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FDA Moving Cautiously on Lab-Developed Tests

The issue of what to do about lab-developed tests (LDTs) is a thorny one that has vexed both the industry and the Food and Drug Administration (FDA) for years. While the FDA has made clear that it plans to exert its discretionary authority over LDTs, the agency is taking a cautious approach in deciding exactly how to enforce oversight.

The topic was the subject of a lively discussion at Washington G-2 Reports' 28th annual Lab Institute this fall, where the head of FDA's Office of In Vitro Diagnostic Device Evaluation and Safety stressed that the LDT oversight process is one that will take a while to develop and will be done with input from both the industry and consumer groups.

The discussion continued Nov. 22 at a meeting in Washington, D.C., convened by the American Clinical Laboratory Association (ACLA), where stakeholders gathered to discuss the best approach to developing a regulatory framework for LDT oversight. For more on this story, see our special focus piece starting on p. 5.

Extensions Urged for Pathology Grandfather Protection, Other Expiring Medicare Policies

Fourteen leading health care provider groups, including the American Clinical Laboratory Association (ACLA) and the College of American Pathologists (CAP), have appealed to Democratic and Republican leaders in the House and Senate to take immediate action to extend a host of Medicare policies that expire Dec. 31.

Two of the policies are laboratory-specific: an extension of the pathology "grandfather" protection and an extension of reasonable cost reimbursement for clinical lab services provided by certain small rural hospitals.

The provider groups made their appeal in a Nov. 1 letter to Senate Majority Leader Harry Reid (D-Nev.) and minority leader Mitch McConnell (R-Ky.) and House Speaker Nancy Pelosi (D-Calif.) and John Boehner (R-Ohio), minority leader.

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▲ **Extensions Urged,** *from page 1*

The expiring policies also affect the physician fee schedule, ambulance services, the exceptions process for therapy caps, and extensive rehabilitation services needed to return Medicare beneficiaries to their homes and communities.

There is a chance that the extensions could be attached to an SGR fix before the lame-duck session adjourns in early December. Otherwise, they would be taken up again when the new Congress opens in January. Provider groups advocate extensions of at least through 2011, retroactive to Jan. 1. CAP and ACLA, while calling for an extension of the pathology grandfather protection for at least a year, support making the protection permanent.

Failure to pass legislation to extend these various Medicare policies, the provider groups said in their appeal to congressional leaders, "will prompt limited access to services for beneficiaries in rural and other underserved areas, payment cuts to health care professionals, as well as the creation of an unsustainable health care environment."

There is a chance that the extensions could be attached to an SGR fix before the lame-duck session adjourns in early December. Otherwise, they would be taken up again when the new Congress opens in January.

The groups backed an extension under the Part B physician fee schedule "of the floor on geographic adjustments to the work portion of the physician service through the end of 2010, with the effect of increasing practitioner fees in rural areas. It also would provide immediate relief to areas negatively impacted by the geographic adjustment for practice expenses and require the secretary of HHS to improve the methodology for calculating practice expense adjustments."

The pathology grandfather protection allows independent clinical labs to bill Medicare Part B directly for the technical component (TC) of anatomic pathology services to hospital inpatients and outpatients. It expires Dec. 31, and the Centers for Medicare and Medicaid Services (CMS) has declared its intent to eliminate such billings after that date.

CMS has long advocated this policy change, contending that the TC is reimbursed through the hospital's prospective payment and the lab should seek payment for the service from the hospital, not Part B.

Congress has repeatedly blocked the agency from moving ahead by enacting a series of short-term extensions of the "grandfather" protection, most recently last year by approving a one-year extension, through Dec. 31, 2010. The protection is of special benefit, advocates say, to rural hospitals that cannot afford to perform the pathology work in-house but must send it to an outside clinical lab.

The grandfather protection applies to hospital-lab arrangements in effect as of July 22, 1999, the date when CMS first proposed to eliminate such billings. Further, it applies to the hospital, not the lab, CMS has ruled. Hospitals may switch labs without forfeiting the protection; however, independent labs cannot switch hospitals and still be protected. The TC of pathology services includes anatomic services, cytopathology, and surgical pathology.

Department of Justice Files Brief Opposing Gene Patents
Position at Odds With USPTO, NIH

In an unexpected move the U.S. Department of Justice (DOJ) has filed a brief opposing gene patents in a case that has ramifications for the diagnostics industry.

The brief was filed in *Association for Molecular Pathology, et al. v. U.S. Patent and Trademark Office, et al*., a case challenging the legality of the BRCA gene patents held by the Utah Research Foundation and exclusively licensed to Myriad Genetics (Salt Lake City) to test for increased risk of breast and ovarian cancer.

The case is on appeal to the U.S. Court of Appeals for the Federal Circuit after Judge Robert Sweet of the U.S. District Court for the Southern District of New York in March issued a summary judgment invalidating some of Myriad's patents (*DTTR, May 2010, p. 1).*

The DOJ's amicus brief stated that "isolated human genes, without further modification, are a product of nature and do not constitute patent-eligible subject matter. . . . Common sense would suggest that a product of nature is not transformed into a human-made invention merely by isolating it," the government argued. "The very term—isolated—suggests only that extraneous matter has been separated from the natural product of interest, not that the product itself has been transformed or altered into something man-made."

