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TOP OF THE NEWS

FDA Oversight of LDTs Delayed for Consultation with New Administration, Stakeholders 1

DTC Test Results Don't Lead to Dramatic Changes in Health Care Use 1

INSIDE THE DIAGNOSTICS INDUSTRY

HudsonAlpha Institute for Biotechnology Fosters Genomics Research, Education, Clinical Applications and Workforce Development 5

EMERGING TESTS

Blood Glucose Monitoring Developments Focus on Mobility, Convenience 9

G2 INSIDER

Continuing Rise of Genetics Highlighted at 34th Annual Lab Institute 12

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FDA Oversight of LDTs Delayed for Consultation with New Administration, Stakeholders

The U.S. Food and Drug Administration (FDA) has provided laboratories with some much needed good news—the agency will not finalize its laboratory-developed test (LDT) guidance document before the end of the year. In fact, the FDA confirmed Friday that it will instead work with the new administration on appropriate reforms to ensure LDTs are safe and effective.

According to a statement from the FDA, which G2 received in response to a request for confirmation of the status of the guidance document:

> "The FDA believes that patients and health care providers need accurate, reliable, and clinically valid tests to make good health care decisions—inaccurate or false test results can harm individual patients. We have been working to develop a new oversight policy for laboratory developed tests, one that balances patient protection with continued access and innovation, and realize just how important it is that we continue to work with stakeholders, our new Administration, and Congress to get our approach right. We plan to outline our view of an appropriate risk-based approach in the near future. It is our hope that such an approach will help guide continued discussions."

Agency representatives had previously indicated an intent to release before the end of 2016 a final version of the draft guidance document released in October 2014. That guidance set forth a framework for FDA oversight of LDTs.

Continued on page 2

DTC Test Results Don't Lead to Dramatic Changes in Health Care Use

The U.S. Food and Drug Administration (FDA) has frequently expressed concern about direct-to-consumer (DTC) marketing of genetic testing. For example, the FDA required pre-market approval for 23andMe's Personal Genome Service. One of the FDA's stated concerns is that in the case of DTC genetic tests no physician is involved to provide consumers guidance in utilizing these results and there is a danger that consumers will make their own decisions about treatment or use of prescription medicines that can create risks to their health. Recent studies provide some insight regarding consumers' perceptions of these genetic test results.

Continued on page 8

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■ FDA Oversight of LDTs Delayed for Consultation, *Continued from top of p.1*

> *"Today's announcement by the FDA has paved the way for a transparent discussion on meaningful reform that would protect diagnostic innovation and patient access."*
>
> —Alan Mertz, President, ACLA

Industry reaction mostly positive

The American Clinical Laboratory Association commended the agency's decision to work with lawmakers on LDT reforms, after having vigorously opposed the draft framework—even hiring high profile legal counsel and issuing a white paper in early 2015 detailing legal arguments against the FDA's authority to impose the framework. ACLA's legal team, former Solicitor General Paul D. Clement, now a partner with Bancroft PLLC, and Laurence H. Tribe, Professor of Constitutional Law at Harvard University, prepared a White Paper asserting that: FDA regulation of LDTs is not supported in the language of the Food, Drug & Cosmetic Act (FDCA), the proposed regulation interferes with the practice of medicine, and FDA guidance flouts administrative law requirements for rulemaking.

"We appreciate the FDA's acknowledgment that stakeholder input and the ongoing bipartisan work carried out in the House and Senate is the appropriate process to advance comprehensive statutory reform of the LDT regulatory framework," said ACLA President Alan Mertz in a statement. "Today's announcement by the FDA has paved the way for a transparent discussion on meaningful reform that would protect diagnostic innovation and patient access."

Other laboratory industry stakeholders expressed similar happiness at the delay, as did congressional leaders who had been promoting alternatives to the FDA's framework, including Energy & Commerce Committee Chairman Fred Upton who stated it "was the right call" and imposing regulations "via non-binding guidance documents is not the best approach." He indicated the committee is working on bipartisan solutions and "forging significant consensus among a number of patient groups, labs, and manufacturers around a 21st century approach uniquely designed with all diagnostic tests in mind from the outset."

