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Special!

Inaccurate Vitamin D Results Result in Patient Retest/Recall Program!

From the Desk of R. Lewis Dark...

THE DARK REPORT

RELIABLE BUSINESS INTELLIGENCE, EXCLUSIVELY FOR MEDICAL LAB CEOs / COOs / CFOs / PATHOLOGISTs

Restricted information, see page 3

COMMENTARY & OPINION by...

R. Lewis Dark
Founder & Publisher

Patient Retest Effort Is Extraordinary Event

IT IS NOT OFTEN THAT WE DEVOTE AN ENTIRE ISSUE TO A SINGLE TOPIC. The last single-topic special issue of THE DARK REPORT was almost exactly one year ago, when we provided the laboratory industry's most detailed assessment of the Medicare Part B Competitive Bidding Demonstration Project, the details of which had finally been made public on December 5, 2007.

Obviously this Medicare competitive bidding demonstration project was a high-profile news story—one that had the potential to negatively affect the finances of every laboratory in the United States and lead to an erosion in the current high standard of lab testing in this country today.

So why devote this full issue to the topic of Vitamin D testing and the acknowledgement by **Quest Diagnostics Incorporated** that, for certain periods of time, it had reported inaccurate results on certain patients? After all, it is an extremely rare event because well-run clinical laboratories are consistently good at producing accurate, reliable, reproducible results every day, on every shift, and on every instrument. When questionable test results are produced, well-run labs are generally quick to recognize that fact and take timely action so that the physician gets an accurate result and patient care is not adversely affected by that particular laboratory failure.

The uncommon nature of this lab retest/recall program is precisely the reason that Vitamin D testing is the sole theme of this DARK REPORT. The Vitamin D test recall is an extraordinary event. Anecdotal reports from certain communities indicate that many thousands of physicians may have been sent notices of inaccurate testing on their patients, along with an offer for a retest at no charge. It is also a noteworthy story because it involves the nation's largest laboratory company—a company that continually reminds Wall Street investors that it is committed to Six Sigma quality.

Every laboratory in this country that offers Vitamin D testing is experiencing strong increases in test volume. Thus, plenty of important laboratory management lessons can be learned by watching how this laboratory company manages its relations with physicians, patients, payers, and the press on the very touchy subject of having inaccurate Vitamin D results on some patients.

This recall/retest campaign by a prominent laboratory is also a reminder to other lab organizations that anything can happen at any moment. It is why contingency plans and disaster preparations should always be kept up to date. TDR

Vitamin D Test Issues Trigger Doctor Discussion

Meet two protagonists and two antagonists in this unfolding and important lab industry story

CEO SUMMARY: In recent months, Quest Diagnostics Incorporated quietly launched a campaign to notify certain patients and their physicians that they had received "inaccurate results" for Vitamin D tests it had performed. This notice includes an offer to retest the patient at no charge. There are several unprecedented dimensions to this story which have the potential to trigger long-lasting ramifications that touch the entire clinical laboratory community.

OFF THE RADAR SCREEN OF THE WIDER LABORATORY INDUSTRY, an interesting tussle over the accuracy of Vitamin D results produced by a home brew assay has been unfolding over the past 18 to 24 months.

Protagonist, or the central character in this important story, is **Quest Diagnostics Incorporated**. The antagonists, or forces opposing the protagonist, are a cadre of physicians who refer tests to Quest Diagnostics and, as early as two years ago, began questioning the accuracy of Vitamin D test results reported by Quest Diagnostics on their patients.

The overview to this story is simple and goes like this: toward the end of 2006, Quest Diagnostics did a national roll-out of a new home brew assay for Vitamin 25-hydroxy D. This assay is performed by liquid chromatography–tandem mass spectrometry (LC-MS/MS, or mass spectrometry). That fact is notable because it represented a shift in the common practice of most laboratories in recent decades to offer clinicians a Vitamin D test based on radioimmunnoassay (RIA) or immunoassay (IA) methods.

Within months of implementing its national introduction of this home brew Vitamin 25(OH) D assay to its referring clinicians, a growing number of physicians began to contact Quest Diagnostics to express their concern that the results reported by the mass spectrometry method were not consistent with earlier Vitamin D results that had been reported on these same patients. One common theme in these concerns was the higher number reported to the patient by Quest Diagnostics' home brew Vitamin 25(OH) D assay. Some of these physicians tell

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R. Lewis Dark, Founder & Publisher. Robert L. Michel, Editor.

SUBSCRIPTION TO THE DARK REPORT INTELLIGENCE SERVICE, which includes THE DARK REPORT plus timely briefings and private teleconferences, is $13.10 per week in the US, $13.70 per week in Canada, $14.85 per week elsewhere (billed semi-annually).

THE DARK REPORT that the mass spectrometry results reported by Quest Diagnostics during this time were consistently higher than what they were accustomed to seeing from the RIA/IA Vitamin D test methods.

Apparently, here was merit to some criticisms directed by vocal physicians at Quest Diagnostics and its use of the home brew assay for Vitamin 25(OH) D. Earlier this fall, Quest Diagnostics quietly initiated what it describes as a "voluntary Vitamin D retesting program." In certain communities, particularly around New York City and the Northeastern States, surprisingly large numbers of physicians have received letters from Quest Diagnostics advising them that "questionable Vitamin D test results" had been reported on certain of their patients. Quest Diagnostics then offered to retest these patients at no charge, upon the direction of the physician receiving the retest letter. *(See pages 16-18.)*

Testing Deficiencies

News that the nation's largest laboratory company was informing client physicians and patients that it had produced and reported inaccurate test results for some extended period of time is a remarkable event for the laboratory medicine profession. "Old timer" pathologists cannot recall a similar such episode where a respected, financially successful laboratory organization publicly acknowledged that it had discovered that, for specified periods of time, it had deficiencies in some of its internal testing programs and would offer a free retest for the physicians and patients who had received inaccurate test results.

As with any news story, there is a cast of characters. On the pages that follow, THE DARK REPORT presents interviews with individuals involved in some relevant way with this story. Of course, each has a motivation—a vested interest—and readers should understand that each person will spin in support of his or her perspectives on this story.

The views of two antagonists are presented. First, on pages 6-9, is John Jacob Cannell, M.D., who is a psychiatrist who works at **Atascadero State Hospital** in Atascadero, California. Eight years ago, his professional interest in Vitamin D led him to found the **Vitamin D Council** as a platform to educate clinicians and the public about the importance of Vitamin D for good health. Cannell was among the first to publicize the news, on the Vitamin D Council Web site, that there was a consistent and notable difference in the Vitamin D results reported by Quest Diagnostics and **Laboratory Corporation of America**.