Acknowledging that its position runs "contrary to the longstanding practice of the Patent and Trademark Office, as well as the practice of the National Institutes of Health and other government agencies that have in the past sought and obtained patents for isolated genomic DNA," the DOJ said that it is not against all gene-related patents.

"New and useful methods of identifying, isolating, extracting, or using genes and genetic information may be patented (subject to the prohibition against patenting abstract ideas), as may nearly any man-made transformation or manipulation of the raw materials of the genome, such as cDNAs," the government added. "Thus, the patent laws embrace gene replacement therapies [and] engineered biologic drugs."

A Supreme Court ruling in June in the case of* Bilski et al. v. Kappos *addressed method patents but raised more questions than it answered (*DTTR, July 2010, p. 1*). Given the opportunity to define the scope of patent law to take into account emerging technologies, the high court allowed business method patents to survive, although the extent of the patent protection remains unclear.

In its brief, Myriad holds that the court's findings were "erroneous." Myriad, supported by briefs filed by other industry representatives, warned that if upheld, the ruling "would have far-reaching negative consequences" for the biotechnology industry.

While the U.S. Patent and Trademark Office is currently maintaining the status quo, John Conley, an intellectual property lawyer at Robinson, Bradshaw & Hinson (Charlotte, N.C.) says that advances in technology and the growing use of multiplex testing is making patents on individual genes a hindrance to innovation.

"I think the reaction is overwrought. Isolated individual gene patents are declining in importance anyway," says Conley. "The other side of this case that has received less attention, but is more important, is challenging the method patents. . . . It is very important, and the justice department didn't address it."

Pharmacy-Based Program Increases Warfarin and Tamoxifen Testing Rates

A pharmacy-based genetic testing program appears to significantly increase the utilization of testing for patients newly prescribed warfarin and tamoxifen, according to a new study. The data, presented in early November at the annual meeting of the American Society for Human Genetics, provides a model for how pharmacogenetic testing can be implemented on a more widespread scale, potentially expanding the use of personalized medicine in routine clinical practice.

Researchers from Medco Research Institute, a subsidiary of Medco Health Solutions Inc. (Franklin Lakes, N.J.) analyzed data from the ongoing clinical testing program the company initiated in 2008. They found that with the initiation of a coordinated testing program, the incidence of pharmacogenomics testing in patients prescribed warfarin was 45 times higher and testing in patients prescribed tamoxifen was seven times higher than rates prior to the program.

Benchmark analysis conducted by Medco, in collaboration with the Food and Drug Administration (FDA) in 2008 (prior to the implementation of the testing program), found that just 1.7 percent of patients taking warfarin and 2.3 percent of patients taking tamoxifen received genetic testing in routine practice.

"The predominant view of pharmacogenomics testing has been that in theory it's a very good thing, but it's not practical for widespread use at this point in time," said Eric Stanek, PharmD, the study's lead researcher. "This study proves, given the right process, physicians are ready to put it into practice, as are their patients."

The program utilized the capabilities of a national pharmacy benefit manager and included identifying appropriate patients for testing from a prescription database in "near-real time," educating physicians and patients about the genetic tests and gaining their consent for testing, coordinating the collection and shipment of DNA samples from patients using a home-based self-collection method to a partner laboratory, and communicating and interpreting results to physicians. The full cost of the service and genetic tests were covered by the patients' prescription drug benefit plan.

"Outside the auspices of programs like this there is no real coordination. It is not convenient, people don't know their options, and [testing] just doesn't happen out there," says Stanek, senior director of personalized medicine research at Medco. "By doing this under a pharmacy befit plan it takes down one of the major barriers—insurance reimbursement." More than 4,200 physicians participated in the warfarin testing program, and more than 1,500 physicians participated in the tamoxifen program.

"We found that, in general, for prescribers and patients in half of the instances consent is provided. In clinical medicine that is quite on par with any elective testing," says Stanek. "If [patients] know what is available to them, the process is convenient to prescribers, patients, and laboratories, you give them the information to help make decisions, and it all comes together in one package, they will opt for it and act on it."

Labs Urge Caution as FDA Moves Forward on Lab-Developed Test Regulation

The evolving policy of the U.S. Food and Drug Administration (FDA) toward laboratory-developed tests (LDTs) emerged as one of the hottest topics at Washington G-2 Reports' 28th annual Lab Institute, held Oct. 13-15 in Arlington, Va. A lively panel discussion provided insight into how the FDA is approaching the issue as well as how clinical laboratories and other stakeholders view increased regulation of LDTs in the wake of the two-day public meeting convened by the FDA in July.

The FDA's move to actively regulate this class of in vitro diagnostics (IVDs), which are manufactured and offered within a single clinical laboratory, is a response to public health risks created by LDTs that may not provide a reasonable assurance of safety and effectiveness.

