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Diagnostics 2018: Steady Progress And The Big Get Bigger

by Mark Ratner

If the beginning of 2017 was marked by doubts around whether and how the FDA would act with respect to complex diagnostics, we enter 2018 feeling that slow-moving vessel may finally be turning.

- We predict that artificial intelligence tools for diagnosis and patient monitoring will continue to gain traction as pharma and medtech gear up in digital health, with diabetes care leading the way.
- The diagnostics deal front was largely quiet in 2017, but for a smattering of big-money financings and acquisitions.
- So what? Regulatory pathways around innovative cancer tests – especially the long-standing issue of whether and how to regulate LDTs – will continue to be a hot topic. Even as FDA seeks input for greater technical and clinical clarity, the use of complex assays in routine care remains far off.

FDA product reviews were the lead story for the year, as Class II device designations emerged for large-panel tumor-profiling assays and direct-to-consumer (DTC) genetic health risk assessment (GHRA) tests.

In early November, the agency put forth its plan to regulate DTC GHRAs, exempting them from premarket review under certain conditions, when it allowed *23andme Inc.* to launch a set of FDA-validated direct-to-consumer tests predicting individuals' predisposition to genetic diseases and conditions. (Also see "*US FDA Implements 'Firm-Based' Regulatory Approach To DTC Genetic Health Risk Tests*" - Medtech Insight, 6 Nov, 2017.) Under the proposed scheme, manufacturers of these types of tests would have to come to FDA for a one-time review, after which they may enter the market with new tests without further premarket notification. The agency also established special controls for these tests in a separate *de novo* classification order. Several categories of tests remain outside the new rules: those intended for prenatal screening, determining

predisposition to cancer that could lead to taking medical action, pharmacogenetics testing, or assessing the presence of deterministic dominant variants.

Critics of DTC testing generally maintain their opposition on the basis that it needs to be done in collaboration with a provider. But they appear willing to wait and see how the agency applies the special controls, which among other things seek to assure that labeling will adequately inform consumers of the limitations of the tests.

Two weeks later, FDA turned its attention to next-generation sequencing-based (NGS-based) large-panel tumor-profiling assays when it granted authorization to *Memorial Sloan Kettering Cancer Center*'s *MSK-IMPACT* laboratory-developed test (LDT).

As with DTC GHRAs, subsequent NGS-based tumor-profiling tests need only show substantial equivalence to a predicate device. MSK's *de novo* submission to FDA included and extended information previously submitted to the New York State Department of Health (NYSDOH), which had approved use of the test on samples from the state. (Also see "*A New York Minute: US FDA Leverages State's Health Department To Expedite NGS Reviews*" - Medtech Insight, 15 Nov, 2017.) The FDA used that information in its review, and said that going forward NYSDOH could function as an FDA third-party reviewer of IVDs, including tests similar to MSK-IMPACT. Other accredited, third-party FDA reviewers also may become eligible to conduct such reviews and make clearance recommendations to the agency – a tacit acknowledgment of the need for greater resources to build an inspection program that can handle the increasing numbers of LDTs that may cross the transom. As a result, developers of NGS-based tumor-profiling tests may not need to submit anything directly to FDA in the future.

These moves seemingly opened the door for similar LDTs, but that door may have been slammed shut on December 1, when *Foundation Medicine Inc.*'s *FoundationOne CDx* received a full marketing approval as a companion diagnostic to 15 targeted cancer drugs, benefiting from the agency's expedited access pathway as a breakthrough-designated diagnostic. (Also see "*First Expedited NGS Test Breaks Through FDA Review*" - Medtech Insight, 1 Dec, 2017.)

Along with the nod from FDA, Foundation Medicine obtained a positive proposed National Coverage Determination from the Centers for Medicare and Medicaid Services, which had reviewed the product at the same time as FDA under the FDA/CMS Parallel Review Program. The NCD effectively prevents other laboratories with NGS-based tumor-profiling LDTs from being reimbursed for running their tests, an indirect way of regulating them by kicking the issue to CMS to articulate a payment policy. The molecular diagnostics community, understandably, is taking issue with this action and will no doubt be seeking a compromise position, perhaps arguing for a lesser amount of reimbursement for non-FDA approved LDTs: the public comment period will end in early 2018.

