ACMG
American College of Medical Genetics and Genomics
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November 30, 2023

Robert M. Califf, M.D.
Commissioner, U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: FDA Proposed Rule – Medical Devices; Laboratory Developed Tests (Docket No. FDA–2023–N–2177)

Dear Commissioner Califf:

The American College of Medical Genetics and Genomics (ACMG)[1] appreciates the opportunity to provide feedback on the FDA proposed rule for Medical Devices; Laboratory Developed Tests (Docket No. FDA–2023–N–2177). The ACMG is deeply concerned about the impact the proposed rule would have on development of and access to clinical testing if implemented in its current form. Further, we raise issue with the lack of evidence provided by the Agency to support the need for the proposed rule.

As a medical association representing medical genetics healthcare professionals throughout the United States, including those relying on clinical testing to diagnose, treat, and manage patients, **we ask that FDA abandon this proposed rule and continue to work with Congress and all stakeholders to identify true regulatory gaps and develop solutions that support patient access to innovative, timely, and high-quality testing.** Laboratory developed tests (LDTs) are clinical procedures provided by highly trained, board-certified healthcare professionals. They are not finished goods introduced into

[1] Founded in 1991, the American College of Medical Genetics and Genomics (ACMG) is a prominent authority in the field of medical genetics and genomics and the only nationally recognized medical professional organization solely dedicated to improving health through the practice of medical genetics and genomics. The only medical specialty society in the US that represents the full spectrum of medical genetics disciplines in a single organization, the ACMG provides education, resources and a voice for more than 2,600 clinical and laboratory geneticists, genetic counselors and other healthcare professionals. ACMG's mission is to improve health through the clinical and laboratory practice of medical genetics as well as through advocacy, education and clinical research, and to guide the safe and effective integration of genetics and genomics into all of medicine and healthcare, resulting in improved personal and public health.

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interstate commerce as are the devices, including in vitro diagnostics (IVDs), that FDA traditionally regulates. The regulations set forth under the 1976 Medical Device Amendments are not designed for clinical procedures, and trying to force such services through this pathway will significantly disrupt, and ultimately harm, critical clinical testing services in the US.

Through several public statements and presentations over the past couple of years, the FDA has made it very clear that it supports the need for a legislative approach to address this issue and to develop a diagnostic-focused framework. Further, even if rulemaking is finalized, the FDA does not have the staffing capacity to implement such a large volume of new premarket reviews. This was clearly demonstrated during the first year of the COVID-19 pandemic when FDA could not handle the volume of Emergency Use Authorizations (EUAs) it received and had to continually adjust its policies regarding which EUAs it would or would not review. The FDA estimates that approximately 50% of LDTs would require premarket review, although they also acknowledge in the proposed rule that they won't know the real estimate until they enforce registration and listing requirements. A recent report described a registry of over 175,000 genetic tests in clinical use, the majority of which are LDTs.[2] Thus, 50% of genetic tests alone would be a staggering number of reviews that far exceeds the total volume of COVID-19 EUAs received by the FDA. A legislative solution will be needed regardless. Therefore, it is unclear why resources would be spent finalizing a rule that is likely to face significant implementation hurdles and ultimately highlights the need for a legislative solution. Resources could be better utilized by working with clinical testing laboratory professionals to identify solutions that support, rather than hinder, clinical testing in the US.

Even where a legitimate regulatory need may be identified, solutions must be considered within the full scope of the testing landscape. The Institute of Medicine (IOM; now the National Academy of Medicine) identified six domains that must be considered for healthcare systems: safe, effective, patient-centered, timely, efficient, and equitable. In exploring improvements to regulation of clinical testing, policymakers must also consider these domains. Proposals, such as the current FDA proposed rule, do not consider all six pillars and risk patient care through unintended effects. The current FDA proposed rule narrowly focuses on safe and effective procedures with no consideration given to the other four pillars. Patient-centered, timely, efficient, and equitable procedures are best served by practitioners, licensed by law to administer the right test, for the right patient, at the right time. The focus must be placed on policies that improve healthcare and drive innovation.