Variation in Vitamin D Results

He saw this difference within his own practice at the Atascadero State Hospital, which has used Quest Diagnostics as its reference laboratory during the eight years he has practiced at the institution. Cannell is an advocate for more physician and patient knowledge about Vitamin D, as well as a practicing physician who saw the variation over time in the Vitamin D test results Quest Diagnostics was reporting on his patients. Cannell recently noted that Atascadero State Hospital has received test recall letters from Quest Diagnostics about inaccurate Vitamin D results along with offers of free retesting to the patients at Atascadero who received these results.

An Interesting Individual

The second antagonist is Bruce W. Hollis, Ph.D., of the **Medical University of South Carolina** in Charleston, South Carolina, where he is Professor of Pediatrics, Biochemistry, and Molecular Biology; and Director of Pediatric Nutritional Sciences. *(See pages 10-12.)*

Hollis is an interesting figure in this story, for several reasons. First, he is recognized as a leading researcher in the field of Vitamin D metabolism and nutrition for the past 30 years and has 150 published papers to his credit. Second, back in the 1980s, Hollis was among the first in the nation to develop a radioimmunossay for Vitamin 25(OH) D. This led to an RIA kit

sold by **DiaSorin, Inc.** (then called **Immunonuclear Corp.**). By 1993, this assay had been further developed and gained FDA clearance for the clinical diagnosis of nutritional Vitamin D deficiency. Hollis continues to consult for DiaSorin and thus has a significant motivation to support the clinical accuracy and relevance of DiaSorin's Vitamin D assays.

Representing the protogonist, Quest Diagnostics Incorporated, are two individuals. First is Wael Antoine Salameh, M.D., Medical Director, Endocrinology at **Quest Nichols Institute**, based in San Juan Capistrano, California. In response to questions from THE DARK REPORT, Salameh provided written answers about the home brew Vitamin D assay. His comments are found on page 13.

Speaking next for the protagonist is Richard Reitz, M.D., Medical Director, Quest Nichols Institute and Medical Director, Endocrinology/Metabolism, Toxicology at Quest Nichols Institute. He discusses different aspects of the Vitamin D mass spectrometry testing program. *(See pages 14-15.)*

Readers Free To Decide

Of course, the two experts speaking for the protagonist are motivated to characterize events at their company in the best possible light. That is equally true of the antagonists on their positions. Clients and regular readers of THE DARK REPORT can draw their own conclusions from the remarks of these protagonists and antagonists.

THE DARK REPORT is first in the nation to call attention to this development. It is a story with several implications that may be unfavorable to the entire laboratory industry. A few questions illustrate the land mines that might await, not just Quest Diagnostics, but all clinical laboratories in this country.

First, could this turn into a story that catches the attention of national media? After all, it is a rare event when thousands of doctors have been notified by a nationally prominent laboratory about the reporting of inaccurate lab test results on an unknown number of patients.

Would the media take an adversarial perspective on this problem and cause the American public to lose trust in the integrity of their local laboratories? Past events, such as the cytology testing scandal of the 1980s that led Congress to pass the Clinical Laboratory Improvement Act (CLIA), demonstrate how the media can magnify a lab failure story into a national concern.

Ammunition For The FDA

Second, might the **Food and Drug Administration** (FDA) decide that this situation gives it an ideal opportunity to attack the issue of home brew assays? The fact that some physicians have contacted the agency to complain about receiving inaccurate Vitamin D results may have givin the FDA the right kind of ammunition to justify expanding its oversight of home brew tests. That would be a very unpopular development among laboratory professionals.

One very important dimension to this story as it unfolds is that it provides a contemporary opportunity to learn the "do's and don'ts" of how a laboratory should execute a lab test recall program. Pathologists and laboratory staff are ever-aware of the potential for a test run to go awry without detection, causing inaccurate results to unknowingly be reported to patients. Thus, having a case study example of a significant campaign to notify physicians and patients and offer free retests will be a valuable learning experience for laboratories across the country.

Finally, for pathologists and laboratory administrators, these developments are reminders that every laboratory can find itself surprised in unwelcome ways. The complexities of operating a modern, high-tech laboratory can be overwhelming, particularly if increased volumes of specimens come flooding in at unexpected times. TDR

Doctor Notices Different Vitamin D Results over Time

With an eight-year history of Vitamin D testing for his patients, California doctor noticed the change

CEO SUMMARY: Psychiatrist John J. Cannell, M.D., was in a unique position to see the noticeable upward shift in the Vitamin D results reported on his patients by Quest Diagnostics Incorporated over the past 24 months, along with the recent decline in test result levels in recent weeks. His Vitamin D Council and his newsletter, with 28,000 readers, became a public clearinghouse where physicians and patients could get information about why the two national labs were reporting different Vitamin D results.

BECAUSE OF A KEEN CLINICAL INTEREST in Vitamin D and its role in various diseases, John Jacob Cannell, M.D., quickly recognized that an upward shift in the results of Vitamin D tests performed on his patients had occurred. He also believed this upward shift, combined with what readers of his newsletter were reporting, made it possible that a major American reference lab was reporting what he described as "falsely elevated" Vitamin D levels to many patients across the United States.

Cannell is a psychiatrist, a Vitamin D researcher, and holds a position at **Atascadero State Hospital** in Atascadero, California, which is the nation's largest hospital for the criminally insane. He is the founder of the **Vitamin D Council** (*www.vitamindcouncil.org*). His newsletter is read by 28,000 people.

Interest in Vitamin D

"Vitamin D caught my attention eight years ago as I worked with my patients," recalled Cannell. "I realized Vitamin D is not a vitamin at all, rather the only known substrate for a potent steroid hormone that regulates 2,000 human genes. Over the next year, I came to slowly realize that Vitamin D deficiency is probably involved in most of the diseases of civilization.

"Seven years ago, I founded the nonprofit educational organization, Vitamin D Council, so there could be a clearinghouse of information for healthcare professionals and patients," noted Cannell. "I began publishing my theories in the newsletter, a year or so before they were published in refereed medical journals, including my theories about Vitamin D's role in influenza and in the autism epidemic. I also began to closely monitor all my patients' Vitamin D levels.

"I work at a hospital that treats some very dangerous individuals with severe mental illnesses," stated Cannell. "Many of my patients have very dark skin, none have fatty fish in their diet, and many come from prison, having been in solitary confinement for long periods of time. My hospital uses **Quest Diagnostics Incorporated** for laboratory testing.

"When I began monitoring the Vitamin D levels of my patients, as you can imagine, their Vitamin D levels were very low, just what you would expect when a person has: very dark skin, minimal

exposure to the sun and no Vitamin D in the diet," said Cannell.

"Vitamin D is generally obtained in the diet only from fatty fish. Most other sources, including multivitamins, contain inconsequential amounts of Vitamin D," Cannell added. "For the first seven years, Vitamin D levels for my patients were at the level I expected. They were very low.

