Proposed Rule Affirms Consequences for Patient Access to Laboratory Developed Tests
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AMP & Molecular Pathology

- 2,900 physicians, doctoral scientists, and medical technologists who perform or are involved with molecular laboratory testing.
- Molecular pathology is the heart of precision medicine, where experts apply knowledge to develop molecular and genetic testing approaches to diagnose, characterize, and monitor human disease, and help select therapies.

Infectious Diseases

Hematopathology

Solid Tumors

Inherited Disease

Informatics

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AMP respectfully requests that OIRA pause the FDA rulemaking to provide Congress the opportunity to enact legislation to establish a modernized and appropriate regulatory pathway for LDTs

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Reason #1: Molecular Pathologists are Healthcare Professionals, NOT Manufacturers

- Complete extensive post-graduate education and clinical training, taken board-certification examinations administered by the American Board of Pathology or the American Board of Medical Genetics and Genomics under the umbrella of the Accreditation Council for Graduate Medical Education, or other recognized professional boards.
- Prefer the term ***"laboratory developed testing procedure"***
  - LDPs ≠ boxed and shipped test kits

Reason #2: FDA Review is Costly, Burdensome, and Resource-Intensive

	Cost Per LDT	
	Stanford University Study	FDA Analysis
PMA	**$75 million**	**$4.3 million**
510(k) Method Comparison	**$24 million**	**$275,000**
510(k) Moderately Complex Clinical Study		**$518,000**
510(k) de novo		**$565,000**

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Reason #3: Compliance with Rule is Not Feasible for the Vast Majority of Labs

- FDA estimated one-time cost during phaseout period per laboratory: **$29.6 million**.
  - Does not include the cost of user fees
- 90% of the assumed 1,200 laboratories impacted by the proposed rule are small businesses
- Those entities' average revenue during phaseout period: is **$19.5 million each**

Reason #4: FDA does not have the appropriate resources to handle the added workload

- 144 human genetic tests authorized to date
- Recent estimate of human genetic tests available for clinical use today: >175,000 tests (hereditary disease and oncology only)
- FY24 Appropriations: flat funding, directs agency to shift at least $50 million to cover existing obligations

FDA is anticipating more than 40,000 existing LDTs will need to be reviewed and an additional ~4,000 applications per year afterwards.

Estimated increase in FDA workload

>5000% PMAs

>800% 510(k)