FDA's Proposal to Regulate Clinical Testing as Devices

As written, the proposed rule lays out FDA's intentions to regulate LDTs as medical devices and treat highly trained, board-certified medical laboratory professionals as manufacturers. If implemented, the FDA's proposed rule would impose significant regulatory and financial burdens on clinical testing laboratories that would simply be unsustainable for many. The

[2] Concert Genetics, "Genetic Test Price Transparency Report." 2023. Available at http://www.concertgenetics.com/wp-content/uploads/2023/11/Concert-Genetics-2023-Genetic-Test-Price-Transparency-Report-07Nov2023.pdf

medical device pathway would be cost-prohibitive for laboratories that rely on medical reimbursements, an already strained financial setting made worse with implementation of the Protecting Access to Medicare Act (PAMA).

This is in stark comparison to the true test kit manufacturers that FDA currently regulates who distribute, market, and sell IVD products. The financial strain of the medical device pathway would result in many clinical testing laboratories significantly reducing test offerings or may result in laboratory closures. This would lead to consolidation of testing to a smaller number of large laboratories that could financially handle the costs associated with this proposed rule. Most clinical testing laboratories and their institutions do not have the cost advantages that larger commercial entities ('manufacturers') can reap, i.e., the economies of scale cost advantages when production becomes efficient, and costs are distributed over larger volumes of goods. This is not a phenomenon limited to medical laboratory procedures. In fact, the Biden-Harris Economic Blueprint outlines that "Corporate consolidation squeezed small businesses and entrepreneurs, raised costs for consumers and lowered wages for workers, while exacerbating supply chain challenges that imposed billions of dollars of costs when the economy was hit by global economic and public health shocks."[3] The FDA proposed rule could provide an innovation and cost advantage to these organizations, which if uncontrolled could create a (near) monopoly of LDT providers, further limiting the availability of equitable genomics informed healthcare.

Further, given a competitive advantage with rule implementation, those laboratories would likely change their test offerings to maximize return on investment; low-volume, high complexity tests with high labor costs would be significantly altered or discontinued. This is especially concerning for rare diseases or other specialty tests that, although low volume, fill critical patient needs.

This will also significantly impact newborn screening, one of the most successful public health programs in the country. Most newborn screening tests are LDTs, and the proposed rule makes no exceptions for public health laboratories. While the screening tests are used on almost every baby born in the US, the tests used for diagnostic testing following a screen-positive result are much lower in volume. As described above, such low-volume tests could potentially disappear altogether which would significantly diminish the success of newborn screening. The FDA must address how they will ensure that such tests remain on the market and how they will implement a framework that is realistically feasible for clinical testing laboratories, especially those at academic medical centers.

Clinical testing laboratories serve patients by researching, developing, and refining clinical tests to meet a wide variety of clinical needs. Outsourcing clinical testing often means slower turn-around times and less opportunities for customization to meet unique patient needs (a cornerstone of precision medicine), such as rapid validation for a different specimen (e.g.,

[3] Biden-Harris Economic Blueprint, September 2022. Available at https://www.whitehouse.gov/wp-content/uploads/2022/09/Biden-Economic-Blueprint-Report-720PM-MASTER-DOC.pdf

blood) when the typical specimen type (e.g., tissue) is not an option. The proposed rule provides no flexibility for customized patient needs and would require FDA review for any such modifications. This would result in significant delays in testing for patients and add exorbitant and unnecessary costs for such testing. The FDA must address how they will avoid causing harmful disruptions in access to clinical testing for all patients, including those with rare diseases, which collectively affect an estimated 30 million people in the United States.[4]

The proposed rule also does not include any exemptions for tests currently used in the clinical setting. This means that, if implemented, laboratories would be forced to remove current clinical tests from their offerings until they submit their applications to the FDA and pursue the lengthy and costly process of FDA review and approval. In many cases, LDTs are used because there is no FDA-approved IVD equivalent. Removal of such LDTs from the market would result in a complete loss of testing capabilities in the United States for certain conditions. Even if temporary, this gap would be devastating for patient care and physicians' ability to make clinical care recommendations.

