December 4, 2023

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

Re: ASCLS Comments on Proposed Rule, “Medical Devices; Laboratory Developed Tests”  
(Docket No. FDA-2023-N-2177)

The American Society for Clinical Laboratory Science (ASCLS) shares the FDA’s view that a new framework enacted via legislation is a preferable approach to regulating Laboratory Developed Tests (LDTs) and has actively worked for passage of Verifying Accurate Leading-edge IVCT Development Act (VALID). ASCLS also recognizes FDA’s authority to regulate LDTs under current statute.

Unfortunately, the approach proposed in this proposed rule has cast a very broad net that will ensnare small volume and low-risk tests created for vulnerable patient populations. ASCLS is concerned with the dangerously false premises that undergird this needlessly broad approach endangering, instead of protecting, patients. FDA should recognize the high degree of variability among LDTs in the United States and not classify all LDTs as the same based on the most extreme examples.

As currently proposed, the wide elimination of enforcement discretion, even phased in, is likely to have profoundly negative effects on access to critical diagnostic testing.

**General**

FDA lacks the necessary resources with the required competence and expertise at the scale necessary to regulate the Laboratory Developed Tests, even with the proposed, phased approach: in particular for tests related to rare diseases and pediatrics. Piling additional requirements on clinical laboratories suffering from significant workforce shortages will amplify the negative effects of this policy.

Given FDA’s limitations, ASCLS strongly supports FDA leveraging programs such as the New York State Department of Health Clinical Laboratory Evaluation Program (NYSDOH CLEP) and those within the Veterans Health Administration (VHA).
ASCLS also believes it is reasonable to require clinical laboratories developing and running LDTs to report adverse events, regardless of risk or volume.

**Enforcement Discretion**
Virtually all of FDA’s claimed authority is predicated on a very broad definition of “manufactured.” Not all LDTs are the same and FDA seems to acknowledge that but chooses to broadly describe all with the same descriptor.

If the FDA makes significant changes to its proposal to focus enforcement, ASCLS believes there is a structure that would allow for FDA to provide reasonable and safe oversite while mitigating effects that would limit access.

The FDA proposes continuing enforcement discretion on “1976-Type LDTs.” However, ASCLS believes the exemption must be interpreted within the contemporary realities of a clinical laboratory system decades in the future. FDA should continue enforcement discretion for ANY LDT performed by laboratory personnel with specialized expertise; using components legally marketed for clinical use; and designed, developed, validated, and used within a single CLIA-certified high complexity laboratory regardless of the method used.

The FDA can further mitigate public health concerns around limiting access to diagnostics by stratifying its enforcement approach based on two variables, continuing to provide enforcement discretion in most cases, except for tests with these characteristics:

- **Risk**: FDA should focus premarket approval on high-risk tests exclusively. Low risk LDTs should be largely exempt from oversite, while moderate risk testing may require oversight if produced at volume and commercialized.
- **Commercialization**: High and moderate risk LDTs commercialized and offered outside of the legal entity that owns or operates the CLIA-certified laboratory should receive the most attention from FDA.

**Phase In**
It is a mistake for the FDA to disconnect enforcement discretion from the risk level of the laboratory developed tests as it proposes in Step 2. FDA rejecting its own earlier, sensible, risk-based approach is arbitrary and is not justified by the narrative provided. The lack of clarity around implementation details like this will have a chilling effect as laboratory professionals and laboratory leaders, uncertain if their work to provide customized diagnostic testing for patients, will require volumes of federal paperwork and fees because they have inadvertently crossed a poorly defined and uncertain threshold, will eliminate tests from their menus.
The FDA asks, “Is there a public health rationale to have a longer phaseout period for IVDs offered as LDTs by some laboratories with annual receipts below a certain threshold (e.g., $150,000)?”

FDA should continue its enforcement discretion for many laboratories as noted earlier, but revenue is an inappropriate measure. The experience determining applicable laboratories for reporting under the Preserving Access to Medicare Act of 2014 (PAMA) clearly demonstrates the difficulty determining what revenue is generated by any single CLIA-certified laboratory. Exemptions should be provided based on the risk profile and commercialization of LDTs performed in those laboratories.

Finally, FDA provides no convincing justification for discontinuing general enforcement discretion under Stage 5. ASCLS urges FDA to continue general enforcement discretion of all low and most moderate risk LDTs indefinitely.

**Academic Medical Centers**

ASCLS is unable to imagine a consistent, objective, and enforceable definition of Academic Medical Centers (AMCs) and finds no definition for such entities in current law. While AMCs have considerable expertise housed within their walls, they should not be exempt from enforcement if they produce high risk LDTs and commercialize them at significant volume to warrant oversight.

**Economic Projections as Basis for Policy**

The FDA simultaneously overestimates the revenue generated by these tests and underestimates the number of laboratories and LDTs that will fall under its new enforcement actions. The overall market for clinical laboratory services in the United States is generally believed to be $100 billion per year. If the FDA’s estimates for LDT revenue of $28.6 billion are accurate, the Agency is asserting that nearly 30 percent of the entire industry’s revenue is due to LDTs, which is simply not believable if, as FDA asserts, just 10 percent of the 12,000 high complexity laboratories are marketing LDTs.

FDA’s economic analysis lacks the very precision it seeks to enforce while failing to recognize the degree to which LDTs exist in high complexity laboratories. Basing important public policy decisions on economic analysis that doesn’t pass basic logic will fail badly and injure the very patients claimed to be the beneficiaries of this enhanced enforcement.

There are certainly some LDTs that have been commercialized that generate significant revenue for its makers, but the distribution of revenue production per LDT is likely to follow a Pareto
distribution where a small number of tests produce the vast majority of the total revenue. The FDA’s proposed policy, however, is dependent on a relatively even distribution of revenue across all tests.

The FDA must make significant and meaningful adjustments to this proposed rule, or it will put patients in grave danger. Understaffed and under-resourced clinical laboratories, unable to comply with a heavy administrative burden, will simply stop offering low volume tests. FDA must focus its enforcement in those areas with the highest volume, commercialized testing.

With our shared interest in the highest quality care for patients, ASCLS and its members welcome the opportunity to lend our expertise further to this process as the agency might find helpful.

Sincerely,

James R. Flanigan, CAE
Executive Vice President/CEO