But not everyone is ecstatic about the delay. Andrew Fish, executive director of AdvaMed Diagnostics, a trade association serving the medical device industry issued a statement saying that "AdvaMedDx is disappointed that FDA final guidance on LDT oversight is not forthcoming at this time." Echoing Upton's comments, Fish mentioned the need for a broader look at diagnostics oversight as a whole saying AdvaMedDx was "encouraged by congressional interest" in LDT oversight "in the context of broader diagnostics reform legislation." The statement emphasizes the organization's commitment to working with all stakeholders to achieve legislation addressing "risk-based oversight of all diagnostics, including LDTs" and stated it was "imperative that this legislation recognizes FDA's critical oversight role and serves public health and innovation, and we hope FDA will share its current thinking on LDT oversight to help inform the legislative discussion."

Delayed but not forgotten

As can be seen from AdvaMedDx's reaction to the delay, continued conversation is welcomed but concern regarding LDTs isn't going away.

Health care attorney Danielle Sloane, of Bass Berry & Sims in Nashville, commented that "Laboratories are collectively breathing a sigh of relief at the FDA's announcement in conjunction with the knowledge that congressional action is also less likely

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to come to fruition under the new administration. However, the issues that drew the FDA's concern remain, so I expect to see continued FDA vigilance in the market, particularly with respect to direct-to-consumer marketing of laboratory tests and situations in which the ordering practitioner is affiliated with the performing laboratories."

Highlighting the same concerns Mertz mentions in ACLA's statement, Jen Madsen, MPH, a health policy advisor at Arnold & Porter in Washington, DC points out that "the FDA's announcement focuses on balancing patient protections and innovation which is really where the sticking point has been in the whole debate." She predicts that if Congress does not pass compromise legislation in the upcoming user fee negotiations in 2017, it could be a significant period of time before a revised regulatory approach emerges, given that it will take some time for the new administration to get people sworn in, including a new HHS Secretary. "One barrier to congressional action is the lack of consensus in the community" about the right path to regulate LDTs, so the situation "will remain ambiguous for at least a while." Noting various stakeholders favor modernization of CLIA in addition to or in place of heightened FDA involvement in LDT oversight [see Box], Madsen adds "the device industry has also been arguing that statutory change is needed" because the FDA's medical device regulatory framework doesn't apply perfectly to diagnostics, she says, "so there are arguments that a different review process is needed for all diagnostics, not just lab tests."

Madsen and Sloane participated in a panel presentation at G2's recent Lab Institute in Washington, D.C. (Oct. 26-28, 2016) and highlighted the FDA's growing concern about LDTs marketed direct-to-consumer as well as surveyed the number of alternative regulatory proposals being promoted in efforts to influence the structure of any regulatory oversight of LDTs.

This latest status update regarding FDA efforts is not a vast change from the agency's prior statements other than to step away from its indication it would finalize the framework this year. In December 2015, at a hearing before the U.S. House of Representatives Energy and Commerce Committee, Jeffrey Shuren, director of the Center for Devices and Radiological Health at the FDA, had outlined the steps the FDA planned to take going forward which included:

- Coordinating with CMS on laboratory oversight and FDA plans to develop draft guidance regarding quality system requirements for LDTs, "to provide clarity for laboratories on how they can leverage compliance with CLIA requirements to satisfy those applicable FDA guidelines";
- Working with CMS and accrediting bodies and CLIA-exempt state laboratory programs, "to identify any potential overlaps between CMS and FDA activities" and look for ways to increase efficiency; and
- "Ongoing meetings with stakeholders, including laboratories, patients, traditional IVD manufacturers, and medical practitioners."

The FDA's current comments reflect a similar path, yet simply expanded to accommodate a change in administrations.

At that same hearing, Patrick Conway, CMS deputy administrator for Innovation and Quality and chief medical officer, deferred to the FDA on the issue of clinical validity of lab tests, stating that CMS through CLIA "merely regulates how and by

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whom the test is conducted and reported out, rather than the scientific principles behind or the clinical validity of the test system itself." Conway explained that "CLIA does not regulate the scientific principles behind or the clinical validity of any test – that is, the ability of the test to identify, measure, or predict the presence or absence of a clinically relevant condition or predisposition in a patient." Further he added: "CMS does not have a scientific staff capable of determining whether a test is difficult to successfully carry out or likely to prove detrimental to a patient if carried out improperly. This expertise resides within the FDA, which assesses clinical validity in the context of premarket reviews and other activities aligned with their regulatory efforts under the Food, Drug, and Cosmetic Act." G2

Alternatives to FDA LDT Oversight Framework Proposed

Here are brief summaries of several proposals put forth by stakeholders in the laboratory industry as alternatives to the FDA's 2014 draft guidance document.

