ann. § 333.030); Nevada (Nev. Rev. Stat. Ann. § 652.080); Rhode Island (R.I. Gen. Laws Ann. § 23-16.2).

[55] N.Y. Pub. Health Law § 574.

cleared or approved, CLIA-waived, LDT etc.), laboratories are generally required to submit both analytical and clinical validation data.[56] In general, the submitted data must be generated in the same laboratory from which a test will be offered.

Since CMS interprets CLIA's mandate to assure "the validity and reliability of the laboratory examinations"[57] as requiring laboratories to establish analytical validity, it has not acted to explicitly require laboratory practices to verify the clinical evidence underlying tests performed. While these state LDT regulations may fill this federal clinical validity gap, the level of LDT oversight is lacking, or at most inconsistent across states.

C. Fluid FDA Authority Over LDTs

Meanwhile, the current FDA LDT regulatory regime remains fluid. On one hand, FDCA grants the FDA authority to regulate IVDs as a subcategory of medical devices.[58] FDA has long taken the position that it has jurisdiction over LDTs. In a response denying a citizen petition submitted by the American Clinical Laboratory Association (ACLA) challenging FDA's regulation of LDTs, FDA stated that (1) the statutory definition of IVD includes LDTs; (2) laboratories performing LDTs are medical device manufacturers and do not fall within the "practice of medicine" exemption; (3) CMS and FDA have "concurrent, complementary jurisdiction" over laboratories that manufacture LDTs; and (4) FDA may issue enforcement policy for LDTs through guidance process, rather than through notice-and-comment rulemaking.[59] Some

[56] *See* N.Y. Dep't. of Health, Wadsworth Ctr., *Test Approval,* https://www.wadsworth.org/regulatory/clep/clinical-labs/obtain-permit/test-approval.
[57] 42 U.S.C. § 263a(f)(1)(A).
[58] 21 C.F.R. § 809.3(a).
[59] U.S. Food & Drug Admin., *Citizen Petition Denial Response*, Docket No. FDA-2013-P-0667-0008 (Jul. 31, 2014).

LDTs have already received approvals and clearances from FDA—meaning they must be medical devices (as these forms of marketing authorization are reserved for devices).[60]

On the other hand, nothing in the legislative history or the language in law suggests that Congress contemplated FDA would be overseeing clinical laboratories. FDA have yet formally promulgated the criteria for what constitutes an LDT. In fact, the term LDT was not even used by FDA in an official document until 2007.[61] The 2014 draft guidance defining LDT as "an IVD that is intended for clinical use and designed, manufactured, and used within a single laboratory" is never finalized.[62] In general, FDA exercises enforcement discretion not requiring LDTs to undergo premarket. Clinical laboratories traditionally have taken the position that the proprietary LDTs that they develop are "services" and not "products" and therefore are subject only to CMS regulation under CLIA.[63] Clinical laboratories pushed back when FDA decided to exercise its enforcement power, protesting that LDTs constitute practice of medicine rather than medical products subject to FDA review.[64] The same argument was used to criticize FDA's assertion of its authority over COVID-19 LDTs.[65]

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[60] In fiscal year 2020, FDA issued three LDT 510(k) clearances and nine LDT PMA approvals. Agenda for Quarterly Meeting on MDUFA IV (FY 2018-2020) Performance, 40, 129 (Mar. 17, 2021). https://www.fda.gov/media/146795/download.

[61] U.S. Food & Drug Admin., *Draft Guidance for Industry and Food and Drug Administration Staff: In Vitro Diagnostic Multivariate Index Assays*, 72 Fed. Reg. 41,081, 41,082 (Jul. 26, 2007).

[62] U.S. Food & Drug Admin., *Draft Guidance for Industry, Food and Drug Administration Staff, and Clinical Laboratories: Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)*, 5 (Oct. 3, 2014) https://www.fda.gov/media/89841/download

[63] 42 U.S.C. § 263a; *see also* Laboratory Requirements, 42 C.F.R. § 493 (regulations implementing CLIA).