>6000% de novo

Reclassification/Exemptions Won't Resolve Concerns with Economic Burden

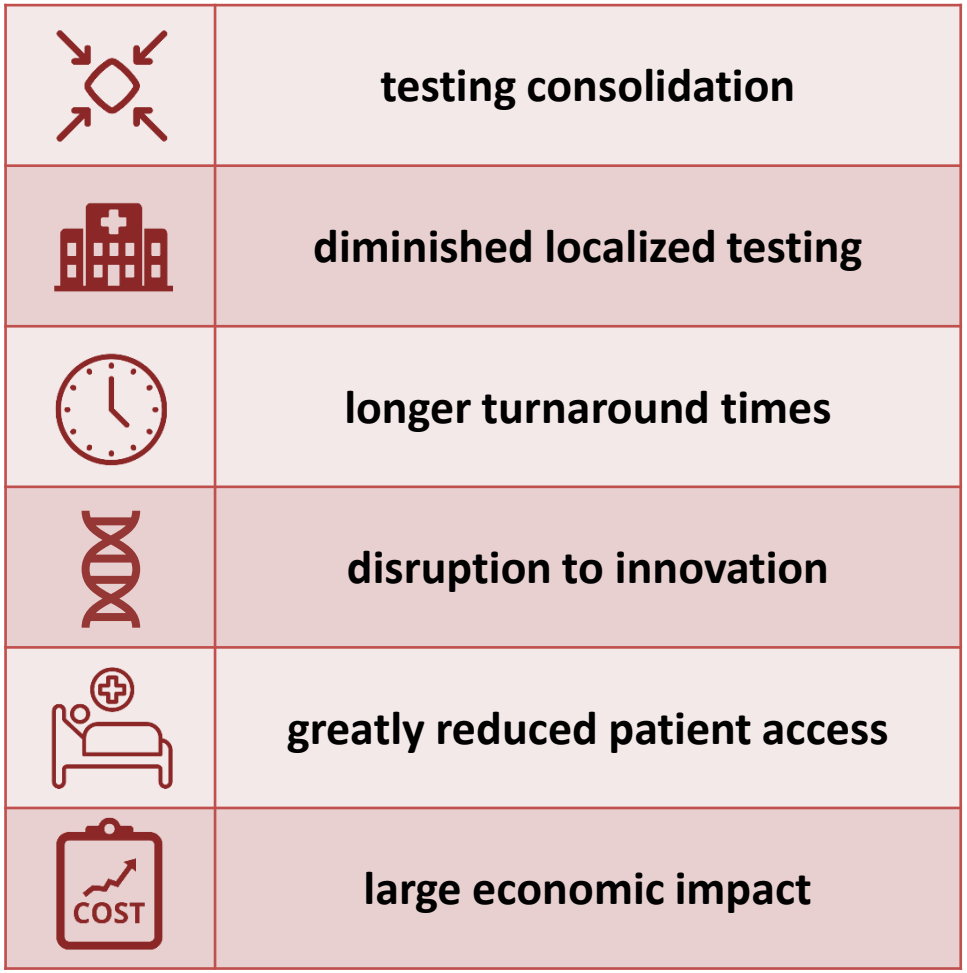
- Preemptively reclassifying high-risk tests to moderate-risk test only shifts, not reduces, the agency's workload
  - Given the lack of predicate devices, most will be more costly and resource intensive *de novo* submissions
  - Reclassification is not a simple process, but requires advisory committee meetings, pre-submission requests, etc. and is unfeasible that the impact of this will be seen during the four years laboratories have to comply with the rule
- The proposed rule included several requests for information on possible exemptions, which will not meaningfully address the economic burden on laboratories and subsequent barriers to patient access.
  - For example, grandfathering freezes tests in time and the inability to modify the tests without premarket review limits ability to meet patients' needs

Reason #5: Highly Flawed Economic Analysis

- Underestimated projected costs to laboratories & basis of economic analysis
- FDA does not account for the impact on health outcomes and costs if laboratories were to close or to reduce their testing menus
- No benefit assigned to LDTs
- Lack of scientific literature to support rule's claims regarding healthcare impact of "flawed" tests
- Fails to consider performance issues with FDA-authorized tests
- Violates the Unfunded Mandates Reform Act:
  - FDA did not take the least burdensome approach to laboratories
  - CLIA modernization not considered

Reason #6: Unnecessary Duplicative Regulation Reduces Patient Access

- Consolidation of clinical laboratories, especially small community-based laboratories and academic medical center laboratories
- Consolidation of test menus as labs focus regulatory resources on highest volume/profitable tests
  - Highest impact likely on tests for pediatric patients and rare diseases
- New patient access barriers due to increases in test price and delayed turnaround times
- Slow, unpredictable regulatory review will delay access to innovation



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Impact on Academic Medical Centers, Public Health, & Community Hospital Laboratories

