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HIGHLIGHTS

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Labs Want Congress to Intervene on LDT Regulation

With the U.S. Food and Drug Administration on the threshold of releasing final rules for its oversight of LDTs, the lab sector is taking a run at preserving the current regulatory model by essentially asking Congress to bring the agency to heel.

Contained in the pending FDA/agriculture appropriations bill in Congress is a provision that would suspend final regulations for the FDA's oversight of laboratory-developed tests. Instead, the agency would be directed to work with federal lawmakers to create a pathway for regulating such assays.

The bill was approved by the House Appropriations Committee on a voice vote and likely has a significant swath of supporters in both the House of Representatives and the Senate, according to Alan Mertz, president of the American Clinical Laboratory Association (ACLA).

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Point-of-care Molecular Testing Poised to Take Off

A new report concludes that the market for molecular point-of-care testing is heating up.

Kalorama Research has predicted that the current molecular point-of-care market, which currently is valued at less than $100 million a year, could be worth as much as $1 billion a year by the end of this decade.

The demand will be driven not necessarily by highly sophisticated molecular assays that could detect forms of cancer, but the need to create a better "mousetrap" for traditional non-molecular assays that are highly accurate but suffer from lengthy turnaround times. Many POC molecular tests provide results even faster than rapid immunoassay testing, according to the report.

"There's a large unmet need in the developed world for better testing solutions for upper respiratory infections and sexual health conditions, and a large unmet need in the developing world for (diseases) such as HIV and malaria," said Kalorama Publisher Bruce Carlson.

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Point-of-care Molecular Testing Poised to Take Off, *from page 1*

"Together, that should add up to a sizable market for manufacturers."

According to the report, rapid testing for the detection of influenza is in demand, because the virus can drive huge numbers of outpatient visits during the winter and early spring months. Kalorama envisions a market for that and other respiratory disorders where hospitals can set up triage points during potential outbreaks.

> *"While healthcare consolidation will likely discourage greater diffusion of testing resources, it should not bar the implementation of patient outcome-impactful and cost-saving POC testing."*
>
> — Kalorama Research Report

Overseas, traditional tests for hepatitis, malaria and HIV currently sell for $1 or less per unit. Although many molecular POC tests cannot currently match such prices, Kalorama expects their prices to drop significantly in the coming years and some manufacturers will offer discounted prices to developing countries in need of such testing, driving up demand.

There are some obstacles to a significant expansion of POC tests. The report noted that hospitals, which have been consolidating and acquiring physician practices, may wish to keep up their traditional laboratory volumes and discourage the use of some POC assays (as well as physician office testing) and that in-lab testing may still be less expensive. But the report did note that "while healthcare consolidation will likely discourage greater diffusion of testing resources, it should not bar the implementation of patient outcome-impactful and cost-saving POC testing."

Reimbursement also remains an issue. Kalorama noted that molecular POC assays are often still more expensive than their older counterparts. That, along with provider unfamiliarity with such tests, "is likely to stall the market penetration."

Takeaway: The point-of-care testing segment is expected to take off in the coming years, both in the U.S. and globally.

Theranos Now Under Criminal Investigation

The plot continues to thicken for Theranos. As the California-based startup tries to strain toward greater transparency, it is now apparently the subject of a criminal investigation. Both the *Wall Street Journal* and the *New York Time*s have reported that federal law enforcement officials have been examining whether officials at Theranos may have misled investors about the state of its technology and the progress it was making in developing it.

In a statement, Theranos said it "continues to work closely with regulators and is cooperating fully with all investigations."

That the company is under criminal investigation is merely the latest of its problems. They include faults with its platform to perform laboratory tests with just a few drops of blood. Theranos has approval from the U.S. Food and Drug Administration to perform a single assay using the technology, although it apparently conducted testing on other widely available commercial platforms under the guise of using its own equipment. The Centers for Medicare & Medicaid Services has declared that Theranos' laboratory in Northern California poses an immediate danger to patients because of a variety of faults in both equipment and management of the facility. Moreover, CMS

has rejected many of Theranos' corrective actions to address the issues and is moving to shut the lab down and possibly ban Chief Executive Officer and company founder Elizabeth Holmes and President Sunny Balwani from operating any laboratory for two years. And while Holmes and her Theranos employees had been highly secretive about its testing technology, that veil could be lifted shortly. The American Association for Clinical Chemistry recently announced that Holmes will present testing data at its 68th annual scientific meeting in Philadelphia on Aug. 1.