During the Lab Institute panel, Alberto Gutierrez, Ph.D., director of the FDA's Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD), emphasized that the agency is still in the phase of gathering ideas and having discussions after extending its public comment period to Sept. 15. "We're working through the comments and figuring out where we go from here," he said. "What we hope to do fairly soon is set a framework so people understand what the process [of regulating LDTs] is, how long it is going to take, and whether it would affect them. We would hope to put that framework together fairly soon, so that people can plan and have an idea whether this is going to affect them. It may not."

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>
> ***–Alberto Gutierrez, FDA***

When pressed for a more specific timeline for proposed regulations, Gutierrez demurred. "Whatever we do, this is a long-term process," he explained. "We will likely put our thoughts together, including publishing the comments that we have received and giving answers specifically to the comments." And the dialogue will be ongoing. "We'll put together our ideas and then everybody will have a chance to comment on those," said Gutierrez. "This is not going to be a short process in any way, and it's going to give plenty of opportunity for everybody to comment and have their voices heard."

Some widespread views of the clinical laboratory community were voiced by another panelist, Ron Weiss, M.D., staff hematopathologist at ARUP Laboratories (Salt Lake City) and a past chairman of the board of the American Clinical Laboratory Association (Washington, D.C.). "Many people, myself included, believe that there clearly is a group—a small group—of laboratory-developed tests that really deserve an enhanced approach to regulatory oversight and one that's risk-based and clearly would be at the highest level of risk to patient safety," he said.

A broad-based approach would pose significant logistical challenges to the agency and its limited resources. Weiss offered ARUP, a high-complexity and CLIA-certified laboratory, as an example. "We have a test menu of perhaps 2,000 different tests, and depending upon how you define a laboratory-developed test, that may encompass anywhere from 40 to 50 percent of our entire test menu," he said. "So

we're talking about hundreds if not a thousand different tests."

Also supporting a risk-based approach to LDT regulation is Genetic Alliance (Washington, D.C.), a nonprofit health advocacy group with a network of approximately 1,000 disease-specific advocacy organizations. "What we want to see is that risk be the basis for the [regulatory] decision rather than the technology," said Sharon Terry, president and CEO of Genetic Alliance. "We're really hoping that technology changes and changes fast and that we not make any decision based on the complexity."

"What we want to see is that risk be the basis for the [regulatory] decision rather than the technology."
–Sharon Terry, Genetic Alliance

Concerns that the technology employed by a test would figure prominently into regulatory decisions about LDTs are rooted in the FDA's 2006 draft guidance concerning in vitro diagnostic multivariate index assays (IVDMIAs), a term coined by the agency to refer to tests that incorporate multiple biomarkers and a computer algorithm that is used to analyze the set of test results. The agency has since decided not to issue final guidance on IVDMIAs.

Terry emphasized that the FDA should focus first on the value of test results. "We want to say what is that information being used for and then the context in which that information is being used is much more critical than whether I did it by a simple assay or something more complex," she noted. "I'm not saying that a complex technology shouldn't also be assessed in the evaluation of risk, but that it shouldn't be the sole source."

The FDA agrees that a risk-based approach is the only logical way to proceed. "Our law in medical devices is risk-based," said Gutierrez. "We actually regulate based on risk, so those devices that are the riskiest go through the most thorough review and post-market controls. The devices that are moderate-risk go through less, and all they have to show usually is that they're equivalent to something that is out in the market. And those that are low-risk don't even come to the agency for review. They tend to just have to follow general controls that the agency has published, essentially requiring good manufacturing practices."

In fact, one of the factors that led the FDA to consider stepping up regulation of LDTs is the agency's historically anomalous approach toward this group of tests. "One of the issues that we have with laboratory-developed tests has been that since we started exercising enforcement discretion, based on a law passed in 1976, it is not risk-based," Gutierrez said. "So it makes for a very different type of regulation than what we have for the rest of in vitro diagnostics."

Commercially distributed tests and LDTs now take divergent paths to market. The proportion of tests taking the LDT route, which does not require FDA submission, has climbed in the past 10 to 15 years, and the volume and variety of LDTs has grown exponentially.

However, many believe that there are good reasons for this bifurcated approach. "The difference between a laboratory-developed test and an in vitro diagnostic, in my mind, is that in vitro diagnostic manufacturers develop, design, manufacture, package, market, sell, and distribute diagnostic kits across the United States.

They're designed to be stored and then used in a variety of different settings," said Weiss. "Laboratory-developed tests are a medical service that's developed under the auspices of the laboratory medical director under CLIA and is really a way in which that laboratory can, with relative speed, deploy new technology as a medical service."

Weiss highlighted what he views as the distinction between practicing medicine and manufacturing a diagnostic kit, but that distinction has become increasingly blurred. Commercially offering LDTs through a CLIA-certified laboratory created specifically for that purpose is now frequently used as a mechanism for market entry, allowing novel tests to reach the national market without going through the FDA. Closing this loophole, which allows what the FDA views as "preliminary medical data" to be packaged as medical information, is among the key goals of a revamped regulatory approach.