Should a test go through the FDA premarket review as currently written, modifications would require a new FDA review and delay implementation of up-to-date, timely test innovation. Instead, costly and time-consuming FDA reviews of each test modification would stymie innovation and be counterproductive to precision medicine. The proposed rule makes no effort to work within the clinical testing framework, including existing laboratory regulations such as the Clinical Laboratory Improvement Amendments (CLIA), to support an approach that fosters timely patient access to high-quality, innovative clinical testing, which is counter to the FDA's prior suggestions to implement focused oversight.[5] The proposed rule does acknowledge concerns about innovation delays and attempts to justify the concerns by pointing to flexibility in the device review pathway. The FDA estimates that approximately 50% of LDTs would require some form of premarket review, although in the proposed rule the Agency also acknowledges that it does not actually know the scope of LDTs currently in use. They also note that most tests would only require a new review for significant changes or modifications to design, components, method of manufacture, or intended use. However, it is not clear what changes, including common updates to LDTs, would be considered significant in this context. Regardless, this is an effort to force clinical testing procedures through a review process designed for an entirely different type of product.

FDA Rationale

Section III.B. of the proposed rule describes FDA's view of why the rule is needed. We are concerned that the perceived problems with clinical laboratory testing have not been clearly identified and are not supported by solid evidence. In the proposed rule, the rationale – which is acknowledged in the rule – relies on mostly anecdotal information. References for the section

[4] Rare Diseases: Although Limited, Available Evidence Suggests Medical and Other Costs Can Be Substantial (GAO-22-104235). US Government Accountability Office, Report to Congressional Committees. October 2021. Available at https://www.gao.gov/assets/gao-22-104235.pdf.

[5] Discussion Paper on Laboratory Developed Tests (LDTs). US Food and Drug Administration. January 13, 2017. Available at https://www.fda.gov/media/102367/download.

on “Need for the Rule” contain scant reliance on peer-reviewed evidence. Instead, the FDA relies heavily on news stories and reports from private industry groups that have not been reviewed for bias. Notably, the FDA chose to omit studies demonstrating the high accuracy of traditional LDTs which are used to support diagnostic decision-making.

For example, the FDA often points to a 2022 New York Times (NYT) article on cell-free DNA prenatal screening (referred to in the proposed rule as noninvasive prenatal screening).[6] The NYT article was deeply flawed and a prime example of why news reports cannot and should not substitute for scientific evidence.[7,8] At its core, the article mischaracterizes screening tests as if they were for use in diagnosis. All tests, including those approved by FDA, will inherently result in some false positives (FPs) and false negatives (FNs). The confusion between a screening assay and diagnostic tests is dramatic as the acceptable FP and FN rates differ substantially. The very nature of screening tests is that they are designed to be highly sensitive to ensure affected individuals are not missed; they are expected to have a much lower FN rate than might be accepted for a diagnostic test. Because screening tests are designed to prioritize sensitivity, they often have a higher FP rate than would be accepted for a diagnostic test. Follow-up diagnostic testing should always be used following a positive screening result. No clinical decisions should be made based solely on a screening test result – a note often indicated on the clinical reports for screening test results and explained when proper pre-test counseling is provided. The NYT article recounts instances in which clinical decisions were inappropriately made based on a screening result but incorrectly attributes the issue to test performance. Moreover, medical decision-making based on a test result, whether it be a screening or diagnostic test, is outside of the FDA’s scope and would not be managed by FDA premarket review of screening tests. Such issues relate to the practice of medicine and must be addressed through training and continuing education of healthcare professionals and incorporation of genetics professionals on healthcare teams.[9]