Organization	Proposal
AACC	LDTs should be defined as new or significantly modified tests for which the modification alters the clinical claims. CLIA should be updated to require laboratories demonstrate that LDTs are clinically valid for use in medical decisions with CMS credentialing third-party organizations to review a laboratory's clinical validation data for LDTs. CMS and deemed accrediting organizations should include on inspection teams individuals with expertise to evaluate LDTs.
AMP	Update CLIA provisions with tiered, risk-based structure. Uses term Laboratory developed procedure defined as a professional service. Relies on CLIA, lab accreditation and professional certification for oversight. Expanded CLIA regulation should include verification of LDP clinical validity with clinical consultant reviewing appropriateness of test ordered and interpretation of results; public CLIA registry of labs and test offerings and public information about adverse events in labs; third party review for moderate and high risk LDPs. Multianalyte assays with algorithmic analyses with proprietary algorithms submitted to FDA
ACMG and AMA Coalition (also includes AMP, American Association of Bioanalysts, American Society for Clinical Pathology, Bioreference Laboratory, infectious Diseases society of America and National Independent Laboratory Association)	Suggest modernizing CLIA by setting standards for clinical validity and strengthening existing standards for quality control, quality assurance, personnel standards and regular proficiency testing. Limited role for FDA.
ACMG	Position statement on genetic testing and LDTs claims LDTs used for genetic testing should be treated differently than routine diagnostic tests. Such tests involve the practice of medicine. Espouses approach closer to radiologic imaging oversight model rather than that based on devices. Proposes enhanced CLIA regulations with tiered and risk based approach, third party review system, public reporting of test performance, CMS and FDA coordinate oversight. Third party genetic testing laboratory accreditors assess analytical and clinical validity of new tests. Precertification of clinical validity under CLIA by third party accreditors for low and moderate risk genetic tests. High risk tests subject to CLIA/FDA/third-party review. NIH support for common data sharing regarding clinical significance of variants facilitating test validation and post market surveillance.
CAP	Opposes FDA framework and proposed alternative in 2009 with tiered, risk-based approach focused on analytic and clinical validity. Differed from FDA on defining LDTs and risk classifications and the role of CLIA and CMS. Also recently updated accreditation requirements to address LDTs and impose requirements for "a minimum number of samples to ensure analytic accuracy."
Diagnostic Testing Working Group	Defines "In Vitro Clinical Tests" as distinct from medical devices and proposes a new FDA entity to oversee design and manufacture of these tests; risk-based approach requires evidence supporting reasonable assurance of safety and efficacy for high risk tests with moderate risk tests subject to requirements for evidence of analytical validity and "reasonable belief" of clinical validity. Adverse event reporting required post market and changes that affect clinical impact of moderate or high risk tests could require post market submissions.

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Inside The Diagnostics Industry

HudsonAlpha Institute for Biotechnology Fosters Genomics Research, Education, Clinical Applications and Workforce Development

Richard Myers, Ph.D., HudsonAlpha Institute for Biotechnology

In just eight years, the HudsonAlpha Institute for Biotechnology (Huntsville, Ala.) has grown to be a sequencing powerhouse, ranking among the top laboratories in the world in terms of sequencing volumes and attracting some of the nation's top genetic scientists to its campus. But the institute does not stop at just building a stellar reputation for its research; HudsonAlpha is also on a mission to drive public genomic education, workforce development, and economic growth. *DTET* recently spoke to HudsonAlpha's president and science director, Richard Myers, Ph.D., to learn about the institute's growth and ambitious plans.

"We ask ourselves all of the time. Are we just doing this or do we have metrics that guide us? The answer is a little of both. If you were doing research and you had to meet milestones every day imposed by outside sources, you will just not be as creative and make interesting discoveries."

