ASSOCIATION FOR MOLECULAR PATHOLOGY
Providing global expertise in molecular testing that drives patient care
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March 10th, 2025

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2024-D-2707, Validation of Certain In Vitro Diagnostic Devices for Emerging Pathogens During a Section 564 Declared Emergency; Draft Guidance for Industry and Food and Drug Administration Staff; Availability

Comments submitted electronically via www.regulations.gov

To Whom It May Concern:

Thank you for the opportunity to submit these comments in response to the draft guidance titled "Validation of Certain In Vitro Diagnostic Devices for Emerging Pathogens During a Section 564 Declared Emergency." The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 3,100 physicians, doctoral scientists, and medical technologists involved with laboratory testing based on knowledge derived from molecular biology, microbiology, genetics, and genomics. Our membership includes professionals from the government, academic medicine, private and hospital-based clinical laboratories, and the in vitro diagnostics industry. AMP members are experts in molecular pathology and regularly perform this type of testing.

Many of AMP's members served on the frontlines of the country's response to recent pandemics including H1N1, Zika, COVID-19, and Mpox. While AMP maintains that laboratory-developed tests (LDTs) are not medical devices and, thus, should not be subject to the Food and Drug Administration's (FDA) medical device regulations, we provide these comments to inform the agency's work to ensure an adequate and robust response in future outbreaks.

AMP appreciates the FDA's effort to be proactive in providing guidance to enable rapid response and collaboration with *in vitro* diagnostic (IVD) manufacturers and clinical laboratories throughout the United States in the event of an outbreak or new emerging infectious disease. In a non-emergent scenario, AMP believes that the validation requirements outlined in the document are comprehensive, reasonable, and appropriate. However, during the first year of the COVID-19 pandemic, the reality on the ground for those needing to validate and implement diagnostic testing was far from ideal. For instance, in August 2020, AMP found that over 80% of

laboratories surveyed reported experiencing supply chain interruptions that delayed or decreased their ability to provide patient testing. Control samples were scarce, and laboratories struggled significantly with supply chain disruptions, requiring them to pivot often to maintain critical testing capacity.

While the validation requirements outlined in the draft guidance may be considered standard practice for validating a new IVD, in a rapid response situation, flexibility is necessary to accommodate the highly-qualified laboratory professionals working to meet the needs of patients in critical circumstances. For this reason, AMP strongly recommends that the agency state that the information in the final guidance represents an ideal validation approach, but given the many challenges during public health emergencies, the FDA acknowledges differing recommendations and adaptations will be made as needed to ensure that the lack of diagnostics does not constrain the country's response.

As an example of where flexibility is warranted, the draft guidance requires that a test be validated using 30 negative and 30 positive samples. While this may be reasonable in a non-emergent situation, this requirement may delay the availability of tests, especially at the outset of an infectious disease outbreak when accessing characterized samples may be difficult. AMP appreciates that the draft guidance allows the use of synthetic controls and contrived samples, but as experienced in 2020, these too may have limited availability. In addition to the FDA stating the agency will exercise general flexibility regarding its testing validation expectations, AMP specifically requests that the FDA also allow for flexibility in the number of samples if the circumstances warrant it as well.

When using synthetically-generated samples as validation materials, the draft guidance also requires that the sample closely mimic the pathogen, e.g. if it's an RNA virus, the synthetic material should be RNA. However, it should be noted that in the early weeks of the COVID-19 pandemic, which was caused by an RNA virus, clinical laboratories had to use synthetic DNA to generate samples until an RNA option was available. Laboratories switched when feasible and eventually used the whole virus derived from clinical samples for validation studies. It was an important lesson learned that to deploy tests, laboratories needed to adapt validation protocols to use what samples were available at the time to ensure a testing option was available to serve their patient population. As the virus mutated, laboratories further updated and revalidated testing protocols as circumstances dictated.

The guidance also fails to acknowledge that laboratories continuously work to ensure the quality of the test, and it is standard practice to validate and revalidate the test on an ongoing basis as clinical circumstances change. This approach was particularly important during the COVID-19 pandemic when conditions were constantly in flux and new variants frequently emerging. AMP appreciates that FDA encourages the use of predetermined change protocols in the draft guidance, but even more critical, would be for the FDA to incorporate language acknowledging the inherent challenges in early response to an outbreak and the need to be flexible to adapt to a rapidly changing scenario. Reflecting on the lessons learned from the COVID-19 pandemic, it would have been impossible to anticipate all of the immediate changes needed day to day to

adapt to supply chain issues and create predetermined change protocols to accommodate those possibilities.

Thank you again for providing these validation requirements to assist manufacturers with validating IVDs for use in a public health emergency. AMP views them to be reasonable in ideal situations, but requests that the final guidance include flexibility to enable rapid response in infectious disease outbreaks. If AMP may be of further assistance, please contact Annie Scrimenti, AMP Director of Public Policy and Advocacy at ascrimenti@amp.org.

Sincerely,

Jane S. Gibson, PhD
President, Association for Molecular Pathology