Looking beyond LDTs in oncology, the first traditional IVD (kit) companion diagnostic to identify multiple cancer mutations using next-generation sequencing also gained FDA approval. *Thermo Fisher Scientific Inc.*'s *OncomineDx Target Test* in lung cancer, developed in collaboration with *Novartis AG* and *Pfizer Inc.*, which helps direct the use of Pfizer's *Xalkori* (crizotinib); *AstraZeneca PLC*'s *Iressa* (gefitinib); and the combination of the Novartis drugs *Tafinlar* (dabarafenib) and *Mekinist* (trametinib), got the OK in June. (Also see "*Podcast: Thermo Fisher Talks Regulatory Experience With Oncomine*" - Medtech Insight, 6 Jul, 2017.)

Diagnostics Deal-making

Genetic technology was also the foundation for the biggest oncology diagnostics-oriented acquisition in 2017. In a push to expand its health care offerings with an emphasis on precision medicine, *Konica Minolta Inc.* agreed to pay $800 million in cash plus up to $200 million in earn-outs for privately held genetic testing firm *Ambry Genetics Corp.[See Deal]* The deal was partly funded by the public/private Innovation Network Corporation of Japan. It will create new diagnostic technologies for oncology and drug discovery, and bring a comprehensive genetic-diagnostic portfolio to Japan, among other markets.

The Asian market was also the focus of diagnostics' biggest acquisition of the year. In a bid to further grow its presence outside the US, especially in China and the emerging markets, *PerkinElmer Inc.* paid $1.3 billion in cash for German IVD multinational *EuroImmun AG*. *[See Deal]* (Also see "*PerkinElmer Solidifies OUS Presence With $1.3bn EUROIMMUN Buy*" - Medtech Insight, 19 Jun, 2017.)

Top Diagnostics Deals Of 2017

- Top M&A: Perkin Elmer Buys EuroImmun for $1.3bn
- Top Oncology-focused M&A: Konica Minolta Buys Ambry Genetics for $800m cash, $200m earn-outs
- Grail closes first tranche of billion-dollar B round, merges with Cirina
- Liquid biopsy play Karius raises $50m A round
- Verily gets $800m from Temasek

Although *Abbott Laboratories Inc.*'s $5.8 billion acquisition of *Alere Inc.* in February was technically the year's biggest, we included that deal, which took more than a year and a half to complete, in our 2016 Year in Review. *[See Deal]* (Also see "*Diagnostics In 2016: From Alere To Zika*" - In Vivo, 24 Jan, 2017.) Last year also ended with *Grail Inc.* on the cusp of completing a billion-dollar Series B round, for which the first tranche, of $914 million, finalized in February 2017. *[See Deal]* Two months later, the developer of liquid biopsy technology merged with China's Cirina Ltd., which is also focused on early-stage cancer detection using blood-based markers. *[See Deal]* (Also see "*M&A Analysis: Grail's Chinese Merger Wraps Up Busy May*" - Medtech Insight, 9 Jun, 2017.) Another liquid biopsy firm, infectious disease-focused *Karius Inc.*,

took in $50 million in a Series A round in August. *[See Deal]*

Our other noteworthy private placement of 2017 was to *Verily Life Sciences LLC*, which received an $800 million investment from Singapore investment company Temasek in January in exchange for a minority stake in the company. *[See Deal]* The two companies will also collaborate on expanding Verily's programs outside of the US.

A major focus of Verily is in diabetes, where it has partnered with *Dexcom Inc.* around smart glucose monitors. We predict that artificial intelligence tools will continue to gain traction as the pharma and medical device industries gear up in digital health, with diabetes care leading the way. *Roche*, for example, bolstered its diagnostics division in June via the acquisition of *MySugr GMBH*. The deal gave Roche a set of apps and services that combine diabetes coaching, therapy management, test-strip supply and automated data tracking to blend with its own glucose monitoring systems and services. *[See Deal]Medtronic PLC* has licensed diabetes prevention and self-management programs and developed a cognitive app that harnesses IBM Watson Health's computing power to process information from Medtronic's pumps and glucose sensors to help patients better manage their disease.

Looking Ahead

In a year dominated by cataclysmic storms, the Northwestern hemisphere was at least spared having to contend with a major viral outbreak. The same may not be true of 2018.

Scott Gottlieb, MD, has pushed hard to streamline FDA regulations following his installation as commissioner in May 2017. The strength of leadership at other federal health agencies, however, is less certain: at Health and Human Services, Alex Azar's nomination is still under review and the Centers for Disease Control and Prevention has felt pressure from the Trump administration to ban terms including "science-based" and "evidence-based." (Also see "*HHS Nominee Azar And The Taint Of Industry*" - Pink Sheet, 6 Dec, 2017.) [*Editor's note: Azar was confirmed on January 24.*] As we also said last year, it is difficult to gauge how the current administration will respond to a significant public health threat.