[64] *See e.g.,* Paul D. Clement & Laurence H. Tribe, Am. Clinical Laboratory Ass'n, *Laboratory Testing Services, As the Practice Medicine, Cannot Be Regulated as Medical Devices* (2015). https://www.acla.com/wp-content/uploads/2015/01/Tribe-Clement-White-Paper-1-6-15.pdf

[65] *See* Evans BJ. & Clayton EW, *Deadly Delay: The FDA's Role in America's COVID-Testing Debacle*¸ 130 Yale L.J. Forum 78 (Jul. 29, 2020).

To further complicate this matter, HHS issued and later withdrew a directive on its website stating that FDA did not have the premarket review authority of LDTs "absent notice-and-comment rulemaking."[66] The directive was characterized as a "recession" of guidances and other "informal issuances" aimed at FDA's prior attempts to use guidance to provide a regulatory framework for LDTs. Although HHS later issued an FAQ document on its website further elaborating on the reason for and impact of the announcement[67], it is still unclear as to exactly how HHS interprets the applicability of FDCA to LDTs. Perhaps, HHS's rationale is that there is sufficient ambiguity as to exactly which LDTs are subject to the requirements of FDCA (i.e., which LDTs are devices), and under what circumstances, that rulemaking should be issued to offer a reasoned interpretation of the statute in lieu of the widespread application of enforcement discretion via informal guidance.

HHS was essentially encouraging FDA to engage in rulemaking perhaps to mitigate the risk of any foreseeable litigation. Since FDA's assertion of authority over LDTs has never been challenged in litigation, no court has evaluated the agency's informal interpretation of FDA's statutory authority over LDTs. Case law generally holds that *Chevron* deference does not apply to all agency interpretations of agency-administrated statutes.[68] Judicial deference may only be afforded to an agency's statutory interpretation promulgated via formal or notice-and-comment rulemaking. Further, if FDA engages notice-and-comment rulemaking, it can overrule court's

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[66] U.S. Dep't of Health & Human, Servs., *Recission of Guidance and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests* (Aug. 19, 2020) (withdrawn). https://www.hhs.gov/coronavirus/testing/recission-guidances-informal-issuances-premarket-review-lab-tests/index.html

[67] Cong. Research Servs., *HHS Announcement on FDA Premarket Review of Laboratory-Developed Tests (LDTs)* (Dec. 3, 2020). https://crsreports.congress.gov/product/pdf/IN/IN11548

[68] *See U.S. v. Mead Corp.*, 533 U.S. 218 (2001) (holding that *Chevron* deference did not apply to statutory interpretations adopted in the informal tariff classification ruling letters).

decision.[69]. But history suggests that it would be very challenging and time consuming for FDA to initiate rulemaking on LDT regulation.[70]

The HHS's "recission statement" itself amounts to non-binding informal guidance, and HHS itself is not bound by it. Even after the statement was removed from the HHS website, it may be challenging to issue a revised statement, because doing so would potentially require HHS and FDA to develop a more specific position on LDTs, which they were not able to do successfully for number of years. Thus, this HHS directive would create more Congressional interest in IVD legislative reform discussions.

[69] *See National Cable & Telecom Services Ass'n v. Brand X Internet Services*, 545 U.S. 967 (2005).
[70] *See supra* note 61. FDA failed several attempts to finalize LDT standards, and the latest attempt was the 2014 draft LDT guidance.

III. A Common Legislative Framework for IVCTs

A. A New Class of Medical Product — IVCT

The draft VALID Act directly addresses the issue that the medical device regulatory framework is not a good fit for clinical diagnostic tests. As mentioned previously, diagnostics differ greatly from conventional medical devices in terms of product characteristics, and this distinction should be reflected in the regulatory approach. To make a distinction between diagnostics and other types of medical devices, VALID created a new class of medical product within FDA's jurisdiction, which is defined as "*in vitro* clinical test" (IVCT). The term IVCT broadly includes all tests, both traditional IVDs and LDTs. Under VALID, an IVCT would mean