UNC HEALTH	420 LDTs; results were critical in the treatment of 68,319 patients over 1 year period; anticipated cost of FDA review >$30 million; UNC's operating income = loss of $81 million (comments)
Children's National	Offers several hundred LDTs; predicts that most would be Class II or III; often use pediatric specific instrumentation; FDA review would "further strain our capacity to meet the needs of the children in our care today" (comments)
Washington University in St. Louis School of Medicine	118 LDTs to conduct over 110,000 tests per year; FDA would "would bring the system to a complete halt" (comments)
UHealth University of Miami Miller School of Medicine Pathology & Laboratory Medicine	>100 LDTs; "FDA proposal would make it impossible for our health systems to maintain our existing testing menu" (comments)
Vanderbilt University Medical Center	92 LDTs; nearly all would require PMA; provides rapid turnaround time for patients; "a substantial number of tests will have to be outsourced"; concerned that will extend the turn-around time and delay patient care (comments)
Memorial Sloan Kettering Cancer Center	168 LDTs; "many LDTs would simply disappear" (comments)
Texas Health and Human Services	83 LDTs; "would need more financial resources to comply with the rule"; "cannot profit from its fees for testing performed as specified in Texas statute and due to these tests being provided to uninsured or underinsured individuals, the laboratory cannot recoup the costs for performing the tests" (comments)
Department of Health	Summaries the LDTs it offers including for NBS and NGS; "the rule will cause public health laboratories operating on a thin financial margin to cease offering many tests. That will reduce access for some of the most vulnerable populations in the U.S., including minorities, children and rural communities." (comments)
Perelman School of Medicine University of Pennsylvania	"Adding the cost of FDA user fees and hiring staff to manage PMA submissions will drastically alter the calculus of innovative LDTs for our laboratories." (comments)

ARUP Survey: Overwhelming Concern and Opposition to the Rule Among Laboratory Stakeholders

Support for FDA Proposal

Yes 8.2%

No 71.6%

Don't know 13.7%

No opinion 6.6%

Of 503 respondents, only 8% support the FDA's proposed rule.

Negatively Impacted by Rule

Yes 83.9%

No 3.4%

Don't know 12.7%

Of respondents whose laboratories perform LDTs, nearly 84% believe the rule will negatively impact their laboratories.