The FDA then goes on to reference another news article about incorrect genetic variant interpretations related to a cardiac condition.[10] Even if we ignore the fact that this is a news article, the fundamental issue still relates to professional interpretation challenges, not an issue with test performance. The professional interpretation of genetic variants is the practice of medicine and outside the scope of FDA. This is one example of several reports referenced in this section that highlight the challenges of professional interpretation rather than issues with test

[6] Kliff, S., Bhatia, A. “Tests Predicting Rare Disorders in Fetuses Are Usually Wrong”, *The New York Times*, January 1, 2022. Available at https://www.nytimes.com/2022/01/01/upshot/pregnancy-birth-genetic-testing.html.
[7] Klugman, S. Letter to the Editor “Noninvasive Prenatal Tests Are for Screening, Not Diagnosis”, *The New York Times*, January 2, 2022. Available at https://www.nytimes.com/2022/01/08/opinion/letters/prenatal-genetic-tests.html.
[8] ACMG Responds to The New York Times article regarding Noninvasive Prenatal Screening, “Tests Predicting Rare Disorders in Fetuses are Usually Wrong”, Press Release, January 2, 2022. Available at https://www.acmg.net/PDFLibrary/2022_ACMG_Response_NYT_NIPS.pdf.
[9] Liehr T, Harutyunyan T, Williams H, Weise A. Non-Invasive Prenatal Testing in Germany. Diagnostics (Basel). 2022 Nov 16;12(11):2816. doi: 10.3390/diagnostics12112816. PMID: 36428876; PMCID: PMC9689121.
[10] Begley, S., “Genetic Testing Fumbles, Revealing ‘Dark Side’ of Precision Medicine,” *STAT*, October 31, 2016. Available at https://www.statnews.com/2016/10/31/genetic-testingprecision-medicine/.

performance. Interpretive information about genetic findings is rapidly evolving and changing as more evidence is gathered. Clinical decisions are not made on a single test result alone. Rather, the test result, including interpretation of the pathogenicity of a variant, must be considered in light of other clinical findings. This diagnosis, based on a combination of factors, is the practice of medicine.

Next, the FDA relies on their 2015 report of 20 case studies involving LDTs as evidence that LDTs are inaccurate, unsafe, ineffective, or poor quality.[11] The FDA omits the follow-up investigations reported by the Association of Molecular Pathology (AMP) that same year which examined each of these cases.[12] The AMP investigations corrected inaccurate information and provided critical context omitted from the FDA report. For example, the FDA report highlights outlier tests that were never offered, for which the FDA-approved equivalents perform poorly, or for which inappropriate clinical decision-making was used. The AMP investigation concluded that most cases were either irrelevant because there was no patient harm or would not have had a different outcome with the addition of FDA review.

Amid the anecdotal information and news reports, the FDA does reference a few articles (research-based and commentaries) published in peer-reviewed scientific journals. One of the referenced studies, the Sustainable Predictive Oncology Therapeutics and Diagnostics quality assurance pilot study (SPOT/Dx pilot), reported sending the same samples to 19 laboratories for *KRAS* and *NRAS* variant testing using their own manufactured test and found that 7 of those laboratories correctly reported all results.[13] However, the SPOT/Dx pilot study methods differed from proficiency testing programs used to demonstrate laboratory accuracy in detection rates and included instructions that led to laboratories not performing their tests as intended based on their validations. A reanalysis of the SPOT/Dx pilot data using proficiency testing methods found high accuracy in detection rates and concluded that the findings of the original study were not generalizable.[14] This is just one example in which reports were selected to fit a desired narrative rather than providing an accurate, fully informed view of a perceived issue. The FDA continues on throughout this section with references to news articles and other anecdotal information as well as references to issues where professional interpretation of test results (the practice of medicine), not test performance itself, was the issue.

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[11] FDA, "The Public Health Evidence for FDA Oversight of Laboratory Developed Tests: 20 Case Studies," November 16, 2015, available at http://web.archive.org/web/20151122235012/https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM472777.pdf.