> "a test intended by its developer . . . to be used in collection, preparation, analysis, or in vitro clinical examination of specimens taken or derived from human body for the purpose of—
>
> (i) identifying or diagnosing a disease or condition;
>
> (ii) providing information for diagnosing, screening, measuring, detecting, predicting, prognosing, analyzing, or monitoring a disease or condition, including by making determination of an individual's state of health; or
>
> (iii) selecting, monitoring, or informing therapy or treatment for a disease or condition; and
>
> (B) may include—
>
> (i) a test protocol or laboratory protocol;
>
> (ii) an instrument [];
>
> (iii) article for taking or deriving, holding, or transporting specimens from the human body [];
>
> (iv) software, excluding software . . . ; and
>
> (v) [], a component or part of a test, a test protocol, an instrument, an article, or software . . . , whether alone or in combination, including reagent, calibrators, and controls."[71]

[71] VALID Act Section 2 Definitions (amending FDCA Definitions section 201).

IVCTs would be regulated separately from medical devices. But this new medical product class would remain under the authority of FDA's existing medical device review center, i.e., CDRH because FDA expressed the concern that a new review center would require significant financial resources that would be covered by the federal government funding and/or user fees.[72]

VALID would use a classification scheme similar to the existing three-tier risk classification used for medical devices, except that the bill only defined two risk categories: low risk and high risk. The risk description is tailored to IVCTs. It is based on (1) harm to the patient if the test produced an inaccurate result, (2) the likelihood of harm coming to a patient, (3) how well the technology is characterized, and (3) whether other confirmatory tests were involved in treatment decision making. Low-risk IVCTs are those that would likely cause minimal or no harm from inaccurate results, which would be exempted from premarket review. High-risk IVCTs are those that would likely cause serious or irreversible harm or death from an inaccurate result, which would require premarket review. A subcategory of high-risk IVCTs with "risk mitigation measures" would be eligible for the novel "technology certification" pathway.[73]

The elimination of moderate risk class signals the bill sponsors' and stakeholders' preference to move away from the controversial medical device 510(k) program.[74] While the premarket notification pathway (510(k)) was originally intended as a stopgap for regulating

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[72] U.S. Dep't. of Health & Human Servs., *Technical Assistance on VALID Act of 2018* (Apr. 2019), https://dx.advamed.org/sites/dx.advamed.org/files/resource/hhs-technical-assistance-fda_cdc_cms-feedback-on-valid-act-apr2019.pdf.

[73] *See infra* section III B Premarket Review Pathway and Technology Certification.

[74] U.S. Food & Drug Admin., *Guidance for Industry and Food and Drug Administration Staff: The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]*, (July 2014). https://www.fda.gov/media/82395/download

moderate risk devices,[75] the daisy-chain type "substantial equivalence" review standard is much criticized as a "regulatory loophole" exploited by device manufacturers.[76] As discussed in Section II A, this 510(k) pathway is less of a concern in the context of diagnostics because IVD manufactures are often required to independently demonstrate analytical and clinical validity against the "truth," i.e. reference methods or standards.[77] IVCT seem to be an ideal candidate for Congress to experiment whether it can wean FDA from its dependence on the 510(k) program.

Finally, VALID introduced a category of IVCTs as first-of-a-kind (FOAK). FOAK is an IVCT with both a different intended use and indications for use than any legally marketed IVCT. FOAK IVCTs are presumed to be high risk and not eligible for abbreviated form of review (special premarket review) or technology certification. Although FDA could redesignate FOAK IVCTs as low risk IVCTs, the redesignation would only take place after the review has occurred.

In summary, the proposed common regulatory framework establishes a one-size-fits-all, risk-based approach that is tailor fit to oversight all IVCTs. This means that a single premarket review standard would apply to all tests, regardless of where the test is designed, developed, manufactured, or offered. Diagnostic regulators would no longer need to resort to creative rule tweaking to fit IVCTs into medical device regulations.

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[75] The Medical Device Amendment of 1976 mandated that FDA would review all existing types of medical devices by regulation place them in Class I, II, or III. Class II devices would be subject to FDA-established performance standards plus genera postmarket controls. It took FDA 14 years to complete classification, and few performance standards have been issued. *See* 90 Sat. at 540-552, *See e.g.*, 21 C.F.R. § 1000.