"About a year and a half ago, I noticed Vitamin D test results were creeping upward," noted Cannell. "A test result would come back with a 25-hydroxy-vitamin D of 50 for a patient with very dark skin, who had been in solitary confinement, taking no vitamins, and who had no Vitamin D in his diet. So a Vitamin D test result of 50 for this patient meant something was screwy."

Having noticed this change at Atascadero State Hospital, Cannell learned of a similar change from readers who were monitoring the Vitamin D Council Web site. Cannell explained, "People started calling and sending e-mails, stating 'Dr. Cannell, why are you concerned about Vitamin D levels? My doctor did a test from Quest Diagnostics. My level is 60 and I don't get any Vitamin D in my diet. I don't go out in the sun and I don't take Vitamin D supplements. You're a quack!'

Different Test Results

"After reading similar e-mails," continued Cannell, "I began suggesting to these people that they get their Vitamin D levels checked by using **Laboratory Corporation of America** for the test. I started getting calls and e-mails from readers who would say, 'It's incredible! I had my levels checked at both Quest and at LabCorp. At Quest, it was 50 and my level at LabCorp was 25. What's going on?'

"At the same time, I noticed that Vitamin D levels had gone up in my hospital," said Cannell. "In July of 2008, I described these events in my newsletter, which had grown to 28,000 readers. The editorial I wrote caused a firestorm. A week later, at the annual meeting of the **American Association for Clinical Chemistry**, I was inundated by pathologists asking me questions about Vitamin D tests. I suggested that pathologists collect duplicate blood samples from the same patients, then send one to LabCorp and one to Quest and carefully save the results that each lab reported for Vitamin D levels.

No Charge For Retesting

"Two months later, I presented my paper on the role of maternal vitamin D deficiency as an environmental trigger for autism at an autism conference in San Diego. Physicians there told me that Quest was sending them stacks of letters for individual patients that would notify them that the Vitamin D lab tests needed to be redone. Quest was offering to perform retesting for these patients at no charge. I was amazed. I had no idea reference labs did recalls like this.

"From what I can tell, these letters requested patients be retested if their original test had been done anytime in the past year and a half," said Cannell. "Also, it seems like a great number of physicians across the country who ordered the Vitamin D test from Quest during that time were sent these retest letters.

"I understand Quest is performing 500,000 Vitamin D tests per month, so there's a huge number of tests involved," added Cannell. "Which physicians got the letters and how many patients they actually recalled, I don't know.

"There are a growing number of clinical studies that connect low levels of Vitamin D to an increasing number of diseases," explained Cannell. "Go to Google News or PubMed and type in 'Vitamin D' plus any disease you want, then read what comes up. For example, a recent news report on a clinical study done in Germany says people with low Vitamin D are five times more likely to drop dead from a heart attack.

"Recent published studies link low Vitamin D levels with hypertension, Parkinson's disease, virtually all cancers,

Lab Industry Missed this Major Event, But Alert Physicians Were Warning Their Patients

MONTHS AGO, WHEN THE VITAMIN D COUNCIL recognized a significant upward shift in the level of Vitamin D results reported by Quest Diagnostics as compared to Laboratory Corporation of America, it published its assessment of the situation on its Web site and in a newsletter read by 28,000 people.

For pathologists and lab executives, these Web postings demonstrate how the Internet now functions as a news service. Reproduced below is one posting that the Vitamin D Council published in July 2008 to alert its readers to issues associated with Vitamin D testing conducted at Quest Diagnostics during this time period (*http://www.vitamindcouncil.org/newsletter/2008-july.shtml*):

Does it matter what reference lab my doctor uses?

Yes, it might make a huge difference. A number of methods exist to measure 25(OH)D in commercial labs. The two most common are mass spectrometry and a chemiluminescence method, LIAISON. The first, mass spectrometry, is highly accurate in the hands of experienced technicians given enough time to do the test properly. However, in the hands of a normally trained technician at a commercial reference lab overwhelmed with 25(OH)D tests, it may give falsely elevated readings, that is, it tells you are OK when in fact you are vitamin D deficient.

The second method, chemiluminescence, LIAISON, was recently developed and is the most accurate of the screening, high throughput, methods; LabCorp uses it. Quest Diagnostics' reference lab uses mass spec. Again, both Quest and LabCorp are overwhelmed by 25(OH)D requests. The problem is that the faster the technicians do the mass spec test, the more inaccurate it is likely to be.

If your 25(OH)D blood test says "Quest Diagnostics" on the top, do not believe you have an adequate level (> 50 ng/ml). You may or may not; the test may be falsely elevated. Let me give you an example. A doctor at my hospital had Quest Diagnostics do a 25(OH)D. It came back as 99 ng/ml of ergocalciferol. He is not taking ergocalciferol (D2), he has never taken ergocalciferol, only cholecalciferol, and he is not taking enough to get a level of 99 ng/ml, 50 ng/ml at the most. His email to Dr. Brett Holmquist at Quest about why Quest identified a substance he was not taking went unanswered other than to say "any friend of Dr. Cannell's is a friend of ours."

Long story short: if your lab report says "LabCorp" on the top, it is probably accurate; if it says Quest Diagnostics, it may be falsely elevated. While LabCorp has also been overwhelmed with 25(OH)D requests, the LIAISON method they use is relatively easy to do and does not rely on technician skill as much as the mass spec methods do. I'm not saying this because I'm a consultant for DiaSorin, who makes LIAISON, I'm saying it because it is true. If you don't believe me, get Quest to make me an offer to be their consultant at 10 times what DiaSorin is paying me and see how fast I turn Quest down. If Quest fixes their test, I'd love to consult. The ironic thing: I've made both Quest and LabCorp lots of money via this newsletter, the Web site, and by repeatedly telling the press that people need to know their 25(OH)D level, which has contributed to the skyrocketing sales of 25(OH)D blood tests.

depression, schizophrenia, stroke, multiple sclerosis, diabetes, dementia, even obesity," said Cannell. "It's very important that people not be told that their Vitamin D levels are okay when they're not. That's the real problem—falsely elevated test results.

"The Vitamin D Council continues to urge people to have tests done at both Quest Diagnostics and LabCorp and to send us the results," said Cannell. "During the past two years, we saw a period of time when the Vitamin D test levels from Quest started sneaking up and then got unbelievably high. Now, in the past month or so, I noted that Quest's Vitamin D results have come back down to where they would be expected to be. Readers now email me that the Vitamin D results they get from Quest are closer when compared to the results they get from LabCorp, although Quest's results remain higher. Quest Diagnostics did a substantial patient recall on this test. That is an implied admission that there were issues and I respect them for taking that step.