[12] Association for Molecular Pathology. Facts FDA ignored: An analysis of the FDA report, "The public health evidence for FDA oversight of laboratory developed tests: 20 case studies". December 13, 2015. Available at https://www.amp.org/AMP/assets/File/position-statements/2015/AMPResponseFDACaseReportFinal.pdf?pass=58.

[13] Pfeifer, J.D., R. Loberg, C. Lofton-Day, et al., "Reference Samples To Compare Next-Generation Sequencing Test Performance for Oncology Therapeutics and Diagnostics," *American Journal of Clinical Pathology*, 157(4):628-638, 2022. Available at https://doi.org/10.1093/ajcp/aqab164.

[14] Zehir A, Nardi V, Konnick EQ, Lockwood CM, Long TA, Sidiropoulos N, Souers RJ, Vasalos P, Lindeman NI, Moncur JT. SPOT/Dx Pilot Reanalysis and College of American Pathologists Proficiency Testing for KRAS and NRAS Demonstrate Excellent Laboratory Performance. *Arch Pathol Lab Med*. 2023 Sep 30. doi: 10.5858/arpa.2023-0322-CP. Epub ahead of print. PMID: 37776255. Available at https://pubmed.ncbi.nlm.nih.gov/37776255/.

The FDA's website notes that the Agency "is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA also provides accurate, science-based health information to the public."[15]. However, the proposed rule relies largely on reports narrow in scope, or even flawed, and does not provide an accurate, science-based, or well-informed view of the clinical testing landscape. Without this foundation, the FDA proposes to regulate LDTs as devices and significantly change the clinical testing landscape so essential to patient diagnosis and care. Decisions to protect public health should never be made based on anecdotal information. The FDA is well-respected for its evidence-based decisions. However, this proposed rule simply does not reflect the "gold standard" expected from the FDA. The issues with this proposed rule, and the recent history of legislative efforts, point to the need for unbiased, nationwide collection of information on the LDT landscape. Neither the FDA nor individual stakeholders can perform this analysis alone. **The ACMG again calls on the FDA to abandon rulemaking and instead work with Congress and all stakeholders to collect accurate, unbiased information about the LDT landscape. Only then can all stakeholders have an informed discussion to identify where changes are needed and identify solutions that achieve the end goal of ensuring high-quality testing without disrupting patient access or creating new unintended consequences.**

<u>Lessons from the COVID-19 Pandemic Response</u>

The first case of COVID-19 in the US was confirmed on January 20, 2020. Eleven days later, the Secretary declared a public health emergency. The FDA responded by announcing that they would end enforcement discretion for SARS-CoV-2 tests and require EUAs for such tests. While clinical testing laboratories were ready to respond and address the local spread of COVID-19, they were prohibited by FDA. Rather than using available procedures, laboratories had to wait while COVID-19 spread in their communities.[16] In early February, the FDA issued its first EUA to the Centers for Disease Control and Prevention (CDC), and the tests were shipped to public health laboratories in the US. However, the CDC test was flawed, leading to continued delays in laboratories' ability to test for COVID-19. On February 26th, more than a month after COVID-19 was confirmed in the US, the FDA acknowledged the need for greater flexibility and allowed certain public health laboratories to modify the CDC test so that it could accurately detect SARS-CoV-2.[17]

Throughout the following month, the barriers created by FDA's policies continued to persist such that FDA was forced to change their policies to allow more flexibilities, such as by allowing

[15] https://www.usa.gov/agencies/food-and-drug-administration#:~:text=The%20Food%20and%20Drug%20Administration,and%20products%20that%20emit%20radiation. Accessed on 11/21/23

[16] Konnick EQ, Laser J, Weck KE. The Role of Clinical Laboratories in Emerging Pathogens—Insights From the COVID-19 Pandemic. JAMA Health Forum. 2021;2(10):e213154. doi:10.1001/jamahealthforum.2021.3154