"There is no better place to present Theranos' technology than at the AACC Annual Scientific Meeting, where leaders in laboratory medicine can evaluate Ms. Holmes' data and research," said AACC CEO Janet B. Kreizman in a statement. "AACC members have been asking for this information, and we are thrilled that Ms. Holmes is presenting the science behind the technology for the first time at AACC."

Takeaway: The downward spiral of Theranos is being accelerated by a potential criminal investigation.

FDA Recalls Focus Diagnostics Test Kit

The U.S. Food and Drug Administration has issued a rare recall of a laboratory test kit, claiming a fault in its manufacturing process could endanger patients. The test in question is manufactured and distributed by Focus Diagnostics, based in Cypress, Calif. The test, branded as Simplexa, tests for the herpes simplex virus and the group A version of streptococcus bacteria. Focus' specialty is on assay kits that rapidly test for herpes and similar viruses.

According to the FDA, the recall is connected to "poor lamination between the sample reaction wells. This poor lamination may lead to leakage into adjacent wells causing cross-contamination between samples, which could yield false positive, false negative, or invalid test results. Inaccurate diagnostic test results may lead to improper patient treatment for herpes simplex or group A streptococcus and may cause serious adverse health consequences, including death."

According to the regulatory agency, the recall affects 1,658 test kits that were manufactured between last July and this February. The FDA regulates laboratory test kits as a medical device. It currently does not regulate tests that are designed to be performed in a laboratory setting.

Focus issued a statement trying to blunt the notion the FDA recall was an ongoing issue for the company, and that it had been resolved last March. The FDA did remark in its recall notice that Focus had taken corrective actions.

"There is no new product recall related to Simplexa Direct Test kits. In close collaboration with the FDA, we notified our customers in February 2016 about the affected test kits," the company said. "We have since resolved the issue with the manufacturer of the discs, which were the principal source of concern. We are confident in the corrective actions that we have implemented."

Takeaway: The U.S. Food and Drug Administration has issued a rare recall of a laboratory test kit.

Inside The Lab Industry

First Quarter Venture Capital Investments Suggest Uncertainties Ahead

Illumina is best known for its sequencing platforms, genomic testing and rapid growth. But the San Diego-based company is taking a leap into new territory: It recently committed $100 million to the creation of a new venture capital fund to help move forward new applications in nucleic acid sequencing, which is the crux of many genomic laboratory tests. The new fund, Illumina Ventures, is headed by Nicholas Naclerio, Illumina's former vice president of corporate and venture development.

> *"Illumina has for many years been making such investment via an internally managed fund, but as the market grows and scales, we believe we can obtain greater reach via an independent venture that has access to additional capital."*
>
> — Eric Endicott, Director of Global Public Relations, Illumina

"Under Nick's leadership, internal venture investing has worked well for Illumina, providing strategic insight and connections to key technologies and channels in our industry," said Illumina Chief Executive Officer Jay Flatley in a statement. "Participating in an independent fund led by Nick that can leverage capital and know-how from other investors who share our strategic interests is an even more effective way for us to utilize Illumina's capital to create incremental shareholder value."

Company officials were reluctant to discuss outside forces that may have dictated the decision, other than the fact that such an arrangement might yield better results for the company in the long term.

"Illumina has for many years been making such investment via an internally managed fund, but as the market grows and scales, we believe we can obtain greater reach via an independent venture that has access to additional capital," said Eric Endicott, the company's director of global public relations.

The commitment is relatively small: the $100 million is callable in increments over the next decade. But the fund could raise another $100 million from additional investors if they are not in the business of sequencing, Endicott said.

It is becoming clearer that the laboratory sector may need that kind of investment in the coming months and years, as venture capital funding is trending unevenly at best.

Although MoneyTree, the venture capital tracking organization, does not keep specific tabs on the laboratory sector, it does track biotechnology, medical devices and health care services, the three areas that include laboratory operations.

Biotech showed some promising growth, up 11 percent for the first quarter of 2016 compared to the fourth quarter of 2015, reaching investments of $1.8 billion compared to $1.63 billion, with 118 deals consummated during the quarter versus 99 in the fourth quarter.

Inside The Lab Industry

"The first quarter appears to tell us that investors still have faith in the venture ecosystem. However, the increase in expansion and later stage financing, combined with the drop in first-time financing, suggests a shift towards relatively mature startups."