— Richard Myers, Ph.D.

HudsonAlpha has comprehensive offerings in the areas of research, clinical services, and sequencing support. How do these pieces fit together?

We started HudsonAlpha Institute for Biotechnology a little more than eight years ago with the idea of doing research, teaching, and more recently, clinical medicine all in the same building. The unusual part is that on the same campus we also have for-profit life science companies. Rather than nearby or across town we actually lunch together and run into each other. The idea of our founders was to put it together and see what happens. The companies keep their finances separate and as a non-profit we can do philanthropy, write grants. The idea is that we stew around together to exchange ideas and collaborate. We see that it is really working.

The overarching mission is genomics. The idea of HudsonAlpha is to focus on a very powerful technology, and it is not just machines, but it is a discipline, a way of thinking about things. Instead of looking at one gene and one protein, we cast a wide net and look at all of our genes. Genomics has so many applications that we are not worried about this being short lived. It is decades of research, teaching, clinical work, and the companies collaborating to make discoveries about human health and disease, the environment, forensics, plants, and animals.

With such a broad range of goals, how do you measure success?

We ask ourselves all of the time. Are we just doing this or do we have metrics that guide us? The answer is a little of both. If you were doing research and you had to meet milestones every day imposed by outside sources, you will just not be as creative and make interesting discoveries.

The metrics of success are different in our workforce development, our education and outreach, and our research. One measure of our growth is that from a relatively small

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Inside The Diagnostics Industry

number of scientists we are publishing of a lot of papers in high-impact journals. That is not enough, but that is one measure. I would argue that it is impressive what we are able to do with a modest number of people. It is possible because of the economies of scale resulting from building a genomics infrastructure. Other metrics have to do with reputation of the institute and the scientists.

> *"The vision is that we want to make a major difference in the health of the planet—that is people, animals, plants, and the environment—by applying these tools and learning as much as we can. But then we work to get the knowledge gained from that out there as soon as possible. Education and outreach are a major part of that."*
>
> — Richard Myers, Ph.D.

We are still small, but a measure of success is the number of serious collaborations with 1,000 groups of scientists. A lot of that comes from our Genomic Services Laboratory where we can do outreach because of our marvelous infrastructure and expertise. It is not just the machines and computers, but the expertise of the scientists and our experience. We have developed a reputation of doing it and doing it really well.

Of course the ultimate impact is that it changes medicine or the way we do agriculture in a positive way. Because our research leans towards the applied side we are seeing this. We are seeing tests come out of the discoveries from the research side. Out of the 36 companies over our eight years, so far, six have been acquired in the $60 million to $80 million range. I joke with my Bay Area biotech and venture capital friends that out there that would, maybe, be considered a failure. Not really, of course, but the idea is that we take on problems that are important and that we are in a sweet spot that we don't have to have a $1 billion fund to make it worthwhile here.

A unique aspect of the institute is the emphasis on education. How and why does HudsonAlpha do this?

The vision is that we want to make a major difference in the health of the planet—that is people, animals, plants, and the environment—by applying these tools and learning as much as we can. But then we work to get the knowledge gained from that out there as soon as possible. Education and outreach are a major part of that. We don't just find genes, we do something about that in the clinic, and our Educational Outreach group uses that to train physicians and educate families.

We spend an enormous amount of money—15 full-time people—on education and outreach. That is not just K-12 students, but junior colleges and four-year universities, too. I feel it is very important. We teach the public, and that includes doctors and attorneys, too. This team identifies gaps in education in various groups and figures out with a scientific approach the best way to fill that gap. In this state every 7th grader and most 10th graders are using lessons and materials we developed here. It is now going outside of the state, region, and country.

HudsonAlpha By-the-Numbers

- 29 next-generation sequencers, including Illumina's HiSeq X Ten sequencing system
- 200 faculty and scientists at the institute
- 1,000 international scientific collaborations
- 18,000 annual whole genome sequencing capacity
- $150 million in grants for genomic research, since 2008

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Inside The Diagnostics Industry

> *"We work in partnership with the physicians to figure out what they need to know. Geneticists have been working with physicians for years. But in the past it was for rare genetic disease. Now we are talking about figuring out how use genomics to wisely impact a much larger part of the population. It is early, but it is starting to happen."*
>
> — Richard Myers, Ph.D.