Accurate Vitamin D Tests

"The Vitamin D Council simply wants all labs to perform accurate Vitamin D tests," he added. "If a bias has to exist, we favor a test bias that understates—not overstates—the level, for a simple reason. We want more people treated for Vitamin D deficiency.

"The danger is the false reassurance a patient gets if an inaccurate test overstated their real level of Vitamin D," explained Cannell. "In this instance, it means the patient won't take action to increase his/her level of Vitamin D. By contrast, there is no clinical danger in telling someone their level is 10 ng, or even 20 ng, lower than it really is."

Pathologists and laboratory executives should take note of another aspect to the Vitamin D story. When both physicians and patients were puzzled by discrepancies in the way Quest Diagnostics and LabCorp were reporting Vitamin D results, they found the Vitamin D Council on the Internet and used it as a clearinghouse.

These physicians and patients were first to publicly report widespread discrepancies with Vitamin D test results delivered by Quest Diagnostics. They shared insights about methodologies, such as mass spectrometry versus the DiaSorin immunoassay for Vitamin 25(OH) D. They also publicly discussed the details of how the lab company responded when it was contacted about these issues.

Cannell, too, played his role in this story. "I felt I needed to speak out about this situation," he said. "It makes no sense that a psychiatrist at a state mental hospital, who runs a shoestrong non-profit organization on his weekends using a home computer, ends up doing quality control for Vitamin D testing in the United States. That makes no sense at all." TDR

Contact John J. Cannell, M.D., at 805-468-2061 or jjcannell@charter.net.

Cannell Criticizes Home Brew And No Regulatory Oversight

"THE VITAMIN D COUNCIL SIMPLY WANTS QUEST DIAGNOSTICS INCORPORATED—and any other laboratories that produced inaccurate Vitamin D results—to fix those problems," said John J. Cannell, M.D., Founder of the Vitamin D Council in Atascadero, California.

"Quest is a major player in laboratory testing. We want them to have accurate tests and do 10 million Vitamin D tests per month to help patients and physicians address the widespread deficiency in Vitamin D," stated Cannell. "But why is a lab like Quest allowed to create it's own in-house test when an FDA-cleared test kit is available, is widely used, and has a long history of accurate results? The immunoassay kit manufactured by **DiaSorin** has a track record with physicians and was used in almost every major clinical study of Vitamin D in the past couple of decades.

"It's nuts that existing regulations allow a laboratory to create its own test and offer it to patients and doctors with little validation of accuracy, nor with any regulatory review," declared Cannell. "After all, people's lives are at stake! Look at the turmoil caused over the past 18 months by one big lab after it decided not to use the FDA-approved test and instead offer its own version of a Vitamin D test. Lack of regulation on this point is unacceptable."

Vitamin D Test Expert Discusses Mass Spec

➤LC-MS/MS Vitamin 25(OH) D test results can be "analytically accurate" but not "clinically relevant"

➤➤CEO SUMMARY: Those labs performing Vitamin 25(OH) D testing by mass spectrometry face an interesting challenge. For more than two decades, physicians, patients, and a majority of credible clinical studies have accepted RIA and IA Vitamin 25(OH) D results as a familiar standard. That is why, to avoid confusing physicians, some labs using the mass spec method correlate those mass spec results to the IA method and report those correlated results with the immunoassay reference ranges.

DO ANY RESEARCH INTO VITAMIN D TESTING and you will quickly find the name of Bruce W. Hollis, Ph.D. Since 1981, Hollis has been a national figure in Vitamin D research and an expert on Vitamin D testing.

Hollis is Professor of Pediatrics, Biochemistry, and Molecular Biology; and Director of Pediatric Nutritional Sciences at the **Medical University of South Carolina** in Charleston, South Carolina. As one of the nation's leading authorities on Vitamin D, Hollis has been closely observing the evolution of Vitamin D testing in this country.

"My interest in Vitamin D testing goes back 25 years," stated Hollis. "I've developed radioimmunoassay (RIA) tests for Vitamin D. In conjunction with **DiaSorin, Inc.**, we developed the first 25-hydroxy-vitamin D (25 OH Vitamin D) test to receive FDA clearance back in the early 1990s. This test has been widely used to determine the normal level of Vitamin D."

In fact, over the past two decades, virtually all major studies of Vitamin D have utilized the RIA or Laision immunoassay tests developed by Diasorin and Hollis. Because of that fact, clinicians are quite familiar with the reference ranges for these RIA and IA assays.

Hollis has watched other assays for Vitamin D arrive in the marketplace. "Back in 2000, **Nichols Institute Diagnostics** (NID), a division of **Quest Diagnostics Incorporated**, introduced the Nichols Advantage 25-Hydroxy Vitamin D Assay," he noted. "This automated test was not RIA. Instead, it used a human binding protein as a binding agent.

➤Protein Binding Agents

"In fact, protein binding agents for Vitamin D testing had been used for years and they never worked satisfactorily in direct assays," continued Hollis. "The NID Advantage 25D test was no exception. It was a disaster that created quite a bit of chaos when it was pulled from the market a few years ago.

"One consequence of the failed NID assay was that many laboratory scientists did not trust any type of binding assay," he said. "It didn't matter if it was an antibody, a protein, or similar binding agent. Several laboratories decided to solve this problem by using mass spectrometry to measure

Vitamin D, a technology which has the potential to be very precise.

"These labs jumped right in and developed their own Vitamin 25(OH) D assay using liquid chromatography–tandem mass spectrometry (LC-MS/MS)," observed Hollis. "Several of these labs then offered this LC-MS/MS Vitamin D test to clinicians without calibrating their results with the DiaSorin 25(OH) D assay.

False Positive Situation

"That created a problem," explained Hollis, "The mass spec method tends to produce a number which can be 40% or more higher than what the DiaSorin test would generate on the same patient sample. Thus, when those labs report their uncalibrated mass spec results against the DiaSorin range, physicians may get mass spec Vitamin D results (uncorrelated to the DiaSorin assay) which look normal against the DiaSorin range, but actually represent a false negative test report."

One of those laboratories that used LC-MS/MS to establish an in-house assay for Vitamin 25(OH) D was Quest Diagnostics. "When Quest began using the mass spec method for Vitamin D testing several years ago, it reported its mass spec results against the DiaSorin normal range, but it had not calibrated those results against the DiaSorin assay," stated Hollis.

Payers Changed Labs

"Meanwhile, during this same period, **Laboratory Corporation of America** was using the DiaSorin method for Vitamin 25(OH) D testing," he commented. "What happened was insurance carriers would switch back and forth between Quest and LabCorp in their provider networks. That meant physicians would use Quest for a long time, until the health insurer switched to LabCorp as the exclusive lab provider.