"Part of the reason the agency began giving laboratory-developed tests enforcement discretion was that there was recognition that laboratories had some oversight through CMS and CLIA, and that they tended to be run by physicians," said Gutierrez. "They tended to be a service to a limited set of patients that they had a relationship with." He contrasted that to the current market landscape, dotted with laboratories that offer a single LDT. "They tend to get samples from all over the United States. They tend not to have a relationship in any way with the patient they're dealing with," he said. "They also tend to advertise and have proprietary data that nobody can necessarily evaluate. It's a different beast all together, and it's very difficult to deal with laboratories like that."

Now the challenge is to leverage the infrastructures of the FDA and CMS to effectively address LDTs. "We have looked carefully as to what CLIA regulates and where would the FDA actually be able to use some of that, and that's part of the discussion," said Gutierrez. "We look forward to working closely with CMS."

Many stakeholders, including the College of American Pathologists and AdvaMed, have suggested using third-party accrediting organizations to assist in carrying out LDT regulation. This appears to be an option that FDA is still considering. "I think that there is a lot of room here for collaborating and for synergy, whether with CMS or the accredited bodies that work through CMS," Gutierrez said. "There is a lot of expertise out there on laboratories that the agency could tap." Existing programs within FDA allow third-party organizations to conduct reviews and inspections.

Finally, the agency remains flummoxed by the lack of information surrounding LDTs. "One of the biggest issues that we have is that there is really no good accounting of what tests are out there," said the OIVD director. "It makes it very difficult for us to actually get our hands around the issue in any form. So a database of some kind that actually has the type of laboratory-developed tests that exist out there is going to be necessary before we can begin to think about how to tackle the problem."

The Genetic Testing Registry (GTR) that is being compiled by the National Institutes of Health (NIH) will offer a starting point. The public database would allow researchers, consumers, health care providers, and others to search for information

submitted voluntarily by genetic test providers, including clinical laboratories, test manufacturers, and entities that report and interpret tests performed elsewhere.

Genetic Alliance has championed the GTR, which is slated to debut in 2011. "We understand the need to make it voluntary in the beginning, but we do believe it should be mandatory, and we look forward to FDA and NIH having conversations about whether or not that registry could serve the need of FDA for more information," said Terry.

The New World of Laboratory Medicine

The world of diagnostics is changing, and clinical laboratories and pathologists need to embrace the ongoing evolution if they want to stay competitive in today's marketplace. That was the message of one of the keynote speakers and thought leaders at Washington G-2 Reports' 28th annual Lab Institute conference, held in Arlington, Va., Oct. 13-15.

Richard Friedberg, M.D., Ph.D., chairman of the Department of Pathology at Baystate Health in Springfield, Mass., and deputy chairman of the Department of Pathology at Tufts University School of Medicine, noted that the evolution of today's diagnostic environment is marked by six primary trends:

1 **Discrete to Multiplex**. This is most evident in clinical pathology (CP), where the field has moved from conducting single tests to conducting multiple tests on a single platform.

2 **Structural to Functional**. This is best evident in anatomic pathology (AP), where the field has moved from simply identifying parts of cells to determining the function of different parts of cells.

3 **Qualitative to Quantitative**. In immunohistochemistry, stains are becoming assays as pathologists use computer alogorithms to quantify them.

4 **Analog to Digital**. Similar to what happened in radiology years ago, pathology is now moving from analog (glass slides) to digital pictures of slides and ultimately to actual digital images.

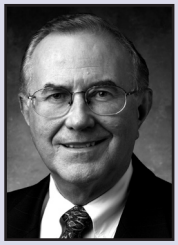
5 **AP Evolution Mimicking CP**. Anatomic pathologists are now more concerned with analytical precision, reproducibility, accuracy, specificity, and reliability.

6 **AP Evolution Mimicking Radiology**. Analog images established the field, market and technology forces drive digital imaging, and digitization allows new applications. This all has significant workload and throughput implications.

The traditional pattern recognition fields of anatomic pathology and radiology are changing, explains Friedberg. Both are now becoming more quantitative with an increased focus on precision, accuracy, reliability, and measurability. "Once information becomes digital, integration shifts into high gear and things really take off. That's where we are getting to be in the world of traditional anatomic pathology."

Cepheid Succeeds With Testing for Health Care Associated Infections

Next Focus Is Testing for TB, Sexually Transmitted Diseases



John Bishop, CEO

Cepheid, based in Sunnvale, Calif., is an on-demand molecular diagnostics company that develops, manufactures, and markets fully integrated systems and tests for genetic analysis in the clinical, industrial, and biothreat markets. The company has strong focus on developing tests for infectious diseases. To learn what's driving growth in the company's clinical diagnostics segment, *DTTR* recently spoke with CEO John Bishop.

What has Cepheid accomplished this year?

We have had very significant growth in the sales of our clinical products—growing in the area of 40 percent throughout the year. This has happened as a result of ongoing expansion with placement of our systems in the marketplace in the face of continuing capital constraints, both in the United States and Europe. In addition, we've had very significant growth of our tests. The company has already achieved the position of market leader relative to products involved in that area of health care associated infections (HAI). Now we're aggressively growing outside of HAI products.