What takeaways are there in your education and outreach for the rest of the genomics industry?

Science and academia and big industry don't do this nearly as much as they should. This is part of our culture. We are more than research. Most scientists would see this as distracting. There are outreach programs in other places, but I am arguing ours is the best in the world simply because of how we built it with long-term legs and it will be here forever. The lessons people can learn from us and the rest of the outreach community nationally is that this is really important. Frankly, I think anybody getting state or federal money for research owes this to the public. If everybody did just a little bit it would demystify genomics. This is not trying to get everybody to be a scientist, although building a workforce is part of the goal, but people need to understand genomics regardless.

How does this outreach impact clinical adoption of genomic medicine?

I taught medical students for years and other than the very few that go into medical genetics and continue to use it; it is a challenge to find the time for students and physicians to learn this. It is a huge challenge to figure out how to get physicians to hear about genomic medicine and incorporate it into practice.

Locally, there are 700 physicians in the Huntsville area, which has about 450,000 people in the city and whole surrounding area. About 10 percent of physicians here deeply embrace genomics and work with us. We work in partnership with the physicians to figure out what they need to know. Geneticists have been working with physicians for years. But in the past it was for rare genetic disease. Now we are talking about figuring out how use genomics to wisely impact a much larger part of the population. It is early, but it is starting to happen.

Part of the physician training is an online tool. The outreach team, with our genetic counselors and research scientists, developed an online tool to show what genomics is. What it can do. What it cannot currently do and what the information means. We also did the same things for families coming in with undiagnosed conditions to get their genomes sequenced. They can go online and see these materials, written in everyday language, before they get here. This model is replicable and can be incorporated with telemedicine. We are still testing it out and we will share it. I predict in two to four years we will go to hospitals and clinics and spread it nationally. It is part of our strategic plan.

Core Laboratories at HudsonAlpha

- **Genomic Services Lab** offers cutting-edge genetic research tools to support academic and commercial partners in their discoveries.
- **Clinical Services Lab** uses whole-genome sequencing to diagnose disease at the Smith Family Clinic for Genomic Medicine.
- **Genome Sequencing Center** specializes in plant genomics.

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■ DTC Test Results Don't Lead to Dramatic Changes in Health Care Use, *Continued from bottom of p.1*

Impact on risk perception and decision making

Consumers buying direct-to-consumer personal genome tests (DTC-PGT) want to believe good news, according to an article published in the September issue of *Nature Biotechnology*. While participants' perception of their personal risk changed after receiving results showing decreased and increased risk, there was an "optimism bias"—with a greater change in perception resulting from good news. Additionally, the researchers found that following receipt of PGT results, consumers primarily seek medical attention in response to large, surprising results.

Despite high-profile regulatory scrutiny of DTC-PGT [see box], there is not much evidence showing how use of these services impacts consumers' medical decision making.

The researchers modeled risk perception as a combination of baseline beliefs and learning in response to genetic news. Health care utilization was assessed as a function of changes in these risk perceptions. Eight conditions were evaluated (Alzheimer's disease, Parkinson's disease, breast cancer, lung cancer, colon cancer, prostate cancer, type II diabetes, and coronary heart disease).

The study included 617 real-world consumers who individually sought out and purchased PGT services from 23andMe before the U.S. Food and Drug Administration (FDA) banned DTC health reports. The participants were enrolled in the Impact of Personal Genomics (PGen) study, a longitudinal study of real DTC genomics customers. Risk perceptions were assessed through surveys at baseline and again six months post results.

The researchers found that participants had a slight "optimistic bias" in perception of baseline risk. This perception varied by condition, but the average level of optimism across the conditions was 42 percent, reflecting below-average risk perception versus an average 19 percent perception of above-average risk.

On average, following receipt of test results, participants updated their risk perceptions. However, the magnitude of this updating was asymmetric, meaning that results showing "good news"—a decreased risk of a condition—led to a significantly bigger drop in risk perception compared to the relative increase in risk perception following the receipt of "bad news" or results showing an increased risk of disease. This pattern in results existed regardless of the participants' initial reason for purchasing the test.

