COLLEGE of AMERICAN PATHOLOGISTS

March 10, 2025

Sara Brenner MD, MPH
Acting Commissioner
U.S. Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Re: Validation of Certain In Vitro Diagnostic Devices for Emerging Pathogens During a Section 564 Declared Emergency. Docket Number: FDA-2024-D-2707

Dear Dr. Brenner,

The College of American Pathologists (CAP) appreciates the opportunity to comment on the draft guidance of **Validation of Certain In Vitro Diagnostic Devices for Emerging Pathogens During a Section 564 Declared Emergency** and looks forward to continuing engagement with the FDA on multiple aspects of diagnostic development to ensure non-onerous rules for pathologists and the safety of patients. As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

Our most significant requested revisions relate to 1) providing greater flexibilities for tests developed within a laboratory setting and 2) highlighting the important role of pathologists in test development and validation.

Providing Greater Flexibilities for Tests Developed within a Laboratory Setting
The CAP's members play a critical role in designing and using laboratory-developed tests (LDTs) to predict and diagnose disease, guide therapy selection, and assess patient responses to specific treatments. An LDT is typically developed because there is no FDA-authorized in vitro diagnostic (IVD) test kit that meets a specific clinical need. For this reason, clinical laboratories often design new LDTs for patients with rare diseases or other unmet needs. Most LDTs serve patients being cared for in a hospital or health care network where the laboratory is located. This allows pathologists overseeing LDTs to interact directly with other physicians caring for these patients.

The FDA should provide greater flexibility for in vitro diagnostic devices that are developed within a laboratory setting as LDTs. The CAP accredits laboratories according to the Clinical Laboratory Improvement Act (CLIA) statute and CAP accreditation standards. As such, CAP-accredited laboratories are overseen by pathologists, use well-established laboratory methods, and incorporate clinical validity as is well-documented in the medical literature. For this reason, we believe that FDA guidance should recognize that tests developed in the laboratory setting under the guidance of highly trained pathologists' merit greater flexibility.

Highlighting the Important Role of Pathologists in Test Development and Validation
As drafted, the guidance fails to recognize the important role of pathologists in the development and validation of IVDs. We urge the FDA to add a provision to the guidance that encourages test developers to involve practicing pathologists in their test development and validation. Pathologists are specialized physicians trained and certified in pathology. In the US, practicing pathologists undergo specialized training after medical school and are most often certified by the American Board of Pathology. Pathologists direct clinical and anatomic pathology laboratory services; perform biopsies; evaluate surgical, cytology, and autopsy specimens; and serve as laboratory consultants to other physicians.

Aside from these two priorities, the CAP is largely supportive of the guidance because it provides necessary guidance for the development of in vitro diagnostic devices during a section 564 declared emergency. The CAP is supportive of the following provisions of the draft guidance:

- Flexibilities for analytical validation testing, and
- Recommendations for development of home collection kits.

Flexibilities for Analytical Validation Testing
The CAP supports the flexibilities provided within the analytical validation testing section includes sufficient flexibility related to the use of spiked genetic material for validation and *in silico* analysis for cross-reactivity analysis. We applaud the allowance made for wet testing with currently circulating variants by testing clinical isolates and/or inactivated materials spiked into clinical matrix at or near the test limit of detection. These flexibilities will help provide more assurance that in vitro diagnostic devices will be available to detect variants throughout the emergency or threat of emergency.

Recommendations for Development of Home Collection Kits
The CAP also appreciates that the FDA included in its draft guidance the recommendation that "developers of home collection kits consider the incorporation of design features that would increase accessibility for users of differing abilities (e.g., vision or hearing deficits) in their device". The CAP agrees that use of these kits is extremely beneficial during an outbreak not only to increase access to safe testing overall but also among vulnerable populations. These considerations are vital for the practice of high-quality medicine and should be maintained in the final guidance. We also support the FDA's recommendation that at-home testing kits should mitigate the risk of inadequate specimens collected by non-clinical persons.

We believe that the following sections of the guidance may benefit from additional flexibilities:

- Use of synthetic genetic material,
- Flexibilities for analytical validation testing,
- Ease of contact with FDA staff, and

Flexibilities for Analytical Validation Testing

We encourage FDA to incorporate our recommended revisions to provide greater flexibility, particularly related to the section covering Specimen Stability. The FDA should provide greater allowance within the Analytical Validation Testing section for use of synthetic genetic material in situations where biological specimens are not available.

Ease of Contact with FDA Staff

The Specimen Stability section *recommends contacting the FDA* if live or inactivated pathogens are not available. While we appreciate the importance of discussing potential options, we also emphasize that connecting with FDA staff can be challenging in emergent situations. In the spirit of transparency and efficiency, perhaps the FDA could consider additional options for steps that could be taken if FDA staff are not immediately available. This would not only lessen the need of the FDA to handle incoming inquiries during an emergency but would allow labs to follow the guidance document and ensure faster development of IVDs.

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The CAP appreciates the opportunity to comment and provide the pathologist's perspective regarding the development of IVDs for emerging pathogens. Please contact Andrew Jackson, CAP Senior Policy Analyst, Scientific Regulatory Affairs and HIT Policy, at ajackso@cap.org if you have any questions on these comments.