ASSOCIATION FOR MOLECULAR PATHOLOGY
Education. Innovation & Improved Patient Care. Advocacy.
6120 Executive Blvd., Suite 700, Rockville, MD 20852
Tel: 301-634-7939 | Fax: 301-634-7995 | amp@amp.org | www.amp.org

May 10, 2021

The Honorable Xavier Becerra
Secretary
United States Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Delivered electronically

Dear Secretary Becerra:

The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 2,500 physicians, doctoral scientists, and medical technologists who perform or are involved with laboratory testing based on knowledge derived from molecular biology, infectious diseases, genetics and genomics. Membership includes professionals from the government, academic medicine, private and hospital-based clinical laboratories, and the in vitro diagnostics industry. Molecular laboratory professionals are a critical part of the medical workforce, most recently serving at the frontlines of this pandemic working with other essential healthcare professionals to care for patients with COVID-19 and stem the spread of SARS-CoV-2.

We thank you for your continued leadership and endeavors to further the mission of the Department of Health and Human Services (HHS) to enhance the health and well-being of all Americans and look forward to working with you on these critical issues. In particular, it is a high priority of AMP to work with policymakers to ensure a rigorous, effective, and adaptable system for the regulation of laboratory-developed testing procedures (LDPs, also known as LDTs). These valued medical services provide essential, clinically-actionable information to serve clinicians and our patient communities, especially now during the COVID-19 pandemic.

We write to restate our support for HHS' statement on the Rescission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests.[1,2] In 2020, AMP was joined by the American Association for Clinical Chemistry and the American College of Medical Genetics and Genomics in our support for the statement.[3] This statement provided much needed clarity by removing the duplicative requirements placed on molecular diagnostics professionals wishing to use their expertise to provide high-quality, innovative LDPs, including those used by clinical laboratories to conduct urgently needed testing for SARS-CoV-2 during the COVID-19 pandemic. AMP has been calling for this clarity ever since the Food and Drug Administration (FDA) began using subregulatory mechanisms in an attempt to inappropriately apply medical device regulations to LDPs.

[1] https://www.hhs.gov/coronavirus/testing/index.html
[2] https://www.amp.org/AMP/assets/File/pressreleases/2020/HHS_Press_Release_082120.pdf?pass=4
[3] https://www.amp.org/AMP/assets/AACC-ACMG-AMP-Joint%20letter%20of%20support%20for%20HHS%20statement%20on%20LDPs-FINAL.PDF?pass=84

HHS' statement provides a clear, transparent pathway for the future, requiring that FDA pursue notice and comment rulemaking, as specified under the Administrative Procedures Act (APA), before seeking to impose any new and significant regulatory requirements on clinical laboratories, hospitals, and health care providers. This statement was released after an HHS internal legal review and ensures that at a minimum, FDA would have to comply with the APA by pursuing a transparent system for policymaking that incorporates stakeholder feedback. While the statement does not address the longstanding issue as to whether the FDA has legal authority to regulate LDPs, AMP believes that FDA does not currently have, nor should it have, this authority.

LDPs are regulated by the Clinical Laboratory Improvement Amendments (CLIA) program at the Centers for Medicaid & Medicare Services (CMS), third party accreditation organizations, and states' requirements. The success of this approach has resulted in tens of thousands of high quality molecular-based laboratory tests being used to inform patient care, including those for cancer, rare diseases, infectious diseases and much more. For years, AMP has communicated its concern about regulatory and legislative proposals that aim to shift or add FDA oversight, not only because it is inappropriate for FDA to regulate the practice of medicine, but also because of the severe disruption to patient care and access that would ensue.[4,5]

The "Original Sin" of the COVID-19 Pandemic

Unfortunately, AMP's concerns regarding FDA oversight of LDPs were realized during the COVID-19 pandemic. As Professor Eric Topol, MD, Director of the Scripps Research Translational Institute, recently stated, "I don't think there's any question that America's original sin was not having a broadly available test by the time COVID-19 was here. We're still living with the fallout of this original sin of not having enough tests. It's the original sin that has become our daily tragedy."[6]

When the public health emergency was declared, instead of relying upon the expertise of molecular professionals across our country under the existing regulatory framework of CLIA, the issuance of a public health emergency was interpreted to require clinical laboratories to obtain an FDA Emergency Use Authorization (EUA) in order to use LDPs in diagnosing COVID-19. This was a drastic and unnecessary addition to the substantial regulatory requirements to which laboratories must already adhere. It took FDA weeks to reverse course and announce policy changes that would allow for the immediate use of LDPs after they had been validated via existing regulatory mechanisms.