Recently we've had two significant events. One, a study published in the *New England Journal of Medicine* involving our TB products used outside of the United States. Some quotes indicated the product could potentially revolutionize the management of TB around the world. Secondarily, we announced collaboration with Novartis in the field of leukemia. The BCR-ABL test is on the market in Europe to monitor patient response to therapy. So a big aspect of that is a more standardized test result as compared to the variable results obtained on lab-to-lab basis with home brew of BCR testing. Additionally, we continue to execute on our product pipeline.

How are you going to grow your clinical offerings in the next few years?

Coming into 2011, [we're working on] the flu product. Although for the 2011 season, flu is not a big focus item which is, frankly, good news for the general population. We are not seeing much of a flu season developing out there. That was certainly the experience in the southern hemisphere and, therefore, might translate to a mild flu season in the United States.

Beyond that, the key product we are working on is our first sexually transmitted diagnostic product—the CT/NG (chlamydia/gonorrhea). We anticipate CT/NG to get to FDA (the Food and Drug Administration) and potentially on the market toward the end of next year and on the market in Europe a little earlier through CE. Hospitals, particularly in view of [the] slowdown in the economy that has occurred, want to bring testing in-house as much as possible instead of sending it outside. . . . As our install basis has grown we are seeing a number of accounts asking what else can we put on the GeneXpert system, and CT/NG is a key item of interest.

The next area we are really flushing out is women's health care. In the 2012-2013 time frame [we're working on] the Vaginitis panel. It is a significant issue for

women and is substantially increasing in incidence. Trichamonas is included and HPV are key products in that area. [Also in that midterm time frame we'll be] moving TB [testing] into the United States and, importantly, moving aggressively into the virology area. For [those who are] immune-compromised, we're looking at a qualitative HIV and HCV.

Cepheid at a Glance

Headquarters: Sunnyvale, Calif.

- Expected 2010 total revenue: $207 million to $210 million
- Clinical diagnostics approximately 80 percent of total revenue
- 1,730 GeneXpert systems in use worldwide
- Xpert test menu includes nine tests in the United States and 13 tests worldwide
- Nasdaq: CPHD

A key trend, we believe, is that the market will want to consolidate menus into one or two platforms to further reduce the overall cost of running the tests. . . . That is a key focus for us. We expect to be a key leading industry consolidator of menus.

What other trends do you see affecting the future of the laboratory and diagnostics industries?

One other very significant trend is a broader dissemination relative to the delivery of health care and will include diagnostics. Historically, diagnostics were concentrated into the hospital laboratory environment. . . . With diseases becoming [drug] resistant and at the same time, in many, becoming more virulent, there is a heightened need to get results substantially faster and to be able to simultaneously identify whether you are dealing with drug resistance or not, so you know how to better effectively manage those patients. As a result, that is going to mean you want to bring the benefit of getting that information closer to the patient. . . . We expect you are going to see . . . an increasing volume and varying types of tests done on an increasingly disseminated basis right in physician offices, outpatient surgical centers, and urgent care centers.

People have been interested, at some level, in dissemination of testing for years, but that was complicated because the technologies of their day were limiting. . . . The technology exists today so that you could get a very accurate determination with a very inexperienced individual and you can rely on those results.

Has the industry begun to understand effects of health care reform?

Yes and no. Right now generally there are a lot of implications of health care reform that are not necessarily positive. The excise tax, enacted as part of that reform package, is highly problematic. The good news for us is we are starting to be profitable. However, there are a number of companies when you are looking at innovations in health care that are out there developing new products and new technologies and obviously they are not yet making a profit . . . and the excise tax [hurts] those companies. That is not helpful for innovation of new technologies.

One of the positive aspects of reform is in fact the focus on comparative effectiveness. One of the things that is very helpful with the initiative is looking at the total cost of delivery of health care on a holistic basis. Up until this point it has primarily been looked at [as] individual parts. As a result, you have people making, frankly, bad decisions as they look at their costs in a silo versus looking at the total cost of health care. So you may end up paying more for a diagnostic, for example, but you end up bringing down the total cost of the health care. That aspect is certainly a positive.

Making the Case for Removing Antiquated Tests From Lab Menus

It is time to remove antiquated tests from laboratory menus, according to a paper published in the September issue of the *American Journal of Managed Care*. Extending the paper's findings into a collaborative effort between medical staff and laboratory directors will allow for the creation of streamlined test menus offering the most appropriate tests, eliminating unnecessary services, and overall improving the effectiveness of laboratory medicine.

Reviewing existing literature, the authors gathered published evidence demonstrating 10 laboratory tests' limited diagnostic and clinical utility. Subscription trends from the College of American Pathologists (CAP) Proficiency Testing Program were used as a surrogate for test volume to examine trends of clinical utilization of these selected tests.

Trend in Enrollment in CAP Proficiency Surveys

TEST	CK-MB	L/S Ratio	ACID PHOSPHATASE	RBC FOLATE	ESR
1996	3234	262	372	-	-
1999	3531	189	274	355	4114
2010	2741	49	35	236	3513
% decline from peak	22%	81%	91%	34%	19%

Source: College of American Pathologists, Proficiency Testing Program

Kinase-MB (CK-MB), myoglobin, serum folate and red blood cell folate, amylase, lecithin/sphingomyelin (L/S) ratio, qualitative serum human chorionic gonadotropin (hCG), prostatic acid phosphatase, bleeding time, and erythrocyste sedimentation rate (ESR) were selected for examination as they are considered antiquated by most clinical laboratory experts, despite the fact they remain in clinical practice.