[76] *See e.g.,* B. Goldberg, *The Evolution of Substantial Equivalence in FDA's Premarket Review of Medical Devices*, 56 Food & Drug L.J. 317, 318, 330 (2001); M. Van Buren, *Closing the Loopholes in the Regulation of Medical Devices: The Need for Congress to Reevalute Medical Device Regulation*, 17 Health Matrix 441, 460 (2007); J. Bauman, *The "Déjà vu Effect," Evaluation of United State Medical Device Legislation, Regulation, and the Food and Drug Administration's Contentious 510(k) Program,* 67 Food & Drug L.J. 337, 360-61(2012).

[77] *See supra* section II A.

B. Premarket Review Pathways and Technology Certification

FDA forecasted under the proposed common IVCT regulatory framework that less than ten percent of the tests would require premarket review.[78] The sponsors of VALD seemed to have foreseen that the expansion of the field of genetic test and laboratory medicine would require a flexible system to accommodate the tens of thousands of tests without overburdening FDA and test developers by requiring premarket review for all new and existing tests. [79]

VALID would exempt a few categories of IVCTs from FDA review, such as grandfathered tests, low-risk tests, tests for rare diseases, tests used for public health surveillance programs, forensic tests, and tests used for law enforcement and employer testing that are not used to make clinical decisions for individual patients. In addition, VALD added that IVCTs to be developed and used under an emergency use authorization during public health crisis.

VALID established several risk-based IVCT pre-market review pathways to balance the needs for innovation and timely access. High risk tests, such as FOAK tests, would be required to undergo full premarket review to verify their analytical and clinical validity. Many components and parts, such as test instruments and software, would receive abbreviated form of review—special premarket review—depending on the type of component or part.

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[78] U.S. Food & Drug Admin., *Speech by Scott Gottlieb, M.D., Commissioner of Food and Drugs-Food and Drug Administration: Blueprint for Breakthroughs - Charting the Course for Precision Medicine,* (Sep.13, 2018). https://www.fda.gov/news-events/speeches-fda-officials/blueprint-breakthroughs-charting-course-precision-medicine-09132018-0.

[79] As of March 2018, there were almost 75,000 genetic tests alone on the market in the United States, which an average of 14 being added each day. *See The Current Landscape of Genetic Testing: Market Growth, Reimbursement Trends, Challenges and Opportunities,* Concert Genetics (Apr. 2018). http://www.concertgenetics.com/wp-content/uploads/2018/04/12_ConcertGenetics_CurrentLandscapeOfGeneticTesting2018.pdf.

Most significantly, to protect test developers' ability to modify tests rapidly and act nimbly to meet patient needs, VALID introduced a new alternative pathway to premarket review: technology certification. This pathway introduced the novel concept of "test groups," which are categorized primarily according to their indications for use and technology. Eligible IVCT developers could choose to apply for the optional technology certification through FDA in lieu of premarket review for certain eligible tests. To obtain a technology certification, the IVCT developer is required to submit a representative test from the test group to FDA for review. If approved, all other tests within the scope technology certification would market without additional FDA premarket review. The certification would be valid for four years. To renew, the certificate holder would be required to submit a different presentative test from the test group for FDA review.

To be eligible for technology certification, the developer must be in good standing, and the IVCT cannot be an instrument, component, specimen receptacle, a reagent used in blood or tissue banking, or a FOAK, home use, high risk, cross-referenced or direct-to-consumer (DTC) IVCT. Most of the technology certification exclusion are categorical in nature, i.e., not risk based, except for high risk IVCTs. For high risk IVCTs, VALID authorized the FDA to establish "mitigating measures" that would render an otherwise high-risk test eligible for technology certification. Mitigating measures are evidence-based requirements that are "necessary for IVCT to meet applicable standard, or to mitigate risk of harm ensuing from an inaccurate result or misinterpretation of any result. They would include "labeling, advertising performance standards, performance testing, clinical studies, submission of clinical data, user comprehension studies, postmarket studies, training, and conformance to standards."