After laboratories were permitted to implement LDPs, they responded rapidly. An AMP survey found that experienced academic medical centers were able to develop, validate, and perform their own COVID-19 tests for patients within a month following the FDA policy change that allowed them to do so.[7] However, while navigating the mandatory, concurrent EUA process, many laboratories reported that FDA set impossible-to-meet requirements. For example, at one point the agency required laboratories to evaluate more positive samples than the actual number of confirmed cases in the US. FDA also required laboratories to validate their tests to ensure they did not inadvertently detect MERS or the original "SARS" viruses that were not circulating here and for which no samples were available. In August, almost a third of laboratories reported that they experienced hurdles of this kind while seeking an EUA in response to our survey. Thus, despite FDA's policy changes, significant barriers to obtaining an EUA still remain.

[4] https://www.amp.org/AMP/assets/File/position-statements/2015/FDAcommentsonLDTguidance-FINAL.pdf?pass=5
[5] https://www.amp.org/AMP/assets/AMPComments-VALIDAct-2-13-2019-FINAL.pdf?pass=40
[6] https://www.theatlantic.com/ideas/archive/2021/03/the-original-sin-of-americas-covid-19-response/618300/
[7] https://www.amp.org/advocacy/sars-cov-2-survey/

Applying Lessons Learned to Future Pandemics, Precision Medicine, and Beyond

It is imperative that we learn from the lessons of this pandemic and ensure that the same barriers do not restrict access to other critical diagnostic tests. FDA recently stated that they received over 5,500 pre-EUA and EUA submissions in 2020.[8] This additional workload led to significant delays resulting in FDA only reviewing applications for tests that were deemed high priority by the agency. Furthermore, FDA has acknowledged that due to their lack of bandwidth, they also had to pause review of applications for non-COVID tests for a minimum of 90 days. These include important tests used in cancer and other vital areas of medicine, which may have contributed to significant increases in morbidity and mortality due to these diseases over the past year. If the FDA was unable to process the volume of 5,500 applications for one type of test within one year, it is unrealistic to expect the agency to review the tens of thousands[9] of additional tests for which review would be required if all LDPs were subject to premarket review.

FDA resources are best spent on their statutory charge and area of expertise – review of drugs and medical devices including manufactured and distributed in vitro diagnostic test kits. Fortunately, the current regulatory system under CLIA is ideally suited to ensure that LDPs for all health conditions, overseen by highly experienced, board-certified, medical professionals, are precise, accurate, and informative. The best way forward is to leverage important features of the current system – considering the laboratory, the laboratory professionals, and their services as a whole, while also modernizing the CLIA statute and regulations to reflect current practices and standards. AMP has developed a detailed proposal on how CLIA should be modernized[10], and we welcome the opportunity to share additional details with you and your colleagues at HHS. AMP also recognizes that legislation would resolve this long-standing lack of regulatory clarity. As such, we support the Verified Innovative Testing in American Laboratories (VITAL) Act[11] that would initiate a transparent and inclusive process for CLIA modernization. This process would also be informed by a report on the availability and utilization of LDPs during COVID-19 pandemic response.

This issue is critically important to our members, the "invisible" heroes at the front lines of pandemic response and caring for patients behind the scenes.[12] Prior to changing current regulatory policy, we urge you to carefully consider the impact of those changes on patient care, innovation, access to testing, and public health. We hope that AMP can be a partner to HHS as you continue your important work during this pandemic and beyond, particularly as it relates to precision medicine. We would greatly appreciate the opportunity to meet with you to more fully discuss the regulation of laboratory developed testing procedures and the best ways to modernize current oversight programs. Tara Burke at tburke@amp.org will be in contact with your staff to explore future opportunities for HHS to meet with AMP leadership and answer any of your questions.

Sincerely,

Antonia R. Sepulveda, MD, PhD
President, Association for Molecular Pathology

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[8] https://www.fda.gov/news-events/fda-voices/year-pandemic-how-fdas-center-devices-and-radiological-health-prioritizing-its-workload-and-looking

[9] In 2018, it was estimated that there are over 70,000 genetic laboratory tests on the market with 14 new tests being added per day. This number only represents a fraction of the LDPs, as this number is not inclusive of all molecular and non-molecular tests. https://www.concertgenetics.com/resources/2018-current-landscape-genetic-testing/

[10] http://www.amp.org/AMP/assets/File/advocacy/AMPCLIAmodernizationproposalFINAL8_14_15.pdf?pass=47

[11] https://www.congress.gov/bill/116th-congress/senate-bill/3512

[12] https://www.nytimes.com/2020/12/03/health/coronavirus-testing-labs-workers.html