"The significance and modest magnitude of observed risk updating suggests that neither excessive overreaction nor complete disregard for the test results was prevalent in our sample," writes lead author Joshua Krieger, from the Massachusetts Institute of Technology. "A pattern of general and moderately increased

FDA Enforcement Efforts Regarding DTC Genetic Testing

The FDA's concerns about direct-to-consumer provision of genomic analysis received mainstream attention in 2013 with its efforts to stop 23andMe from marketing its Personal Genome Service directly to consumers. The FDA has continued to focus on direct-to-consumer marketing of genomic testing with several letters issued to companies since last year:

- **Pathway Genomics**—(Sept. 21, 2015) The FDA said a non-invasive blood test (which could be shipped directly to patients) screening for up to 10 different cancer types was a high risk test requiring FDA approval.
- **DNA4Life**—(Sept. 21, 2015) The FDA said DNA4Life was improperly marketing its Pharmacogenetic Report directly to consumers when the test constituted a medical device requiring FDA clearance. The test predicted patient response to 120 commonly prescribed medications.
- **Interleukin Genetics**—(Nov. 4, 2015) The FDA said the companies' DTC genetic tests for determining risks for diabetes, heart attack and obesity appeared to be unapproved medical devices.
- **Sure Genomics**—(Feb. 16, 2016) The FDA said the company's SureDNA test was a medical device requiring FDA review—the test was a kit allowing consumers to mail saliva samples for genetic testing to determine disease risk and drug reaction risk.

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The concern, of course, is that receipt of DTC-PGT results will prompt consumers to "self-manage their treatments," including changing doses or abandoning treatment altogether, without consulting a physician or pharmacist.

concern across several conditions did not appear to spark decisions to use medical services, whereas a single higher-amplitude risk perception change increased the odds of engaging in follow-up medical action."

The authors caution that the six-month results regarding follow-up medical action may be conservative, given the likelihood some patients will wait until a routine check-up to raise the PGT test results with health care providers.

Impact on prescribed therapies

A separate study, also involving the PGen Study Group, found that pharmacogenomic results indicating an atypical drug response are common among patients requesting DTC-PGT. Receipt of these results is associated with prescription medication changes, although less than one percent of DTC consumers report unsupervised changes to their prescription medications six months following testing.

The concern, of course, is that receipt of DTC-PGT results will prompt consumers to "self-manage their treatments," including changing doses or abandoning treatment altogether, without consulting a physician or pharmacist.

This study relied on data from 961 new DTC-PGT customers (23andMe and Pathway Genomics) who were enrolled in 2012 and surveyed prior to the return of results, as well as six months after receipt of results. "Atypical response" was defined as pharmacogenomic results indicating an increase or decrease in risk of an adverse drug event or likelihood of therapeutic benefit, the authors report.

The researchers found that 91.2 percent of consumers received at least one pharmacogenomic result indicating atypical drug metabolism—a number consistent with previous estimates. In response to the PGT results, fewer than six percent of participants changed a prescription medication within six months of testing and less than one percent reported making changes without consulting a health care provider.

Takeaway: Studies show the impact of DTC-PGT results on changes in risk perception and on health care utilization among real-world consumers.

Blood Glucose Monitoring Developments Focus on Mobility, Convenience

According to the Centers for Disease Control and Prevention (CDC) more than 29 million U.S. residents have diabetes. The agency also reports that medical costs for diabetics are twice as high as nondiabetics. For the diagnostics industry, these statistics indicate a need for products that can help patients monitor their blood sugar and cope with their diabetes. To better manage the disease, diagnostics are striving to make blood glucose testing more convenient and more mobile.

FDA approves new Bluetooth connected mobile system

In late November, the U.S. Food and Drug Administration (FDA) granted Ascensia Diabetes Care approval to market the CONTOUR® NEXT ONE Blood Glucose Monitoring System (BGMS), a Bluetooth connected meter that connects to a mobile app. The app stores and analyzes blood glucose measurements taken by the meter to help patients monitor and manage their blood glucose. Ascensia announced the FDA approval and indicated it expects to bring the device to market early next year. Here are some details about the system:

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"We believe [this non-invasive technology] is a necessary alternative to the finger-stick approach for people living with type 1 and type 2 diabetes. . . . because up to 66% of diabetics avoid doing the finger-stick testing due to the invasive and painful nature that patients must endure between 4-12 times a day."