— Tom Ciccolella, PricewaterhouseCoopers

But investment in medical devices and health care services tell different stories. Investment in medical devices dropped 22 percent in the first quarter compared to the fourth quarter of 2015, from $648.5 million to $508.3 million. Deals also dropped steeply, to 59 from 83.

Deals in the health care services sector dropped even more precipitously, from $341.1 million to $131.2 million. There were 20 deals consummated during this quarter, compared to 23 in the fourth quarter, strongly suggesting that the companies being funded are receiving investments that are significantly smaller in scale.

Combining the three areas of investment where laboratory-related deals take place, the drop in funding is about $360 million for the first quarter compared to the fourth quarter of 2015.

Overall, there was an extremely steep drop in venture capital investments in the fourth quarter of last year. The number totaled just under $12 billion, down from $16.7 billion in the third quarter of 2015 and $17.3 billion in the second quarter. For the first quarter of 2016, the numbers rose slightly to $12.1 billion.

There was also a drop in investments in new or newer companies. Seed stage investments in the biotech sector dropped 4 percent in biotech; early stage investments dropped 72 percent in the health care services sector and 23 percent in the medical device sector, respectively.

"The first quarter appears to tell us that investors still have faith in the venture ecosystem. However, the increase in expansion and later stage financing, combined with the drop in first-time financing, suggests a shift towards relatively mature startups," said Tom Ciccolella, a venture capital and private equity assurance partner at PricewaterhouseCoopers, which helps assemble the report, in a statement.

So far this year, the money appears to be going to more mature laboratories.

Notable First Quarter Ventures

Company Name	Funding Total	Details
Provista Diagnostics	$5.25 million	From existing investors
Clinical Genomics	$15 million	Series A
Veracyte	$45 million	Financing
Stat-Diagnostica*	$28.5 million	NA
Quanterix	$46 million	Series D
Exosome Diagnostics	$60 million	Series B
Jan Medical	$7.5 million	Series C
bioTheranostics	$32 million	NA

* Overseas company

Source: Fierce Medical Devices

Inside The Lab Industry

The biggest funding this quarter is $60 million for Exosome Diagnostics, which will use the proceeds to expand its testing portfolio.

Another big funding this quarter is for the privately-held Quanterix, which manufactures and distributes molecular testing platforms. It received $46 million in series D funding from a variety of venture capital funds. The company said it has reported triple-digit revenue growth for six consecutive quarters.

"With the introduction of immunotherapies, it is more important than ever to invest in developing appropriate diagnostic tests for emerging therapies. Securing this investment allows us to continue to work for the patients we serve."

— David Brunel, CEO, Biodesix

"With the proceeds from this raise, we will launch desktop instruments in 2017, develop 60 new assays by the end of 2016 and further expand our global reach," said Quanterix Chief Executive Officer Kevin Hrusovsky in a statement.

Another big laboratory-related funding this quarter includes Veracyte, whose $49.5 million in 2015 revenue and estimates of $59 to $63 million in 2016 from its thyroid and lung cancer-related assays place it in the mature company category. It snagged $45 million in funding—primarily financing—from New York-based Visium Healthcare Partners. It will receive $25 million upfront, of which it will use $5 million to retire existing debt. It has the option of drawing down another $15 million over the next year.

"This agreement provides Veracyte the funding and flexibility we need to advance our business towards having three revenue generating products by the end of 2018. We have a clear path to profitability and will build the business with financial discipline and measured investments," said company Chief Executive Officer Bonnie Anderson in a statement. But beyond those two investments, there are few in the eight-figure range. GenomeDX Biosciences recently obtained $25.4 million in funding to develop genomic assays to better detect the presence of prostate cancer.

Colorado-based Biodesix brought in $22 million in a series F round of funding to develop new immunotherapy tests and to market its cancer assays.

"With the introduction of immunotherapies, it is more important than ever to invest in developing appropriate diagnostic tests for emerging therapies. Securing this investment allows us to continue to work for the patients we serve," said company CEO David Brunel in a statement.

Most of the other funding deals announced this quarter have been below $10 million. A couple of deals involve laboratories based overseas, demonstrating the sector's global growth and outreach.

Takeaway: Venture capital in the laboratory sector may be spotty and unpredictable for the foreseeable future, with more mature operations the most likely to obtain further funding.

Labs Want Congress to Intervene on LDT Regulation, *from page 1*

"It should send a message to the FDA that Congress is interested in a legislative solution," Mertz said, acknowledging that while Congress has weighed in on reimbursement issues for the sector on multiple occasions, it has not really involved itself on the regulatory end for decades.