"There are many hundreds of antiquated tests. We found the most commonly in use, where change is needed," explains lead author, Alan Wu, Ph.D., professor of laboratory medicine and laboratory director of the toxicology chemistry lab at the University of California, San Francisco. "Lab menus are based on history. You start out doing so many tests. We suggest as you add on, think about removing some."

Many of the examined tests date back to the 1970s, and even beyond. Advancements in testing technologies and discoveries of additional analytes have called their clinical utility into question.

Newer analytes such as troponin, prostate-specific antigen (PSA) and C-reactive protein have replaced CK-MB, myoglobin, and lactate dehydrogenase, prostatic acid phosphatase, and the erythrocyte sedimentation rate, respectively. Improvements in testing technologies make bleeding time, the lecithin/sphingomyelin ratio, and amylase testing redundant or obsolete. Additionally, supplementation of dietary folic acid in the United States and Canada reduced the need for folate testing.

"We make changes, obsoleting tests for two reasons: changes in the pathway of clinical diagnosis, the test results are no longer valuable in diagnosis, or because there is

a better way of testing—technological changes for example," says Ilke Panzer, senior vice president, diagnostic lab, at BloodCenter of Wisconsin.

While laboratory directors may understand the benefits of removing obsolete tests, based both on financial motivations and clinical utility, they must be able to collaborate effectively with the clinical staff to make alterations to a menu. Educating clinicians is key to changing referral habits.

"It is not easy because the physician mindset has been whatever they have wanted, they get. There has never been a question about whether it is useful," says Wu. "Plus it is a business. If a reference lab is denying testing, it will lose money and business."

Additionally, the rapid advancements in diagnostic technologies have made it a challenge for clinicians to stay abreast in a rapidly evolving field.

"With the human genome project it is clear there is so much we don't know. Genetically, there is so much research and there are new insights every minute. It is a deluge coming at clinicians," says Panzer. "The question is how do they sort through the information and how will they stay current?"

Both Wu and Panzer agree it is incumbent upon the laboratory to provide education. The BloodCenter of Wisconsin is in the early stages of implementing a lab education program for referring physicians.

"It really comes down to what is the clinical use of the test," says Panzer. "It comes back to education. From a clinician perspective, how to make the best decision for the patient should be the guiding force. That will set the tone for the lab industry as well."

The authors emphasize that collaboration is necessary for the field of laboratory medicine to develop effective testing pathways to ensure that testing is based on evidence-based medicine and not simply tradition.

Wu acknowledges that change is slow even in his own lab, but he hopes this paper will serve as an educational platform for laboratory directors to initiate conversations with their clinical colleagues.

"We wrote this paper to provide ammunition for labs thinking about doing this," he says. "Now they can cite to a peer-reviewed publication. None of the concepts are new, but we compiled them in the same document with objective evidence."

Supreme Court to Hear Case on Universities' IP Rights in Federally Funded Research

The U.S. Supreme Court has agreed to hear a patent rights dispute involving Stanford University and Roche Molecular Systems (Pleasanton, Calif.) The case could redefine current understanding of the Bayh-Dole Act, a statute that allows federal contractors to retain title to inventions developed with federally funded research and casts doubt on the rights to hundreds of billions of dollars of federally funded research conducted over the past 30 years.

A Stanford scientist, Mark Holodniy, performed some of his research at Cetus Corp. (Berkeley, Calif.), a private biotechnology company. Holodniy's team's research even-

tually led to three patents being issued to the university for detecting HIV viral load levels in a patient's blood using polymerase chain reaction (PCR).

In 1988 Holodniy signed a "Copyright and Patent Agreement" that would assign the rights to his inventions to Stanford, his employer and contractor for the federally funded research. In 1989 he signed a "Visitors Confidentiality Agreement" assigning any inventions resulting from his collaboration to Cetus. Cetus was later acquired by Roche in 1991. The case centers on whether Holodniy, in fact, had the power to assign his rights to Cetus.

Stanford first filed this suit in 2005 alleging Roche infringed upon the three patents by selling a PCR-based test kit that used the contested technology. In 2008 the U.S. District Court for the Northern District of California ruled Stanford had superior claim to the patents but invalidated them based on obviousness. Both parties appealed.

"In 2009, the Federal Circuit ruled that Roche had an ownership interest in the patent. Therefore Stanford lacks standing for suing Roche for infringement. Roche believes that the Federal Circuit's decision was correct and should be upheld," Roche wrote in a statement to DTTR.

In appealing to the Supreme Court, Stanford, supported by briefs from other universities and the U.S. solicitor general, argues that Bayh-Dole supersedes an individual's rights to grant ownership to an invention.

"The court of appeals erred in holding that an individual inventor may contract around the Bayh-Dole Act's framework for allocating ownership of federally funded inventions," said the Obama administration in an amicus brief filed in November.