— Dr. Ronny Priefer

- App is downloadable from Apple App Store and Google Play
- 95% of results within ±8.4 mg/dL or ±8.4% of laboratory reference values for glucose concentrations < 100 mg/dL or ≥ 100 mg/dL (fingerstick)
- Meter provides results, reminders, alerts
- System includes electronic log for patient to report meals, activities and medication
- Optional cloud-based storage of data
- System facilitates email communication of reports to provider

Breathalyzer affords pain-free monitoring

Also in November, two Western New England University Professors announced development of a hand-held breathalyzer that measures the acetone in a diabetic patient's breath to help monitor blood glucose and determine when insulin is needed. The professors presented research regarding their device at the 2016 American Association of Pharmaceutical Scientists Annual Meeting and Exposition (Denver, CO). Currently the device is the size of a small book but the professors indicate an intent to make it smaller. They hope to have the device available next year.

Dr. Ronny Priefer, one of the developers, indicated in a statement, "We believe [this non-invasive technology] is a necessary alternative to the finger-stick approach for people living with type 1 and type 2 diabetes. … because up to 66% of diabetics avoid doing the finger-stick testing due to the invasive and painful nature that patients must endure between 4-12 times a day."

Monitoring system gives providers visual snapshot

Earlier this fall, Abbott received FDA approval for a new glucose monitoring system, FreeStyle Libre Pro, which provides "a visual snapshot of glucose data, known as the Ambulatory Glucose Profile (AGP)" according to the company. The snapshot reports glucose levels and identifies trends in the levels to help drive treatment. Features:

- Clinicians apply a small, round, self-adhesive, sensor on patient's upper arm
- Sensor remains in place up to 14 days, measuring glucose every 15 minutes via a filament inserted below the skin
- Patient reports to provider after wearing sensor and provider downloads data stored in sensor.

"This novel technology provides a solution to the ongoing challenge of the need for complete and dependable glucose data. This data is imperative for not only the doctor but also for the patient to help them achieve optimal health," said Jared Watkin, senior vice president, Diabetes Care, Abbott.

FDA offers guidance for development of test systems

To ensure safety and efficacy of the devices used to monitor diabetic patients, in October, the FDA issued two new guidance documents relevant to blood glucose test systems:

- Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use
- Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use

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These documents finalize draft guidance provided in 2014 and provide manufacturers suggestions about study type and information that should be submitted in 510k premarket applications for blood glucose devices.

"Together both guidance documents can improve the accuracy and safe use of blood glucose meters, giving health care providers and people affected by diabetes safe and effective tools to monitor and manage their blood glucose levels in health care settings and at home," the FDA said in a statement announcing the release of the guidance documents. "The FDA is also reaching out to health care professionals, people affected by diabetes and diabetes patient advocacy groups to provide these guidance documents and to explain how the adoption of these recommendations by industry will result in improved new devices and ultimately benefit these groups."

With that goal of reaching out to stakeholders in mind, the FDA held a webinar to discuss the guidance documents on Nov. 21, 2016. The FDA indicated that previously, manufacturers of such devices sought over-the-counter clearance but the agency believes that a distinction is necessary between different use settings. These guidance documents thus address variables that can affect accurate use of monitoring devices in the clinical setting and at home. They do not address how the meters should be used or how laboratories should validate the glucose meters. In response to concerns raised by the Centers for Medicare & Medicaid Services and the CDC, both guidance documents emphasize the importance of infection control to avoid transmission of blood borne pathogens.