Remove Tests From Menu

Yes 60.9%

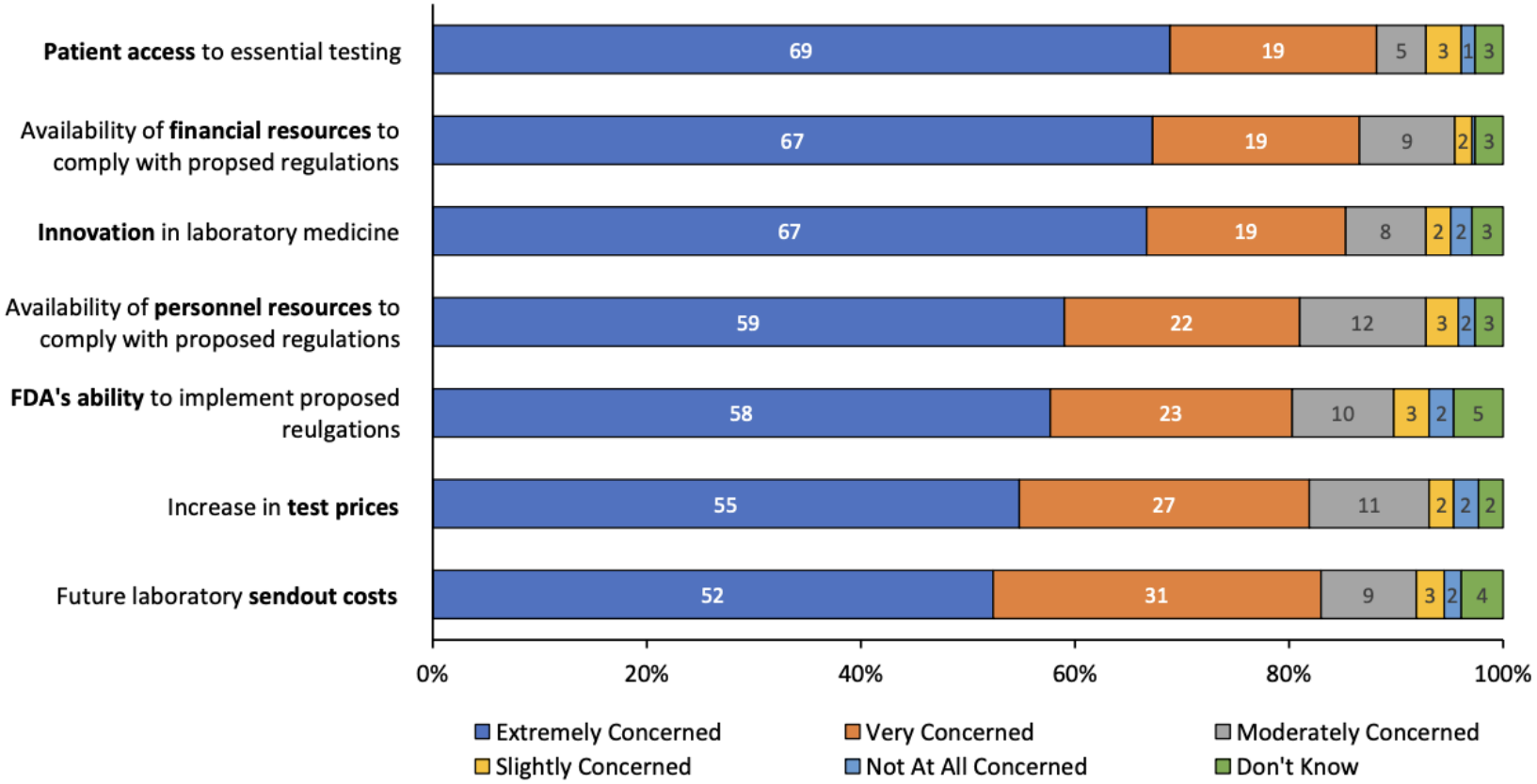
No 5.9%

Don't know 33.2%

The majority of laboratories believe they will have to remove tests from their menus.

Source: https://www.medrxiv.org/content/10.1101/2024.02.28.24303459v2.full.pdf

ARUP Survey Shows Potential Harms if Rule is Finalized



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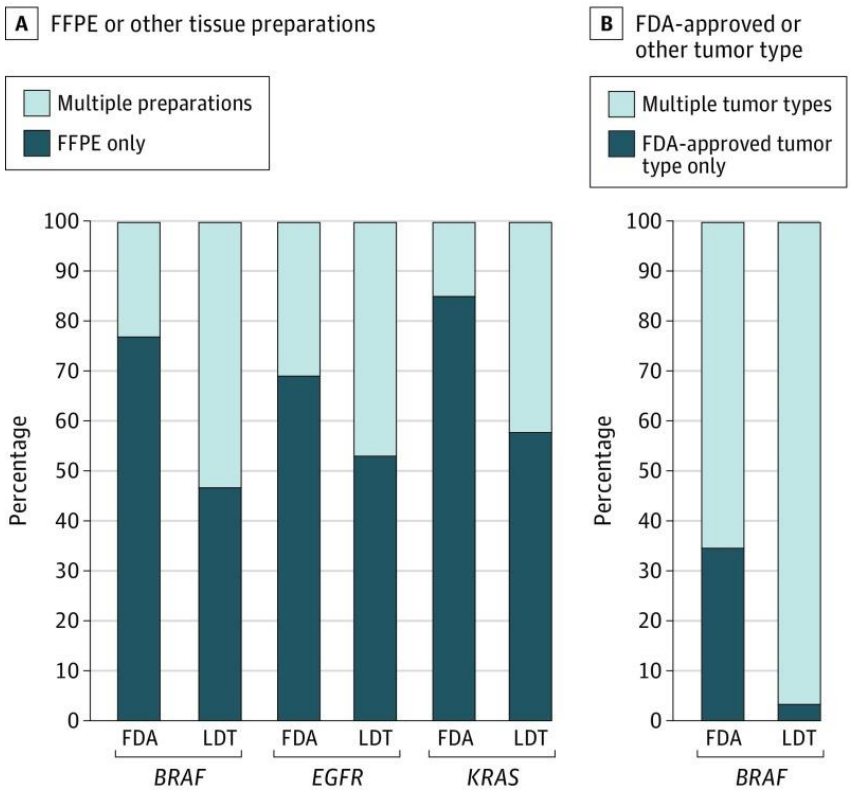
Reason #7: LDPs often perform better than FDA authorized tests