Stanford is expected to file a brief in the case in December and the court is anticipated to hear the case in March.

Health Diagnostic Laboratory Sees Tremendous Growth With Novel Disease-Management Model

Tonya Mallory, President and CEO

Richmond, Va.-based Health Diagnostic Laboratory Inc. (HDL) doesn't just provide lab tests. It is changing the way clinical laboratories do business, and it seems to be working.

HDL Inc. uses a "comprehensive systems biology approach." In addition to providing testing services, HDL also provides patients access to free disease-management services in the hopes of improving compliance with treatment plans and ultimately reversing the increasing incidence of chronic diseases.

"We have a very unique approach. We are a disease-management company with lab testing," says Tonya Mallory, president and CEO of HDL. "The current medical system is backwards. A patient goes to the hospital with an event and receives a diagnosis. But, patients had [the condition] years and years before the event. We form a partnership between the doctor and the patient. Where is the patient on the continuum and what can we do to reverse the disease and prevent the event?"

Both physicians and patients appear to be buying in to this new model. HDL is growing at an astonishing 8 percent a week, says Mallory. The company recently announced that

it is undertaking a $4.2 million expansion at its headquarters in Virginia BioTechnology Research Park that will increase clinical laboratory space to 42,000 square feet and will increase its patient-consulting capacity. The project will create 213 new jobs.

HDL has expanded into 19 states, primarily concentrated in the Southeast's "obesity belt." Testing services are focused on cardiovascular disease, metabolic syndrome, diabetes, and fatty liver disease, with plans to expand into oncology and autoimmune diseases in the future.

HDL at a Glance

Year Founded: 2008

Headquarters: Richmond, Va., presence in 19 states

Employees: 151

Patients Under HDL care: 250,000

Patients Receiving Disease Management Coaching: 5,000

Physician Partners: 2,500

"We are growing rapidly because this approach is common sense," says Mallory. "With cutbacks for reimbursement and insurance, physicians are squeezed to see more patients to make the same income. They don't have the opportunity to educate patients and see about compliance. We fill that gap."

Gen-Probe Sees 8 Percent Growth and Is Poised for More

Gen-Probe Inc. (San Diego) expects 2010 total revenue to top $541 million. Its third-quarter revenue was up 8 percent over a year ago to $132.6 million. Growth was driven by solid blood screening sales and increases in clinical diagnostics sales, particularly in women's health and with the addition of Prodesse products.

The company has completed a year of robust filings, with a total of five Food and Drug Administration (FDA) submissions expected by the end of the year. If approved, the new products are anticipated to jump-start "an important new sales growth cycle for the company."

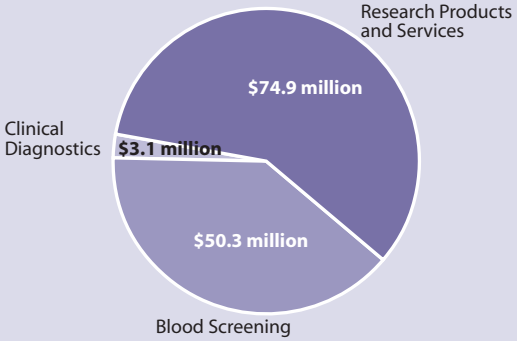
Gen-Probe at a Glance

Headquarters: San Diego

Third-Quarter Revenue: $132.6 million (up 8 percent over one year ago)

Estimated 2010 Total Revenue: $541 million to $546 million

Product Sales (third quarter)



This fall Gen-Probe (Nasdaq: GPRO) filed a Premarket Approval (PMA) for the PROGRENSA PCA3 product, the first urine-based molecular diagnostic assay for prostate cancer. The company filed a 510k submission for the APTIMA Trichomonas vaginalis assay on the TIGRIS system, which can be used with the same samples for existing APTIMA chlamydia and gonorrhea tests. The APTIMA Trichomonas vaginalis assay is already CE marked for sale in Europe. Additionally, the company filed a 510k for a Prodesse assay to detect adenoviruses in the linings of the respiratory tract.

"We have already filed four U.S. regulatory applications this year, a level of productivity that far exceeds our recent past, and the PMA for our APTIMA HPV assay is expected to be submitted within the next month," the company's president and CEO, Carl Hall, told analysts on an investor conference call. "[We] continue to have confidence in Gen-Probe's trajectory, as we should see increasing benefit from our pipeline."

IVD Stocks Gain 3%; OraSure, Abaxis Boosted by Quarterly Results

The G-2 Diagnostic Stock Index rose an average of 3 percent in the three weeks that ended Nov. 19, with 11 stocks up in price, six down, and one unchanged. The G-2 index is also up 3 percent since January, while the Nasdaq has gained 9 percent and the S&P has gained 5 percent over the same period.