The agency highlighted the following issues as having been changed or clarified in this final guidance:

- Clinical Laboratory Improvement Amendments (CLIA) clarifications. Monitoring systems cleared for prescription use at point of care won't be automatically CLIA waived but the FDA is sensitive to the need for waived monitors in the point-of-care setting; studies should support both clearance and CLIA waiver.
- Performance goals. For over-the-counter devices the accuracy goals are unchanged but for point-of-care testing, the accuracy goals were reduced

DRAFT	FINAL
99% within +/-10% ≥70mg/dL and within +/- 7 mg/dL <70 mg/dL	95% within +/-12% ≥ 75 mg/dL and +/- 12 mg/dL <75 mg/dL
100% within +/- 20%	98% within +/- 15% >75 mg/dL and +/- 15 mg/dL <75 mg/dL

The guidance documents are available on the FDA website:

- Self-Monitoring Blood Glucose Test Systems for Over-the-Counter Use http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM380327.pdf
- Blood Glucose Monitoring Test Systems for Prescription Point-of-Care Use http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM380325.pdf

The slides presented by the FDA at the Nov. 21, 2016 webinar are available at: http://www.fda.gov/downloads/Training/CDRHLearn/UCM529929.pdf

Takeaway: Industry seeks to make testing easier, less painful and more convenient for clinicians and the millions of patients battling diabetes.

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G2 INSIDER

Continuing Rise of Genetics Highlighted at 34th Annual Lab Institute

Attendees at last month's G2 Intelligence annual Lab Institute (Oct. 26-28, Washington, D.C.) were treated to a history lesson about diagnostics as well as forward-looking discussions that illuminated the current state and the future of the laboratory industry and clinical diagnostics. Speakers noted that increasing diagnostic options also require more education and better resources to help providers and patients understand their options, select the most appropriate diagnostics, and properly manage utilization.

Keynote speaker Mara Aspinall, chief executive officer of Health Catalysts and Executive Chairman of GenePeeks, highlighted how diagnostics will change with the rising importance of genetic testing. She explained that identification of genetic mutations rather than site of a tumor will drive cancer treatment in the future. The future of diagnostics, Aspinall predicted, will involve algorithms and integrated data gathered from multiple sources—in short, "an information business with a wet lab on the side."

Gillian Hooker, vice president of clinical development at NextGxDx, similarly addressed the explosion in the genetic testing market with tens of thousands of tests currently on the market and new genetic tests being introduced every day. NextGxDx research indicates there are more than 65,000 genetic testing products on the market compared to less than 13,000 just three years ago. Hooker addressed challenges providers face in identifying the right test and a need for standardization in terminology not only to simplify ordering but to facilitate coding and reimbursement as well.

Takeaway: Industry leaders indicate the future of diagnostics is patient and data focused.

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G2 Awards Recognize Diagnostics Leaders and Innovators

Mark Ziebarth, G2 Intelligence president and publisher; Analyte Health Chief Executive Officer Dr. Frank Cockerill; and Jack Redding, senior vice president, sales and marketing, for Halfpenny Technologies

During G2's Lab Institute, two leaders were honored for their commitment to the laboratory industry, public service and innovation in diagnostics. Gregory S. Henderson, M.D., Ph.D. was awarded the 2016 G2 Laboratory Public Service Distinguished Leadership Award, sponsored by Kellison & Company, a revenue cycle management solutions company and presented by Kellison's Chief Executive Officer Scott Liff. This award is presented to a diagnostic laboratory industry executive exemplifying the traits of leadership, excellence, and service to the industry. Dr. Henderson was named President of BioReference Laboratories, a division of OPKO Health, Inc. in March 2016. Previously, he guided business growth and operations of one of the largest laboratory outreach programs in the United States, served on a team charged with rebuilding healthcare infrastructure in New Orleans after Hurricane Katrina, co-developed the first cloud based anatomic pathology information system, and founded a company that leverages cloud technology solutions to provide digital pathology consultations that afford access to quality diagnostics in the developed and developing world.

Dr. Frank Cockerill, Chief Executive Officer of Analyte Health received G2 Intelligence's Lab Innovation Award, designed to recognize innovation in the field of diagnostics. The award, sponsored by Halfpenny Technologies Inc., was presented by Jack Redding, Halfpenny's senior vice president, sales and marketing. As CEO, Cockerill is leading Analyte Health in pioneering online diagnostic services aimed directly to consumers. Cockerill previously led the Department of Laboratory Medicine and Pathology at Mayo Clinic and was Chief Executive Officer of Mayo Medical Laboratories, a global reference laboratory operating within Mayo Clinic. He was also the Ann and Leo Markin Professor of Microbiology and Medicine at the Mayo Clinic College of Medicine, having extensive experience and expertise in infectious diseases and antimicrobial resistance.

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