Further, VALID also included a breakthrough pathway to incentivize test development for patients with unmet medical needs. This pathway is nearly identical to FDA's current device

breakthrough pathway for "more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions compared to existing alternatives."[80]

C. Grandfather and Transition Policies

Grandfathering is a critical feature of VALID, because it would exempt all previously marketed tests from premarket review, including LDTs. This provision is designed to accommodate the needs of LDT developers to protect patient access to currently available laboratory tests.[81] Grandfathered tests must have been developed by a laboratory with a high complexity CLIA certificate and be used at the same laboratory in which they were developed. All LDTs marketed 90 days prior to enactment of the VALID Act would be grandfathered into the new system and would be exempted from premarket review. However, the intended use, analytical or performance specifications or risk level had changed, the LDT would need to be reviewed by FDA. In addition, if the LDT is high risk and was not already approved by the New York State Department of Health for use, then laboratories would need to submit evidence for the test's analytical and clinical validity to FDA within five years.

The narrow definition of a grandfathered test means there will be tests on the market that will not qualify for grandfathered status. Those "transitional IVCTs" include qualifying LDTs first offered after enactment of the Act but before its effective date. Transitional IVCTs may continue to be offered after the effective date so long as a marketing submission is made within 90 days after the effective date. The FDA would retain the authority to enforce the device provisions of the

[80] U.S. Food & Drug Admin., *Guidance for Industry and Food and Drug Administration Staff, Breakthrough Devices Program* (Dec.18, 2018). https://www.fda.gov/media/108135/download.
[81] *See* American Clinical Lab. Ass'n, *ACLA Statement on the VALID Act of 2020* (Mar. 5, 2020). https://www.acla.com/acla-statement-on-the-valid-act-of-2020/.

FDCA and the Public Health Service Act for any transitional IVCTs as necessary to protect the public health.

IV. Proposed Enhancements to VALID Act

VALID caters the unique needs of *in vitro* diagnostic tests, unifies regulation of all tests, and grants FDA the clear authority to set risk-based review requirements for all tests, including those tests developed and used in clinical laboratories. This proposed legislation would promote and protect the public health by establishing consistent regulatory standards for test developers. To secure these public health benefits, I recommend enhancements to refine three aspects of VALID.

A. Address Duplicative CLIA Requirements

While the main goal of VALID is to establish a uniform federal regulatory framework for diagnostics by closing the LDT regulatory gap in CLIA, VALID solidified FDA's authority over LDTs but without removing the burden from CMS's oversight under CLIA—VALID does not include a section to modernize or harmonize CLIA with the amended FDCA. This is a major concern for the clinical laboratory communities, because the new LDT regulatory oversight mandated by VALID may duplicate the current CLIA's requirements.[82] The laboratory stakeholders' concern of duplicative regulation is leveraged by another proposed legislation—VITAL.[83] VITAL sought to remove LDTs from the definition of device in FDCA and from FDA's jurisdiction altogether. Under VITAL, the regulatory oversight would be solely through CMS or through a nongovernmental third party under CLIA. Interestingly, VITAL required laboratories to submit test's information, which would include the purpose of the test, the intended use of the test, test methodology, and analytical and clinical validity information. Any significant modification that would alter the methodology or clinical validity would require an amendment to the

[82] *See supra* note 81.
[83] *See supra* note 7.

submission. Although this proposed regulatory scheme is not pragmatic because it would require CMS to take on the scientific review of all LDTs—a task is neither within the scope of CMS nor its expertise, VITAL made a compelling argument that any oversight approach should be least burdensome without duplicative requirements.