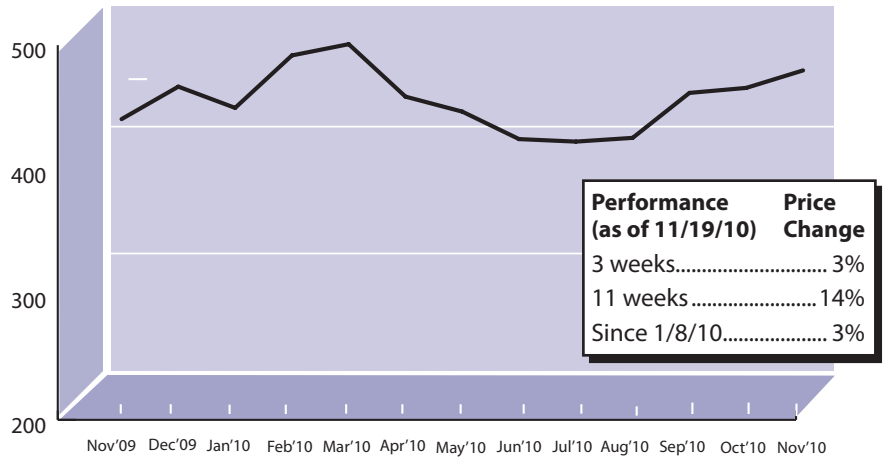
OraSure Technologies (Bethlehem, Pa.) was up 10 percent to close at $4.49 per share with a market capitalization of $233 million. The oral fluid diagnostics company recently announced that revenue and net income for the most recent quarter exceeded guidance. Management attributed the stronger-than-expected performance to increased sales of cryosurgical systems and insurance risk assessment products, offset by decreased sales of substance abuse testing products.

"We also made good progress on our clinical programs in support of a finger stick whole blood claim and CLIA waiver for our OraQuick [hepatitis C virus] test," said OraSure President and CEO Douglas A. Michels. On Nov. 22, the U.S. Food and Drug Administration (FDA) granted an investigational device exemption (IDE) for OraSure to conduct the final phase of clinical testing for FDA approval of its rapid HIV test for sale in the over-the-counter market.

Also gaining ground in recent weeks was **Abaxis** (Union City, Calif.). Shares in the point-of-care test manufacturer gained 9 percent to close at $26.16 per share with a market capitalization of $604 million. Abaxis recently announced record quarterly revenues of $35.3 million, a 17 percent increase over revenues of $30.3 million for the comparable period last year. Sales in the company's medical division grew 7 percent year-over-year and 8 percent quarter-over-quarter.

Abaxis also recently released a new disc-based reagent panel for use with its Piccolo Xpress point-of-care analyzer. Geared to the physician office lab market, the new panel allows users to conduct on-site chemistry analysis in less than 12 minutes for general inflammation and infection in combination with comprehensive liver and kidney function tests.

G-2 Diagnostic Stock Index



Source: The G-2 Diagnostic Stock Index is tabulated weekly by *DTTR* from the average percentage change in the stock price of 18 IVD companies.

Up	Price	% Chg
Abaxis	$26.16	9%
Beckman Coulter	55.52	5
Becton Dickinson	77.84	3
Bio-Rad	95.36	5
Alere	30.59	4
Gen-Probe	50.32	4
Immucor	18.68	7
Nanosphere	5.18	14
OraSure	4.49	10
Quidel	12.82	11
Sequenom	7.17	13
Unchanged		
Johnson & Johnson	63.83	0
Down		
Abbott Labs	47.40	-8
Affymetrix	4.31	-4
Cepheid	20.37	-3
Clinical Data	17.98	-5
Luminex	17.21	-4
Meridian	22.13	-2

G-2 Insider

Public meeting highlights concerns over genetic testing registry... A public meeting in early November showcased some of the 68 comments received by the National Institutes of Health (NIH) and highlighted a range of stakeholder concerns over the genetic testing registry (GTR) that is expected to launch in the spring of 2011.

The GTR database is being developed by the National Center for Biotechnology Information (NCBI) in response to the growth of the clinical genetic testing field and is intended to be a centralized, online resource for consumers and researchers to access information about available genetic testing. While attendees agreed the goals of a transparent information exchange are laudable, they disagreed over necessary safeguards and even the operation of the database.

Some commenters were concerned that test information is voluntarily submitted by test developers and manufacturers with no scientific review. Some fear that tests will be given undo credibility by the very nature of being on an NIH site and that the actual clinical utility of tests may be inaccurately stated or misunderstood by consumers with many stakeholders pushing for independent review and additional safeguards.

"To be honest, it would take resources beyond our means" to review and validate the accuracy of data in the registry, said NIH Director Francis Collins. Trying to assuage fears, officials demonstrated a prototype page in which a "credentials" tab allows companies to list their licenses and certifications and potentially link to published peer-reviewed articles. Additionally, a green marker would indicate approval by the Food and Drug Administration.

Company References

Abaxis 510-675-6500

ACLA 202-637-9466

ARUP Laboratories 800-522-2787

BloodCenter of Wisconsin 877-232-4376

CAP 847-832-7000

Cepheid 408-541-4191

Department of Justice 202-514-2000

FDA OIVD 301-796-5450

Genetic Alliance 202-966-5557

Gen-Probe 858-410-8000

Health Diagnostic Laboratory 877-443-5227

Medco Research Institute 216-363-5730

Orasure Technologies 800-869-3538

UC Toxicology Chemistry Lab 415-206-3540

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