> *"It would be interesting to see where Congress comes down on this debate. However, the real impact may just be a delay in regulation for some time—which, of course, most laboratories would not mind."*
>
> — Danielle Sloane, Esq., Bass, Berry & Simms

Even in Washington's current polarized political climate, appropriations bills are usually passed by Congress and signed into law, because much of the federal government would grind to a halt without the funding they provide. It is also fairly commonplace for lawmakers to insert into appropriations bills only tangentially related legislation that would draw much closer scrutiny if introduced as standalone pieces of legislation.

Is it an actual legislative solution—or an end run around the FDA's regulatory authority? Experts on the FDA and the laboratory sector suggest the latter.

"It would be an end run around the FDA if it were adopted," said Jeff Gibbs, a director with the law firm of Hyman, Phelps & McNamara in Washington, D.C. Gibbs added that the move should also be construed as a "warning shot" against the agency, although he does not believe the FDA would be deterred from issuing the final regulations.

"It would be interesting to see where Congress comes down on this debate. However, the real impact may just be a delay in regulation for some time—which, of course, most laboratories would not mind," said Danielle Sloane, a member of the law firm Bass, Berry & Simms in Nashville, Tenn.

Potential stalling tactics aside, a significant majority of the laboratory sector has been opposed to the FDA's regulation of LDTs. They say that tweaks to the existing CLIA regulations would address the pertinent issues.

However, the FDA has been fairly relentless in its move to try to regulate LDTs, claiming their growing complexity could place patients in danger if their accuracy and efficacy is not closely monitored. Last year, it issued a paper that listed 20 LDTs that possibly placed patients in danger—essentially a first for the agency. Meanwhile, Mertz believes that a bill in some form that preempts the proposed regulations stands a good chance of passing both chambers.

Gibbs is not so sure. He noted that there are still many steps involved in keeping the language in a final bill that would pass both houses of Congress. He also added there is resistance from test kit manufacturers, whose assays are already regulated by the FDA, as well as consumers concerned about safety issues surrounding LDTs.

"This is obviously a very unusual set of circumstances," he said.

Nevertheless, whether Congress or the FDA has the final word, both Sloane and Gibbs expect that LDTs will eventually come under tighter regulation.

"However, the lingering uncertainty is ... unsettling," Sloane said.

Takeaway: The laboratory sector appears to be attempting an end run around the regulation of LDTs.

INDUSTRY BUZZ

Quest Introduces Tests for Efficacy of New Hepatitis C Drugs

Quest Diagnostics has launched some companion tests designed specifically to take advantage of what has become a rapidly mushrooming market for treating patients with hepatitis C.

The New Jersey-based Quest has launched tests that would enable physicians to determine the compatibility of the patient with two new drugs used to treat the virus: Zepatier, which is manufactured by Merck, and Daklinza, manufactured by Bristol-Myers Squibb.

Both drugs, which focus on various genotypes of hepatitis C, represent new fronts not only in the fight against the disease, which was curable only by a liver transplant just a couple of years ago, but as ways to keep the cost of treating the disease in check.

Sovaldi, the first drug brought to market to cure the disease, costs about $84,000 for a regimen. Harvoni, another drug, costs nearly $100,000. The cost has raised concerns that many Americans living with hepatitis C would never receive appropriate treatment.

By contrast, Zepatier costs about $55,000 for a regimen, while Daklinza costs about $63,000, although the latter often must be prescribed in conjunction with Sovaldi.

"These new Quest services underscore the value of diagnostics to advance precision medicine," said Rick L. Pesano, M.D., Quest's vice president of research and development in a statement. "Our new offerings can help improve health care quality and cost savings using specialty pharmaceuticals for an infectious disease that is highly prevalent yet curable when treated appropriately. With insight the physician can better determine if the patient will not benefit from, or develops resistance to, an NS5A inhibitor, so an alternative treatment can be prescribed more quickly."

Having a test readily available that could save tens of thousands of dollars in treating a hepatitis C patient could prove invaluable to providers. A Quest spokesperson did not respond to email and telephone requests for comment.

It is unknown if Quest's major competitor, LabCorp, also offers similar tests. A company spokesperson did not respond to a request seeking comment.

Takeaway: Quest Diagnostics is trying to capitalize on the rapidly growing hepatitis C treatment market by introducing specific companion tests.

References

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