Congress should include a provision in VALID to directly address this concern by eliminating the overlapping requirements in CLIA. FDA's existing regulations on quality system requirements[84] and adverse event reporting[85] overlap with CLIA certification criteria, which controls the quality of laboratory practices to ensure analytical validity of tests performed.[86] Similar duplicative requirements would occur at the state level after VALID enactment, such as those required by the New York State Department of Health. The bill sponsors should consider a practical and reasonable approach to eliminate areas of duplication. For example, the previous reiteration of VALID—the Diagnostic Accuracy and Innovation Act (DAIA) of 2018—includes a separate section that would have updated the CLIA statute and initiated modernization of the CLIA regulations to account for the new authority that FDA would be granted. [87] Specifically, DIDA would have amended CLIA to limit the authority of CMS to exclusively regulate laboratory operations: (1) modernize applicable quality requirements; (2) harmonized FDA and CLIA quality terminology; (3) eliminate requirements related to test development, which would have been regulated exclusively by FDA.

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[84] 21 C.F.R.§ 820.
[85] 21 C.F.R.§ 803.
[86] *See supra* note 50.
[87] *See* Personalized Medicine Coalition, *The Diagnostic Accuracy and Innovation Act: Advancing innovation and safety for patient in diagnostics.* http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/DAIA_Summary.pdf

Further, VALID would update FDCA to eliminate redundant requirements covered under CLIA, the fear remains that FDA would not revise the current medical device regulations to the extent to effectively eliminate duplication with CLIA. History has shown unilateral efforts from one of the coordinating agencies without statutory amendment may not achieve the desired results. For example, FDA took over the responsibility of the Center for Disease Control and Prevention (CDC) in 2000 to categorize IVDs per CLIA level of complexity.[88] CLIA has three levels of IVDs: waived tests, moderate complexity tests, and high complexity tests.[89] To be categorized as a CLIA waived test, a test must meet both FDA's premarket review and CLIA waiver requirements. Despite FDA's efforts to reduce the regulatory burden to meet patient needs[90] (e.g., establishing the dual 510(k) and CLIA waiver by application pathway[91]), IVD manufacturers are required to meet both FDCA and CLIA statutory requirements. As a result, the number of CLIA waivered tests remains low comparing to its non-waived peers.[92]

B. Build in Flexibility and Agility to the Common Regulatory Framework

VALID aims to design a regulatory system flexible and agile enough to evolve along with rapid advances in technology. The key component of VALID is to establish risk-based oversight because an effective and efficient regulatory scheme must balance the need to protect public health and the need to promote innovation. While VALID proposed technology certification as an

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[88] 64 FR 73561 (Dec. 30, 1999); *See also* 69 FR 22849 (Apr. 27, 2004). In limited circumstances, FDA may choose to consult with the Center for Disease Control and Prevention concerning test categorization. 42 C.F.R. § 493.17(c).
[89] 42 C.F.R. § 493.5(a).
[90] As of March 2020, 75% of all CLIA certified laboratories in the United States are CLIA waived. U.S. Ctr. for Medicare & Medicaid Serv., CLIA Statistical Tables/Graphs, *Percent of CLIA Laboratories By Certificate Type*. https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/statcer.pdf.
[91] U.S. Food & Drug Admin., *Guidance for Industry and Food and Drug Administration Staff: Recommendations for Dual 510(k) and CLIA Waiver by Application Studies* (Feb. 26, 2020). https://www.fda.gov/media/109574/download
[92] In fiscal year 2019, FDA issued 13 CLIA waivers. FY2019 Performance Report to Congress for the Medical Device User Fee Amendment, 13 (Sep. 30, 2019). https://www.fda.gov/media/139848/download

alternative, least burdensome pathway to make efficient use of FDA resources, it categorically excludes certain types of tests not based on product characteristics rather than risk. This approach deviates from FDA's well-established risk-based oversight guiding principles. FDA has recognized the important of risk assessment in premarket review process.[93] As described in the FDA's *Benefit-Risk Guidance*, a reasonable assurance of safety occurs when "it can be determined, based upon valid scientific evidence, that the probable benefits . . . outweigh any probable risks," and can be demonstrated by establishing "the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use."[94]

Use of risk-based approach should apply for all IVCTs, regardless of product categories. For example, VALID categorically excludes FOAK IVCTs from exemption, special premarket review and technology certification. Although FOAK IVCTs can eventually be "redesignated," the redesignation would not take place until after the full premarket review has completed. As an industry dedicated to innovation, new diagnostics frequently emerge as technology rapidly advances. As a practical matter, many FOAK IVCTs will be low risk or otherwise not high risk (i.e., low risk with mitigation measures), yet under VALID they would all essentially be treated as high risk.