[17] FDA Repeatedly Adapted Emergency Use Authorization Policies To Address the Need for COVID-19 Testing. OEI-01-20-00380. U.S. Department of Health and Human Services, Office of Inspector General. September 2022. Available at https://oig.hhs.gov/oei/reports/OEI-01-20-00380.pdf.

states to authorize labs within their own state and allowing manufacturers to develop and use SARS-CoV-2 tests prior to receiving an EUA. On February 29, 2020, the FDA issued its first formal guidance on development of COVID-19 tests. The guidance is now in its seventh edition, having been revised three times in 2020 alone.[18] This is in addition to announcements made on FDA's website, such as an October 2020 announcement stating that they would prioritize certain EUAs and decline to review others as the EUA volume exceeded FDA's review capacity. As of September 30, 2021, the FDA had granted EUAs for 412 COVID-19 tests, but there were 370 tests for which they had received EUA requests but not yet reviewed.[19]

The COVID-19 experience highlights the numerous challenges with regulating clinical testing under the medical device pathway. The ability to respond quickly to urgent needs such as this requires flexibility for laboratory professionals to provide the services they are trained to develop and offer. It also requires leveraging existing laboratory regulations, such as CLIA. However, the current proposed rule does not include provisions to appropriately address the lessons learned from this experience. Proper solutions cannot be made unilaterally or by forcing clinical testing procedures through a pathway designed for devices. Stakeholders must be brought together to discuss the lessons learned and identify meaningful solutions that enable our laboratories and test manufactures to rapidly respond to future public health needs.

FDA Economic Justification

The FDA's assessment (referenced in the proposed rule as 'Preliminary Regulatory Impact Analysis (RIA)') of the costs and benefits of this proposed rule was based on assumptions from limited data and drawn for IVDs for certain diseases and conditions. Admittedly, all economic models "rely on information that may be subject to limitations related to: the quality of the methods used to collect the data; the extent to which the data address the same population, industries, or geographic area as the regulation; and the degree to which conditions may change between when the data were collected and when the regulation is implemented." However, the FDA fails to acknowledge that there is exhaustive literature describing best practices for eliciting expert judgments, including relevant choices and methods, along with their strengths and weaknesses, which were not addressed by the FDA RIA. Instead, it suffers from a well-established flaw: "A common mistake is failure to distinguish between variability due to sampling from a frequency distribution and empirical uncertainty that arises from incomplete scientific or technical knowledge". [20]

This flaw leads the FDA to make assertions about the estimated costs to laboratories while also acknowledging major unknowns, including the number or types of LDTs currently in use, information a skilled analyst would recognize as a need to "identify key assumptions or data

[18] Policy for Coronavirus Disease-2019 Tests (Revised). Guidance for Developers and Food and Drug Administration Staff. Available at https://www.fda.gov/media/135659/download.

[19] COVID-19, FDA Took Steps to Help Make Tests Available; Policy for Future Public Health Emergencies Needed. GAO-22-104266. United States Government Accountability Office. May 2022. Available at https://www.gao.gov/assets/gao-22-104266.pdf.

[20] Granger Morgan, M. and Henrion, M. (1990) Uncertainty: A Guide to Dealing with Uncertainty in Quantitative Risk and Policy Analysis. Cambridge University Press, Cambridge, 332 p.

needs" before analysis. Without this fundamental data, the FDA's impact analysis asserts that implementation of the rule would cost the clinical laboratory industry approx. $43 billion dollars within the first several years. Given that most clinical testing laboratories generate very little, if any, revenue, this is an unrealistic cost, which further highlights the problems with using a regulatory pathway that is not designed for clinical testing. In fact, the U.S. Office of Management and Budget (OMB) provides specific guidance on the estimation of regulatory costs and benefits and the preparation of RIAs.[21] It is clearly stated that when key sources of uncertainty are likely to have a significant effect on the conclusions about net benefits (e.g., the ranking of regulatory alternatives or whether net benefits are positive), the agency should consider additional research prior to rulemaking. We suggest this recommendation be followed and re-analysis be completed.

