NY State Database Offers Glimpse Into Laboratory-Developed Testing Landscape

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NEW YORK – The laboratory-developed testing space in New York state is dominated by large national labs with areas like oncology, genetics, immunology, and infectious disease testing as major areas of focus, according to an analysis by 360Dx.

While the analysis looked only at the New York market, it may also provide a glimpse into the larger landscape in the US at a time when such tests are once again in the crosshairs of the US Food and Drug Administration and federal lawmakers trying to provide clarity to a space that has operated under a cloud of ambiguity for decades.

The New York State LDT database contains more than 10,000 such tests available for use by its residents. Because the state has some of the strictest regulations around LDTs — it is one of a handful of states that require state approval for an LDT in addition to federal CLIA certification – the number of LDTs available nationwide are almost unquestionably substantially higher.

LDTs and, specifically, if and how they should be regulated, are contentious topics within the laboratory and diagnostics industries. Unlike in vitro diagnostics, these tests, which are produced and run by individual laboratories under CLIA regulations, have not undergone review by the FDA, which has, nonetheless, long maintained that it has the authority to regulate LDTs, an assertion disputed by many in the lab community.

In recent years, the issue of LDT regulation has come to the fore. In 2022, Congress made perhaps its most serious attempt to date to pass legislation giving FDA oversight of these tests. Called the Verifying Accurate Leading-edge IVCT Development (VALID) Act, the bill would have created a risk-based framework for what it termed in vitro clinical tests (IVCTs) — which would include both IVDs and LDTs — with high-risk tests, such as novel assays, required to go through FDA premarket review and lower-risk tests allowed on the market after passing through technological certification.

Following Congress' failure to pass VALID last year, the FDA announced it would seek to regulate LDTs under its existing authority. In March, the agency said it planned to regulate them through the rulemaking process, and its proposed rule is currently being reviewed by the Office of Management and Budget. The FDA is expected to release the rule sometime this month, after which there will be a 60-day public comment period during which stakeholders can make comments that the agency must address when it produces its final rule.

The FDA and other proponents of increased LDT oversight have argued such regulation is necessary to ensure test quality and to establish a single regulatory framework for both IVDs and LDTs. Opponents, on the other hand, have argued that new regulations

could hamper test development. Of particular concern is that they might prevent hospital and academic labs from developing tests that are not sold as IVDs but which doctors require for patient care.

While LDTs are widely used, there is no central registry that catalogs these tests. This has presented challenges to understanding the scope of LDT applications and, consequently, assessing the possible impact of increased LDT oversight.

The New York State Department of Health's LDT database is potentially useful in this respect. New York requires that LDTs offered for use on specimens collected in the state be approved by its public health laboratory, the Wadsworth Center, which maintains a searchable collection of approved LDTs.

The New York database is not a perfect proxy for the overall LDT market. Because the database contains only tests offered in the state, it is heavily weighted toward laboratories that are selling LDTs on a national basis, as opposed to locally.

Nonetheless, the database offers insight into the applications for which LDTs are crucial as well as what laboratories are the major providers of these tests.

One potential takeaway is that the LDT space can be split into two relatively distinct markets: one consisting of labs marketing their tests on a national basis, as evidenced by their presence in the New York database, and another consisting of labs that are primarily serving a local customer base in another state and so have not taken their LDTs through the New York approval process.

LDTs from large national reference labs like Quest Diagnostics and Laboratory Corporation of America along with more specialized national labs like Invitae and Myriad Genetics comprise the overwhelming majority of tests registered in the New York state database, reflecting these outfits' national customer base.

Out-of-state academic medical center and hospital labs, on the other hand, have a relatively modest presence in the database. Among out-of-state medical centers, Baylor Miraca Genetics — a for-profit joint venture between Baylor College of Medicine and Miraca Holdings — has registered the largest number of LDTs, with 76. The University of Vermont Medical Center has registered 36 LDTs with the state, but its catchment area includes a region of upstate New York. Cincinnati Children's Hospital has registered 27 LDTs. In total, fewer than 30 out-of-state academic medical centers have registered tests with New York, with the majority of those having registered fewer than five tests.

This pattern tracks with claims by many academic medical centers and organizations like the American Association for Clinical Chemistry (AACC) — now called the Association for Diagnostics and Laboratory Medicine (ADLM) — that these institutions primarily offer LDTs to serve their local physician and patient populations and to fill testing needs not met by IVDs. They have argued that FDA oversight of LDTs would

limit their ability to use LDTs for such purposes.

Some in the academic medical center community have also suggested that regulators draw a distinction between LDTs offered locally to serve specifically physician and patient needs and those developed by labs looking to mass market and distribute them nationwide, advocating that the former should be more lightly regulated than the latter.

Gary Gustavsen, a partner and managing director at consulting firm Health Advances, said the notion of two distinct LDT markets is "spot on," noting that a lab's presence in the New York database "demonstrates a national customer base."

