COUNTY OF SAN LUIS OBISPO HEALTH AGENCY
PUBLIC HEALTH DEPARTMENT
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Office of the Center Director
Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Ave, Bldg. 66
Silver Spring, MD 20993

Response to Docket No. FDA-2023-N-2177: Proposed Rule on Medical Devices; Laboratory Developed Tests

Dear Office of the Center Direct and Commissioner Califf:

This letter provides comment on the proposed rule to phase out the FDA's general discretion approach for laboratory-developed tests (LDTs) so that *in vitro* diagnostics (IVDs) manufactured by a laboratory would generally fall under the same enforcement approach as other IVDs. The County of San Luis Obispo Public Health Laboratory is a high-complexity CLIA laboratory that performs clinical and environmental testing to support programs of the County of San Luis Obispo Health Agency as well as hospitals, clinics, physicians, private businesses, citizens, and local, State, and Federal authorities. Together with the broader public health laboratory community, our laboratory has several concerns about the proposed rule:

1. Public health laboratories (PHLs) use LDTs to respond to low incidence, high-priority threats including biologic threats. Many LDTs for rare pathogens and diseases have a high test cost and low demand, and they have been developed by the Centers for Disease Control & Prevention or a state laboratory, and have a proven track record of efficacy and safety over time across a broad network of laboratories. There is a low likelihood that commercial manufacturers will seek FDA approval for these tests because of the lack of financial incentive. The net effect of the proposed rule would be to decrease the response to bioterrorism agents and other high-priority threats throughout the country.
2. Non-commercial laboratories, including PHLs, are not in a position to act as manufacturers for LDTs. The fees and filing process to apply for FDA review of an LDT would be a barrier to adopting and maintaining LDTs that are critical for rare diseases and the populations that we serve. If the test menu of our laboratory was reduced, it could impact not only our reach, but also the laboratory's viability.
3. The proposed rule provides an advantage to large commercial laboratories that have the financial ability and staffing to develop and file for pre-market and 510(k) approval.
4. Many LDTs maintained at PHLs have a significant health equity component. Modifications to assays have been implemented to serve unique patient populations, including individuals at a high-risk for sexually transmitted infections (STIs), incarcerated individuals, etc. The

proposed rule could jeopardize services to certain communities and individuals, further increasing disparities.

5. Turnaround time is essential when diagnosing an infectious disease, and with the rule in place, clinical microbiology laboratories will likely be forced to refer specimens to reference or commercial laboratories for testing.
6. Under the existing rules, modifications to an FDA-approved test serve to recategorize it as an LDT. This facilitates an efficient pathway for laboratories to adapt and refine a test by performing validation studies, particularly in cases where the modifications are relatively minor (e.g., substitution of a similar reagent). By contrast, the proposed rule would require resubmission and review of validation data by the FDA for any modification to a test. Testing response could not move forward during the period required for regulatory review, when timeliness in responding to a local event may be critical.
7. Increased regulatory oversight may impair innovation in cases where cutting edge technology (e.g., whole-genome sequencing) may be applied to address an unmet need in testing.

I agree that Centers for Medicare and Medicaid Services (CMS) through CLIA may not be sufficient to evaluate the performance characteristics of an LDT, and that surveyors may not have sufficient time to review technical data. In addition, test reliability is paramount to laboratories completing their mission. A possible mechanism would be to designate centers of excellence (e.g., CDC, the Wadsworth Center, CDPH) that could serve a two-fold function by: 1) developing new tests and reagents for broader distribution as LDTs to laboratories, especially public health laboratories, and 2) reviewing validation data of a laboratory's LDT for accuracy, precision, sensitivity, specificity, and other parameters and providing recommendations on approval based on the strength of the data. Such a pathway would preserve the integrity and flexibility of LDTs while ensuring both safety and effectiveness of test results.

In the event that the FDA determines that LDTs will fall under the same enforcement approach as other IVDs, I would request that the FDA continue to exercise enforcement discretion on existing LDTs that meet certain conditions. These conditions include:

1. The LDT has been used by an established laboratory that maintains compliance as a high-complexity laboratory under CLIA.
2. The protocol and/or reagent design have been developed by a state or national government laboratory or reference laboratory.
3. The performance of the LDT has been monitored through a CLIA-approved proficiency program.
4. Parameters that potentially affect specificity (e.g., primers and probes for PCR testing) have not been modified. Parameters that potentially affect sensitivity or other performance measures (e.g., extraction method, master mix, collection device) have undergone appropriate bridging or validation studies.

Continued enforcement discretion on LDTs is necessary both to respond effectively to outbreaks and to provide critical services to underserved populations. Moreover, such tests have a proven track record based on initial validation testing and through continued external monitoring.

Below is a list of the laboratory's maintained LDTs and the justification for their use.

LDT name	Description/Justification for Use	Risk
Measles RT-PCR	Qualitative detection of measles virus RNA by RT-PCR from throat swab, NP swab, NP aspirate, and urine specimens. Assay developed by the California Department of Public Health. No known IVD assay exists to test measles virus RNA.	Inability to respond to a measles outbreak, delays when referring specimens
Mumps RT-PCR	Qualitative detection of mumps virus RNA by RT-PCR from buccal swab specimens. Assay developed by the California Department of Public Health. No known IVD assay exists to test mumps virus RNA.	Inability to respond to a mumps outbreak, delays when referring specimens
Norovirus RT-PCR	Qualitative detection of Norovirus genogroup I and II RNA from stool specimens by PCR. Assay developed by the California Department of Public Health. No high-throughput assay exists to test for Norovirus RNA. The Xpert Norovirus assay and Biofire GI panels are available as low-throughput IVDs.	Restricted to a low-throughput response to norovirus outbreaks
CT/NG NAAT for self-collected extragenital sites	Qualitative detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* ribosomal RNA by Hologic Panther from self-collected rectal swabs. Modification to the assay was made to improve reach into the community. No IVD test is available with self-collection for extra-genital sites.	Reduced detection of STIs, increased spread of disease
MALDI-TOF for mycobacterial ID	Identification of Mycobacteria species using the mass and intensity distribution of protein profile from a Bruker MALDI Biotyper. IVD test available on the BioMerieux Vitek MS.	Laboratory would likely drop this capability, leading to slower turnaround time for diagnosis through referral
LRN-B assays	Various PCR assays developed by the CDC Laboratory Response Network to detect bacterial bioterrorism agents including *Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis*. The Biofire Warrior Panel detects many of these agents with the exception of *Brucella suis* and *Brucella abortus*.	Restrictions on sample types that may be tested for BT agents, testing delays for critical results when referring specimens

Thank you for your consideration of these concerns and suggestions.

Sincerely,
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