The FDA goes on to estimate savings to the healthcare sector and argues that the benefits outweigh the costs. However, these estimates are based on speculative figures such as potential reduction in inaccurate test results leading to poor diagnosis and treatment decisions and avoiding potential lawsuits. These loose extractions undermine the reliability of the economic analysis. Simply put, more information about the current LDT landscape and evidence on real harms must be attained before a reliable economic impact analysis can be completed. As stated above, this is not information that FDA or individual stakeholders can realistically obtain. **An unbiased, national-level effort (e.g., through an entity such as the Government Accountability Office) to collect the needed information should be pursued before FDA attempts to move forward with any major regulatory changes, especially one that stands to have such a significant impact on patient care.**

<u>Impact on Medical Education</u>

The FDA's plan to regulate clinical tests as devices would unequivocally incur additional financial burden to laboratories, especially the non-profit laboratories in the academic medical center (AMC). As mentioned above, the LDTs developed in AMC laboratories often fill a void in the markets where FDA-approved IVD kits are not available. These LDTs are often developed to fill an unmet need for patients with rare diseases and cancers. Residents and fellows in Pathology and Laboratory Genetics/Genomics spend a significant amount of their training in AMC laboratories where they learn test development for these diseases. Because AMC laboratories are already operating on small margins with low reimbursement rates, the financial strain created by this proposed rule would force many AMC laboratories to halt offering such low-volume tests (e.g., tests for rare diseases) or even shut down altogether. This will consequently affect the training programs and therefore the available workforce, and pipeline, of board-certified laboratory personnel in this country. Multiple reports, including a 2020 GAO report, have identified notable gaps in the medical genetics workforce.[22] There is already a significant gap between genetic services needed and the workforce capacity, and policies that harm AMC

[21] Circular A-4 (OMB 2003). Office of Management and Budget. September 17, 2003. Available at https://obamawhitehouse.archives.gov/omb/circulars_a004_a-4/.

[22] Genetic Services, Information on Genetic Counselor and Medical Geneticist Workforces (GAO-20-593). United States Government Accountability Office. July 2020. Available at https://www.gao.gov/assets/gao-20-593.pdf.

laboratories will ultimately harm our ability to train new genetics professionals to address clinical needs.

Conclusions

ACMG requests that the FDA abandon rulemaking for LDTs and instead continue to work with Congress and all stakeholders on constructive solutions. The first step must be an unbiased national-level effort to collect better data on the current LDT landscape, including the number and types of tests currently in use, evidence from peer-reviewed literature on real harms being cause by modern LDTs, and gaps in the current regulatory framework that result in said harms. Even within the proposed rule, the FDA states that "*Until FDA systematically collects information on these tests, such as adverse event reports, it will not be able to assess more fully the extent of the risks to patients in the manner it does for other devices*." The same can be said for not knowing the harms to patient access to clinical testing. However, this is the type of information that should, and realistically could, be collected prior to implementing a potential harmful new rule. LDTs are a cornerstone of healthcare, and regulatory changes must be well-informed to ensure that they support rather than hurt clinical care and advances in precision medicine.

There is a clear need for data gathering followed by a broader stakeholder dialogue. Even if the FDA moves forward with finalizing this proposed rule, it is clear that legislative actions are still going to be required. Thus, rather than pursuing a new rule for which FDA does not have the personnel to implement, federal resources should be devoted to starting the data collection process so we can have meaningful conversations about solutions that don't create new, unintended, and potentially catastrophic consequences. Any regulatory or legislative solutions must be tailored to fit LDTs and work with, not against, existing LDT and laboratory regulations. Attempts to force clinical testing procedures through a pathway designed for products that are manufactured and distributed will only complicate and exacerbate already strained clinical testing services that are critical for patient care.

Sincerely,

Susan D. Klugman, MD, FACMG
President
American College of Medical Genetics and Genomics