"When that happened, Vitamin 25(OH) D results reported to physicians by LabCorp came back much lower than what the physicians had seen when these patients had been earlier tested by Quest" he noted. "So physicians called LabCorp saying 'you don't know what you're doing! You don't know how to run a proper test. We've been using Quest and they've told us that mass spec is the gold standard.'

"Also at this time, John J. Cannell, M.D., a psychiatrist in California who founded the **Vitamin D Council**, began receiving a steady stream of questions and complaints from patients and physicians," Hollis stated. "They asked why there was such an unsettling difference in the Vitamin D results reported by Quest and LabCorp for the same patient. Dr. Cannell was one of the first medical professionals to recognize this problem and call public attention to it."

Cannell is interviewed on pages 6-9. He has been outspoken in describing the negative patient consequences when laboratories report mass spec Vitamin 25(OH) D results using the DiaSorin normal range without also calibrating the mass spec test result against the DiaSorin assay.

Mayo Calibrated To Diasorin

"To my knowledge, during this time, Quest had never calibrated its Vitamin 25(OH) D mass spec test to the DiaSorin assay," Hollis said. "That's in contrast to **Mayo Clinic**, From day one, it set up its Vitamin 25(OH) D mass spec assay to be matched and calibrated to the DiaSorin test. Ravinder Singh, Ph.D., at the Mayo laboratory, frequently swapped samples with DiaSorin for calibration reasons to see how samples match up. Singh's mass spec Vitamin D test seems to correlate quite well with the Diasorin assay.

"Some labs offering Vitamin D tests by mass spec did it the right way and correlated results to match the widely accepted ranges familiar to clinicians. If a laboratory wants to report its Vitamin D mass spec result using the higher numbers that can result—as much as 40% higher—then it should raise the range it reports to physician. But there are still some labs using mass spec that have yet to do that."

Hollis recognizes that Mass spec is a detection system with the capability to be

more specific than a UV detection system. But he also cautions that a wide disparity in Vitamin 25(OH) D mass spec results can be seen in the clinical market. "As I travel and give lectures, I often hear it said that mass spec is a 'gold standard' for Vitamin 25(OH) D testing. But if that is true, then why is there such variability in results among different labs?" he asked.

"For example, DiaSorin sent samples to seven labs running mass spec and got seven different results!" commented Hollis, who is a consultant to DiaSorin. "So I ask you, which one of these seven results would you consider the gold standard? This is frustrating for everyone concerned about quality and consistency in diagnostic testing. After all, mass spec is like any diagnostic technology. If you put garbage in, you'll get garbage back."

Integrity Of Test Results

Hollis notes that mass spectrometry is like other diagnostic technologies. Every required step in specimen collection, transport, preparation, and analysis must be done correctly for the test result to be accurate and reproducible. "Variability in the integrity of the test result can be affected by several factors, not the least is sudden, unexpected surges in the volume of specimens to be tested," said Hollis.

"In such circumstances, with a rapid run up in the volume of specimens, to maintain turnaround time, the lab staff may fail to properly prep all the samples," observed Hollis. "There is often a lack of consistency in how different people on different shifts set up and run the test, particularly if the lab is hiring new people to process the extra work.

"Second, these problems are particularly aggravated when the increased volume of specimens overwhelms the technical skills of the lab," he added. "If the Ph.D. and key technologists lack experience and competency in this type of testing, that can affect the quality of results reported by the lab.

Cannell and Mercola First To Alert Docs, Patients

PHYSICIANS JOHN CANNELL, M.D., AND JOSEPH MERCOLA, D.O., were among the first to recognize that differences in how the nation's two largest laboratories reported Vitamin D results had the potential to confuse doctors and patients alike.

Both are opinionated, outspoken individuals who maintain active Web sites which are visited by tens of thousands of people each month. As these two doctors became aware of how variation in the way results were reported by some labs using mass spec for Vitamin 25(OH) D testing was causing confusion with physicians and patients alike, both doctors alerted the public to this situation. Both doctors also publicly recommended that physicians and patients send specimens to both LabCorp and Quest Diagnostics, then compare the results to understand the problem.

"I applaud John Cannell and Joe Mercola for pressing this issue because it was being ignored," noted Bruce Hollis, Ph.D., Professor of Pediatrics, Biochemistry, and Molecular Biology at the Medical University of South Carolina. "They accurately described the problem and provided useful guidance on how physicians and patients should take steps to ensure that, when testing for Vitamin 25(OH) D, they understand the meaning of the different test results they often see from different labs."

"There have been reports that indicate that Vitamin D testing at Quest ramped up rapidly from 50,000 tests per month to possibly as many as 500,000 tests per month in about 24 months," noted Hollis. "That would be overwhelming for any laboratory. It places great stress on quality control and the ability to generate high quality, reproducible test results." TDR

Contact Bruce W. Hollis, Ph.D. at 843-792-6854 or hollisb@musc.edu.

Pathologist Perspectives

Quest Diagnostics Explains Confidence in LC-MS/MS Method

ONE ASPECT IN THE DEBATE about the integrity of Vitamin D tests produced by liquid chromatography–tandem mass spectrometry (LC 0150MS/MS) is the discussion about how this method can produce results that are significantly higher than those produced by immunoassay-based methods. Quest Diagnostics addressed this point directly.

In response to questions from THE DARK REPORT, Wael Antoine Salameh, M.D., Medical Director, Endocrinology at **Quest Nichols Institute**, located in San Juan Capistrano, California, provided a written reply. He wrote:

...we want to clarify four key facts to help you report these complex issues accurately.

First is that LC-MS/MS does not produce results with an upward "bias" relative to immunoassay techniques. This not a bias of LC-MS/MS; rather, the converse is true. Immunoassays tend to underreport Vitamin D2, skewing results lower for total Vitamin D levels.

Second, physicians who use Vitamin D2 therapy—which is the only form of therapy FDA approved for treating Vitamin D deficiency in the U.S.—therefore may not be able to accurately assess a patient's Vitamin D2 levels using immunoassay techniques—possibly impeding effective therapy. Not surprising, NIST [National Institute of Standards and Technology], in developing reference materials for Vitamin D testing, has stated that "accurate assessment of Vitamin D status should include measurement of both hydroxylated forms (25-OH-D2 and 25-OH-D3)." Refer to: http://www.cstl.nist.gov/projects/fy06/food0683904.pdf). Quest Diagnostics' Vitamin D test results (using LC-MS/MS) report separate results for Vitamin D2 and D3, as well as the total Vitamin D level, they comprise.