Under the current IVD regulatory system, the highly successful *de novo* process allows a novel, non-Class III (i.e., low or moderate risk) test to be properly classified and reviewed in

[93] U.S. Food & Drug Admin. *Guidance for Industry and FDA Staff: Factors to Consider when Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications* (Aug. 30, 2019).(Benefit-Risk Guidance) https://www.fda.gov/media/99769/download

[94] *Id.* at 6 footnote 1 (citing 21 C.F.R. § 860.7(d)(1)).

tandem.[95] VALID contains no such mechanism. Congress should consider a similar pathway to allow a test developer to obtain a determination that the IVCT is low risk or otherwise not high risk (i.e., low risk with mitigation measures), at the onset of the review process. In addition, VALID should give power to developers to appeal FDA's risk classification decision, if developer disagrees with the agency.

C. Strengthen Postmarket Powers

VALID proposed a risk-based flexible regulatory framework, which would enable FDA to conduct an agile oversight for large numbers of IVCTs on the market. Since most new diagnostic tests (90% by FDA's estimate)[96] would not be reviewed by FDA, the burden of ensuring safety and effectiveness of IVCTs would shift from premarket to postmarket settings for nearly all tests. This approach only works if FDA has effective postmarket surveillance tools and adequate authorities to detect and respond safety concerns after products enter the market. In this regard VALID needs to make two important changes.

First, legislator should remove restrictions on the important postmarket tool in VALID, the Special Rule. This rule would allow FDA to act quickly when it becomes aware of a test that may pose public health risk. VALID places the burden on the agency demonstrate that there is insufficient scientific evidence to support the validity of the test, and that the test being offered with deceptive or fraudulent claims or is reasonably likely to cause serious patient harm. These requirements are inconsistent with the current agency's postmarket enforcement tools for other

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[95] U.S. Food & Drug Admin., *Guidance for Industry and Food and Drug Administration Staff, De Novo Classification Process (Evaluation of Automatic Class III Designation)* (Oct. 30, 2017). https://www.fda.gov/media/72674/download

[96] *See supra* note 78.

medical products and would place an unnecessary evidentiary burden on the agency to exercise its authority.

Second, Congress should preserve the existing mandatory adverse event reporting requirements. Under the current IVD regulations, there are three mandatory reporter categories: manufacturers, importers, and device user facilities. There is a long-standing mandate that doctors, nurses, and other healthcare providers must report cases of test-related patient harm to FDA because they are listed under the "device user facilities." VALID only listed test developers as mandatory reporters, and they are only required to report adverse events when they are not due to laboratory errors under purview of CLIA. While this change may be an attempt to eliminate confusing and costly jurisdiction overlap between FDA and CMS, [97] the unintended consequence may hamper FDA's ability to detect signals of a potentially faulty test. Reports from healthcare providers regarding harm caused by inaccurate or misleading test results are an essential source of information about the real-world performance of IVCTs.

[97] *See supra* Section II B.

CONCLUSION

The public and private sectors have been working together to tackle the IVD regulatory oversight problem for many years. A comprehensive legislative reform seeking to modernize diagnostics oversight to prevent testing crises and shortages during the public health emergencies as well as during non-emergencies should consider the views of various diagnostic stakeholders: IVD manufacturers, LDT developers, academic pathologists, reference laboratories, commercial laboratories, healthcare providers, regulators, and patients. The common diagnostics regulatory scheme proposed in the draft bill of VALID Act has received a bipartisan support in both the House and the Senate, and it contains the necessary components of a pragmatic oversight aimed at promoting innovation, improving patient and public health. As the bill continues to develop and refine, the stakeholders would find common ground and a reasonable and practical approach to regulator all *in vitro* clinical tests on the market.