Gene	FDA Companion Diagnositcs, No. (%)	Laboratory-Developed Tests, No. (%)	χ^2 Test	*P* Value
BRAF				
All	300 (93.0)	2224 (96.6)[a]	9.1800	.002[b]
Wild type	88 (100)	616 (99.0)	ND	.99
p.V600E	153 (99.4)	1300 (97.5)	ND	.25
p.V600K	59 (66.1)	308 (88.0)[a]	18.0775	<.001[b]

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6145687/



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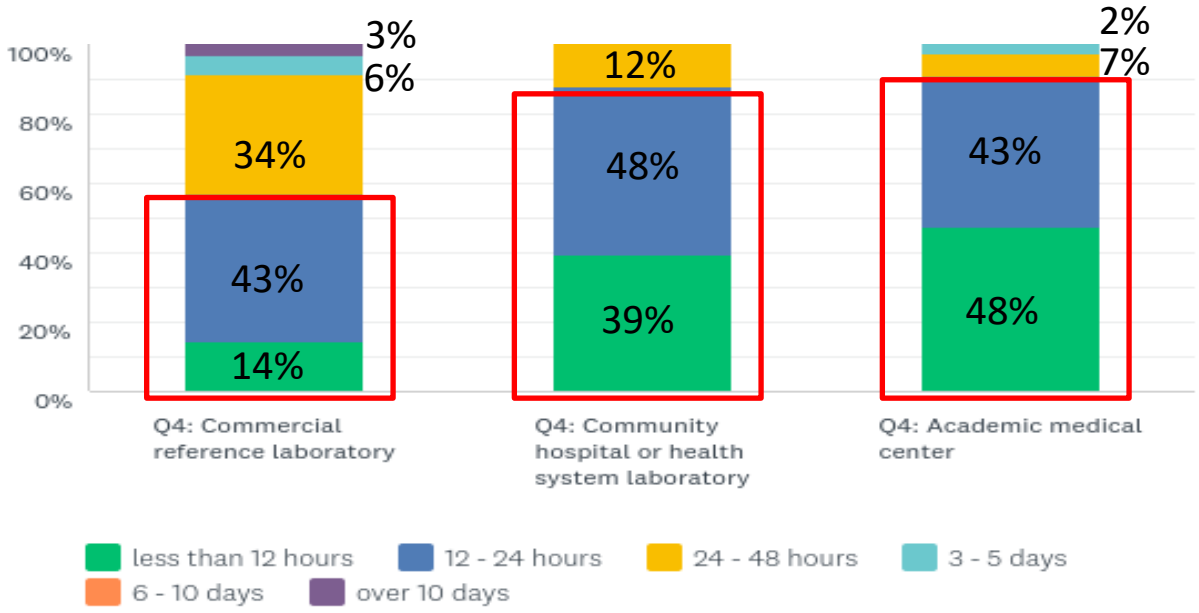
Reason #8: LDTs are Critical to Responding to Public Health Emergencies

COVID-19 2020 Survey Results:

- 38% of respondents were using LDTs as at least one option
- Laboratories deployed multiple testing methodologies due to supply shortages and uncertainties
  - Commercial: 20% had 3 or more
  - AMCs/community hospital/health system labs: 57% had 3 or more
- Laboratories located close to patient care reported a rapid turnaround time for SARS-CoV-2 test results



NOT INCLUDING TRANSPORT TIME

https://www.amp.org/advocacy/sars-cov-2-survey/

A Legislative Solution Would Avoid these Concerns While Assuring Continued Test Quality

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Questions?