Third, as published literature demonstrates, results of immunoassays and LC-MS/MS correlate well for Vitamin D3, with minor variability. Keep in mind that Vitamin D2 can only be introduced into the body. Therefore, unless a person is undergoing Vitamin D2 therapy, a physician evaluating a patients' Vitamin D level using results of different testing techniques can compare Vitamin D3 results from an LC-MS/MS test to the total Vitamin D level reported by an immunoassay test. Significantly, for the same reason, however, if a person is undergoing Vitamin D2 therapy, we believe strongly that the LC-MS/MS methodology will provide the clinician with a more meaningful Vitamin D profile because both Vitamin D2 and Vitamin D3 levels are measured.

To further emphasize this point, Salameh next wrote:

We also reject the notion that most published research on Vitamin D levels is based on a single type of testing technique providing a standard by which others should be based. Nor do we agree that our LC-MS/MS results would need to be correlated to results of other techniques in order to provide medically useful results. Again, we believe these notions are propagated largely by one or more individuals affiliated with one of our competitors... We stand by the LC–MS/MS method. TDR

Quest Discusses Use of Mass Spec Methodology

➤Moving Vitamin D testing to mass spectrometry provides analytically precise results of D2 and D3

➤➤CEO SUMMARY: Having made the decision to perform nearly all Vitamin 25(OH) D testing by liquid chromatography–tandem mass spectrometry (LC–MS/MS), Quest Diagnostics Incorporated found the transition to be challenging. That was particularly true as the volume of Vitamin D specimens tripled at the nation's largest lab company during the period May 2006 to May 2008. Medical Direct Richard Reitz, M.D., shares insights about Quest's experience with LC–MS/MS.

HAVING DECIDED, ABOUT TWO YEARS AGO, to migrate Vitamin 25(OH) D testing onto an internally-developed assay, **Quest Diagnostics Incorporated** was willing to discuss its experience in working with this methodology.

In a recent interview, Richard E. Reitz, M.D., Medical Director, **Nichols Institute**, Quest Diagnostics' esoteric testing center, and Medical Director, Endocrinology/Metabolism, Toxicology at Quest's laboratory in San Juan Capistrano, California, shared information about why Quest Diagnostics decided to use liquid chromatography–tandem mass spectrometry (LC-MS/MS, or mass spectrometry) as its preferred methodology for Vitamin 25-hydroxy D testing.

"Our interest in mass spectrometry has been ongoing," said Reitz. "Since the 1990s, mass spectrometry has played a growing role in steroid hormone testing at Nichols Institute, for example. LC–MS/MS has been a high performance methodology for us.

"This experience encouraged us to look at how LC–MS/MS could be used in Vitamin 25(OH) D testing," he continued. "The technology has the capability of providing very precise analytical results. One benefit of this in Vitamin D testing is the ability of LC–MS/MS to identify and measure both D2 and D3 components of the total Vitamin 25(OH) D."

Quest Diagnostics saw this capability of mass spectrometry as one benefit when compared to the radioimmunoassay (RIA) and the immunoassay (IA) methods. "By comparison, the IA and RIA methods of testing for Vitamin 25(OH) D are not able to recognize the D2 and D3 components separately," stated Reitz.

➤Use For Vitamin D Testing

Following this evaluation, Quest Diagnostics made the decision to make its internally-developed LC–MS/MS assay for Vitamin 25(OH) D testing the primary method. Approximately two years ago, it introduced this assay to physicians and the clinical community.

The timing of introducing the mass spectrometry method coincided with a huge increase nationally in demand for Vitamin D testing. The volume of Vitamin D test requests arriving at Quest

Diagnostics and other laboratories has increased rapidly in recent years. For example, in news interviews, Quest Diagnostics has stated that the volume of Vitamin D tests referred to it tripled in the 24 months between May 2006 and May 2008.

Home Brew Assay

"It is important to note that mass spectrometry is not standardized for Vitamin D testing" observed Reitz. "For example, **Mayo Clinic** uses mass spectrometry for Vitamin D testing and has its own calibrators, just as we at Quest Diagnostics have our calibrators.

"The internal quality control program here at Quest constantly scrutinizes and evaluates the test runs at all sites and across all instrument systems," stated Reitz. "As the LC–MS/MS assay for Vitamin 25(OH) D was brought up at selected laboratories in our system, we maintained a tight QA/QC process.

"Quest Diagnostics has recognized that, starting in early 2007 and into 2008, for some periods of time for a small percentage of tests, there were potentially inaccurate results at certain of our testing sites," acknowledged Reitz. "A thorough review of Vitamin D results reported throughout this time was conducted."

Recognized The Need To Act

According to Reitz, a broad definition was used. "We defined 'inaccurate' to be any result which had the potential to be wrong," he said. "This was the starting point for identifying patients that would be notified of the possibility of an inaccurate result and then offered a retest of their Vitamin D at no charge."

Quest Diagnostics, in assessing the issues that produced what it defined as inaccurate results, determined that its quality management process needed to be strengthened across the laboratory sites within its system where mass spectrometry Vitamin D testing is performed.

"Accuracy and reproducibility over time are very important for every laboratory," stated Reitz. "We saw the opportunity to improve our internal proficiency testing (PT) at all sites. We have intensified our internal program of using blinded daily samples to provide a timely quantitative check on the quality of our Vitamin D testing. We verify our calibrators and keep our quality control within tight parameters."

Another element in Vitamin D testing is the ongoing publication of clinical studies that link Vitamin D to an increasing number of diseases and health conditions. As a result of these new studies, some Vitamin D researchers are calling for guidelines to change. These researchers recommend that some individuals may need significantly higher levels of Vitamin D.

Optimal Reference Range

"We are confident that our results are accurate," stated Reitz. "As we nail down these accurate standards, the separate question is 'what is the optimal reference range for Vitamin D?' For example, is the floor 30 ng/mL, or is it higher? We can't make that statement because it is something upon which the medical community must agree."

On behalf of Quest Diagnostics, Reitz was candid in acknowledging that the laboratory company had delivered results it deemed to be inaccurate for a period of time. "The message here is that, in addressing this issue, Quest Diagnostics is taking the high road with patients and physicians" stated Reitz. "Offering to retest patients who may have received inaccurate results is the right thing to do.

"Further, I want to stress that, as Quest Diagnostics has tightened its quality management, it can verify precision, accuracy, and the clinical relevance of the answers it delivers to physicians and patients every day," he concluded. TDR

Contact Wendy Bost at 973-520-2850 or wendy.h.bost@questdiagnostics.com.

Retest Program Offers Useful Lessons for Labs

➤Vitamin D patient retest campaign can help labs develop their own effective contingency plans

➤➤CEO SUMMARY: Every day in every laboratory, there is the potential for some aspect of the testing process to go wrong and not be immediately detected. In such circumstances, the lab can then unknowingly report inaccurate test results to physicians and patients. That is why lab managers should have a contingency plan in place that effectively addresses the clinical consequences of such an event, along with the ethical, regulatory, and legal issues that are likely to come into play.