"Quest, Labcorp, Mayo, they want to accept samples from New York state residents, so they have to go through this process," he said. "And the NeoGenomics, Exact Sciences, Invitaes, they have to do this, too, because they aren't not going to take New York state patients."

Meanwhile, medical centers and smaller labs without national customer bases have little reason to go through the New York state approval process, Gustavsen noted.

"On the one hand, you could say, well, OK, the labs that are not going after the Wadsworth Center approval are clearly only interested in serving their local community while those that do go for the Wadsworth Center approval are clearly [making] a big national commercial effort, and maybe those are the labs that should be given more [regulatory] scrutiny," he said.

On the other hand, Gustavsen said, one could argue that LDTs that have gone through the New York state approval process have already received sufficient scrutiny and that those tests should therefore be exempted from further oversight.

"I think you can look at it both ways," he said.

In fact, American Clinical Laboratory Association President Susan Van Meter said last year that the organization was advocating that VALID include a "more robust third-party review program" that would allow developers to take their tests through review bodies outside the FDA like New York's DOH, thereby augmenting the FDA's resources. LDTs from ACLA members dominate the New York database. Tests from Quest Diagnostics (approximately 2,040 LDTs registered by the company and its subsidiaries), Mayo Clinic Laboratories (approximately 1,180), Laboratory Corporation of America (approximately 800), and ARUP (approximately 620) accounted for nearly half of the 10,100 tests in the New York DOH database as of Aug. 22.

These national labs' substantial experience with the New York state LDT approval process, which involves on-site surveys and submission of test standard operating procedures and validation data, may also have factored into their relatively open attitudes toward the VALID Act and its call for increased oversight of LDTs. ACLA suggested changes to the bill but did not come out against it as legislators attempted to

pass it last year, a stark contrast from academic medical centers, which, led by organizations like ADLM — were among the more vociferous opponents of VALID.

James Boiani, an IVD, drug, and medical device life sciences attorney at Epstein, Becker & Green in Washington, D.C, said that the low number of LDTs from out-of-state academic medical centers in the New York state database is "really interesting" and "aligns with the fact that with academic medical centers in lots of cases, patients are going to them and collection and testing is performed where the medical center is."

Whether this has implications for how LDTs from such centers should be regulated is a different question, though, Boiani said.

He said he expects that any carve-outs in LDT regulation will be based not on the commercial reach or strategy of the performing facility but on factors like the number of patients a test is meant to serve and whether a particular testing need can be met by IVDs. The VALID Act offered some such provisions, exempting tests for noncontagious disease or conditions that affect no more than 10,000 individuals in the US annually and tests "developed to diagnose a unique pathology or physical condition of a specific patient or patients," provided the test isn't intended for use in more than five patients and isn't included on the performing lab's test menu or in its marketing materials.

There were, however, efforts last year to create carve-outs within VALID specifically for academic medical centers. During a Senate Health, Education, Labor, and Pensions committee meeting, Sen. Tommy Tuberville, R-Ala., proposed an amendment that would provide such an exemption. Additionally, as the legislative calendar wound down in January, lawmakers circulated a version of the bill that would exempt academic medical centers, though some representatives of those centers said this carve-out did not effectively address their concerns.

Boiani also noted that there is a likely some percentage of labs that are pursuing a national commercialization strategy but have not yet taken their LDTs through the New York state process.

Among New York-based medical center laboratories, which must take their LDTs through the Wadsworth Center in order to offer them to their local customer base, Memorial Sloan Kettering has the most approved tests in the database, with 212. Other New York medical centers, including NewYork-Presbyterian/Weill Cornell Medicine, SUNY Upstate Medical University, New York University, and the University of Rochester, have each registered in the range of 100 to 200 LDTs, with others like Mount Sinai, Northwell Health, and Montefiore Medical Center having registered fewer than 100.

The database also provides insight into the testing applications for which LDTs are most commonly used. Among the types of LDT represented in the DOH database, genetic testing is the most common category, with molecular genetic testing accounting for 1,688 tests, cytogenetic testing accounting for 1,488, and genetic testing-biochemistry

accounting for 257, (although some of the registered tests may no longer be available and/or the labs offering them may no longer be in business).

Oncology is also a major testing area, with 1,399 LDTs falling under the molecular and cellular tumor marker category and 125 tests falling under malignant leukocyte immunophenotyping. Infectious disease testing also features prominently, with 719 LDTs for virology and 401 for bacteriology. Other categories with sizable numbers of LDTs include diagnostic immunology-diagnostic services serology, with 811 tests; clinical chemistry, with 532; endocrinology, with 529; clinical toxicology, with 412; therapeutic drug monitoring, with 279; and hematology with 226.

Among the most commonly used technologies are FISH, mass spectrometry, next-generation sequencing, PCR, ELISA, and flow cytometry.