IN SELECTED CITIES AND TOWNS ACROSS THE UNITED STATES, local laboratories are reporting that quite a few physicians and patients in their communities have gotten letters from **Quest Diagnostics Incorporated**. These letters advise the recipient that Quest Diagnostics may have reported "questionable Vitamin D results" and offer to retest the patient at no charge.

The scope and scale of Quest Diagnostics' campaign to notify physicians of a problem with previously reported Vitamin D tests and to offer affected patients a new Vitamin D test remains unknown. However, in various cities, competing laboratories report that a significant number of physicians have received these letters.

These labs also report that certain doctors have been advised that as many as one hundred or more of their patients should be advised of the "questionable results," and come in for a free retest of their Vitamin D levels. These anecdotal reports suggest that, at a minimum, this Vitamin D retest campaign involves numerous physicians and several thousands of patients.

If there is good news in this story, it is the fact that, only on rare occasions, is it possible for an inaccurate Vitamin D result to play a direct role in increasing a patient's morbidity or mortality.

➤Physicians Must Trust Labs

On the other hand, a laboratory is only as good as the trust extended to it by physicians, patients, and payers. For that reason, Quest's campaign to alert physicians about the possibility of inaccurate Vitamin D results, and how it works to restore their trust and confidence, provides a unique case study opportunity for the entire clinical lab industry.

After all, every laboratory, at some time or another, has determined during QA/QC reviews, that certain runs of tests probably produced inaccurate or unreliable results. In these situations, it is common to contact the physicians and patients and arrange to perform that same test again on a new specimen to ensure clinical accuracy. These test "recalls" typically happen within hours or days of the original test report.

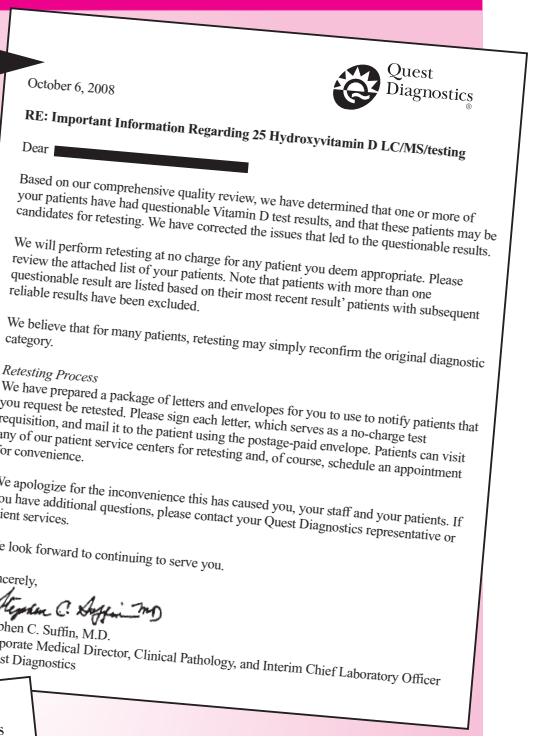
Quest Sends Letters to Doctors and Patients To Notify Them of Inaccurate Vitamin D Results

Quest Diagnostics Asks Doctors to Authorize Retest

AT RIGHT IS THE LETTER SENT by Quest Diagnostics Incorporated to physicians to notify them of inaccurate Vitamin D results reported on their patients.

In carefully chosen language, Quest Diagnostics states that, "We have determined that one or more of your patients have had questionable Vitamin D results, and that these patients may be candidates for retesting."

Quest Diagnostics then asks the physician to authorize retesting. It included pre-printed letters that the physician would sign and send directly to the patient using pre-paid envelopes that were included in Quest's mailing to the physician.



Quest Diagnostics

October 6, 2008

RE: Important Information Regarding 25 Hydroxyvitamin D LC/MS/testing

Dear [redacted]

Based on our comprehensive quality review, we have determined that one or more of your patients have had questionable Vitamin D test results, and that these patients may be candidates for retesting. We have corrected the issues that led to the questionable results.

We will perform retesting at no charge for any patient you deem appropriate. Please review the attached list of your patients. Note that patients with more than one questionable result are listed based on their most recent result' patients with subsequent reliable results have been excluded.

We believe that for many patients, retesting may simply reconfirm the original diagnostic category.

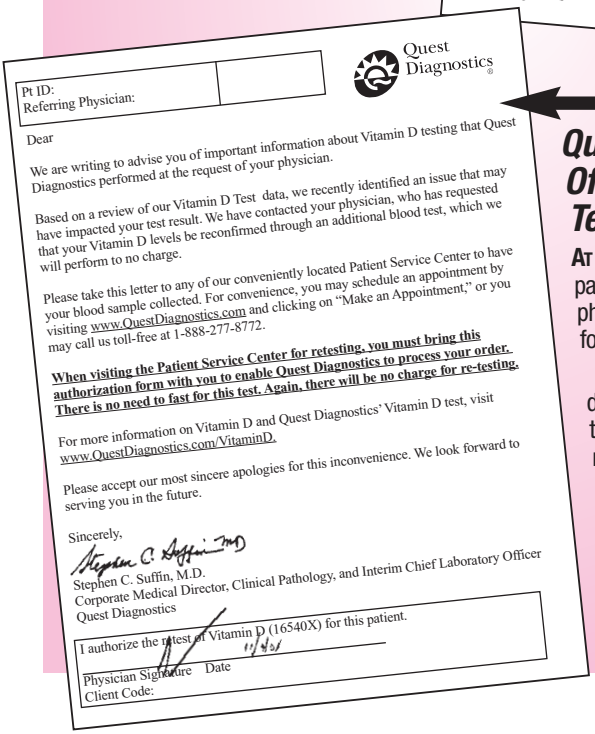
Retesting Process
We have prepared a package of letters and envelopes for you to use to notify patients that you request be retested. Please sign each letter, which serves as a no-charge test requisition, and mail it to the patient using the postage-paid envelope. Patients can visit any of our patient service centers for retesting and, of course, schedule an appointment for convenience.

We apologize for the inconvenience this has caused you, your staff and your patients. If you have additional questions, please contact your Quest Diagnostics representative or client services.

We look forward to continuing to serve you.

Sincerely,

Stephen C. Suffin, M.D.
Corporate Medical Director, Clinical Pathology, and Interim Chief Laboratory Officer
Quest Diagnostics



Pt ID:
Referring Physician:

Quest Diagnostics

Dear

We are writing to advise you of important information about Vitamin D testing that Quest Diagnostics performed at the request of your physician.

Based on a review of our Vitamin D Test data, we recently identified an issue that may have impacted your test result. We have contacted your physician, who has requested that your Vitamin D levels be reconfirmed through an additional blood test, which we will perform to no charge.

Please take this letter to any of our conveniently located Patient Service Center to have your blood sample collected. For convenience, you may schedule an appointment by visiting www.QuestDiagnostics.com and clicking on "Make an Appointment," or you may call us toll-free at 1-888-277-8772.

When visiting the Patient Service Center for retesting, you must bring this authorization form with you to enable Quest Diagnostics to process your order. There is no need to fast for this test. Again, there will be no charge for re-testing.

For more information on Vitamin D and Quest Diagnostics' Vitamin D test, visit www.QuestDiagnostics.com/VitaminD.

Please accept our most sincere apologies for this inconvenience. We look forward to serving you in the future.

Sincerely,

Stephen C. Suffin, M.D.
Corporate Medical Director, Clinical Pathology, and Interim Chief Laboratory Officer
Quest Diagnostics

I authorize the retest of Vitamin D (16540X) for this patient.

Physician Signature Date 12/4/08
Client Code:

Quest's Patient Letter Offers Vitamin D Test at No Charge

AT LEFT IS A COPY of the letter sent to patients by Quest Diagnostics, after the physician has signed his/her authorization for the retest.

Quest uses a rather cryptic deiscription of the need for another test, telling the patient that "based on a review of our Vitamin D test data, we recently identified an issue that may have impacted your test results."

That language is followed with instructions on how to arrange for specimen collection required to retest the patient for Vitamin D levels.

But it is an uncommon event for any laboratory to contact referring physicians and acknowledge that, for a period lasting a number of months—or more than a year—results for a specific type of test were likely to be inaccurate, and thus retesting all patients affected during that period time is recommended and should be done. It is this dimension of the Quest recall/retest campaign that may make it a real world example that is studied by lab managers and pathologists for years into the future.

After all, the monster under the bed of every laboratory scientist is this ever-present concern: "Did anything go wrong today in my lab that caused inaccurate results to be reported and went undetected? Did my lab unknowingly report inaccurate results today that could negatively affect patient care?"

U.S. Labs Among World's Best

It is a testimony to the quality and consistent performance of the thousands of clinical laboratories in the United States that only rarely is there public news about a breakdown in laboratory test quality and test result accuracy that is detrimental to patient care. Compared to the healthcare systems of many developed nations, the quality of laboratory services in the United States ranks with the best in the world.

That is why the current Vitamin D recall/retest campaign initiated by Quest Diagnostics Incorporated has the potential to provide valuable lessons to pathologists and lab managers. Quality management methods, including Lean and Six Sigma, give lab managers proven tools to reduce the statistically-predictable rate of errors generated by work processes and lab testing procedures. But there is little practical experience available to guide laboratory managers about what they should do in circumstances where inaccurate test results are produced and unknowingly reported to physicians. TDR

Few Past Examples of Lab Tests Gone "Bad"

WHAT IS THE LARGEST NUMBER OF PATIENTS involved in other laboratory retesting programs known to have occurred? In the public record since 1990, THE DARK REPORT is aware of only a few public campaigns to alert several thousand patients about problems with their laboratory testing and offer to retest at no charge.

One was the **Maryland General Hospital** lab testing scandal in Baltimore in 2004, when about 4,500 patients were identified as possibly having been given inaccurate infectious disease test results, including HIV and HCV, over a two-year period. Lab managers and staff were aware of the flawed testing process, but it took a med tech whistleblower to alert health regulators, who finally stepped in, closed the laboratory, and initiated a program to locate the patients and have them retested. *(See TDRs, April 5, April 26, May 17, 2004.)*

Another earlier episode happened in April, 1999, when it was discovered that a phlebotomist employed by **SmithKline Beecham Clinical Laboratories** (SBCL) and working in a patient service center in Palo Alto, California, had been reusing butterfly needles for a period of several months.

In this case, SBCL executives offered free infectious disease screening tests to any patient who had blood drawn at any service center during a time period when this phlebotomist was working at that particular patient service center, going back to 1994. At the time, it was estimated that about 15,000 patients were eligible for this testing, and a much lower number actually showed up to have themselves tested. *(See TDRs, April 26 and June 7, 1999.)*

THE DARK REPORT is unaware of any similar cases to the two described above where more than 15,000 patients were involved in some type of lab retest or recall effort.

INTELLIGENCE

LATE & LATENT

Items too late to print, too early to report

Last Thursday, **Sunquest Information Systems, Inc.** of Tucson, Arizona, announced that it would purchase the "Outreach Advantage Solution" software system developed by **Pathology Associates Medical Laboratories** of Spokane, Washington. PAML has spent most of this decade developing a comprehensive, integrated software system designed specifically to give hospital laboratory outreach programs a full service capability to make them competitive with national laboratories. PAML uses the Sunquest LIS, which permitted Sunquest to participate in supporting the development of Outreach Advantage. PAML has been selling Outreach Advantage to hospitals since 2007.

MORE ON: Sunquest

Outreach Advantage makes it easier for hospital lab outreach programs to establish needed support services. It "provides customer relationship management tools, sales and marketing business intelligence, mobile courier management, and connectivity tools for integrating and interfacing with EMRs, Web, LIS, and other enterprise systems." Since its acquisition in 2007 by private equity investors, Sunquest has been actively building its product portfolio of solutions for laboratories.

GENENTECH PETITIONS FDA TO REGULATE LDTS

Genentech lobbed a grenade at the clinical laboratory industry earlier this month by submitting a Citizens Petition to the **Food and Drug Administration** calling for it to regulate predictive "laboratory-developed tests" (LDTs). LDTs are often called home brew tests by the lab industry. Genentech is apparently looking forward to personalized medicine. In its petition, it observes that, were the FDA to assume regulation of these types of *in vitro* diagnostic tests, this "would allow the FDA to focus its attention on high risk LDTs," a definition which Genentech described as tests "used in clinical decision making to determine the use of a particular drug or biologic for the treatment of a patient."

ADD TO: Petition

It didn't take long for the **American Clinical Laboratory Association** (ACLA) to respond to this news. Last Friday, ACLA issued a statement, predicting that, if the FDA adopted this position, it "would have a chilling effect on innovation and patient care while stifling the promise of personalized medicine."

DARK Daily
Clinical Laboratory and Pathology News/Trends

DARK DAILY UPDATE

Have you caught the latest e-briefings from DARK Daily? If so, then you'd know about...

...management changes at **Laboratory Corp. of America** on January 1, when Myla Lai-Goldman, M.D., and Brad Smith, retire. This month, Bill Bonello joined LabCorp to manage investor relations.

You can get the free DARK Daily e-briefings by signing up at www.darkdaily.com.

That's all the insider intelligence for this report. Look for the next briefing on Monday, January 12, 2009.