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Over the past 18 months, we at Beckman Coulter have been spending a great deal of our time focusing on quality, on you (our customers) and on the patients we serve. We’re examining everything we do and we’re working to deliver accurate, reliable, quality products to you.

This issue of Diagnostics Today is a fitting example of the importance we place on accuracy, reliability and quality. Our cover story (page 6), “Assay Standardization and the Laboratory: The Crucial Role We All Play in Improving Diagnostic and Treatment Accuracy,” explains how assay standardization is essential to improving patient outcomes around the world. From standardization successes to challenges, to the important role both manufacturers and labs play, this article demonstrates how, working together, we can increase the accuracy of diagnosis and treatment.

Our Laboratory Spotlight, “Snapshot of Success: How Nix Medical Center Transformed Hematology Productivity with the UniCel DxH 800 Coulter Cellular Analysis System,” (page 4) shows how Nix Medical Center in San Antonio, Texas (USA) helped improve the confidence and quality in their lab results with customizable decision rules on the DxH 800.

Also in this issue, we offer a special two-page feature on our in-booth offerings at this year’s AACC/ASCLS Annual Meeting and Clinical Lab Expo in Atlanta, Georgia (USA) from July 24-28 (Booth #603). Plan to attend presentations in our in-booth theater and learn how we’re helping labs boost performance by collaborating with them to increase productivity, enhance workflow and cut the cost of patient care (page 10).

We know you value accuracy, reliability and quality, too. Whether we’re tackling assay standardization or developing products to increase your productivity, we’re all working to improve patient care. We’re honored that you’ve chosen Beckman Coulter as your partner, and we’re committed to continuing to take steps to ensure that our products are accurate and reliable and, equally important, create confidence that you have the quality products and solutions you need in order to do just that—best serve your patients.

Jack Zakowski, Ph.D., FACB
Director, Scientific Affairs and Professional Relations, Beckman Coulter, Inc.
Located on a picturesque bank of the San Antonio Riverwalk is Nix Medical Center, part of Nix Health Hospital and Healthcare System. Within 24 floors overlooking the city, Nix is a full service, 297-bed hospital complete with a wide range of essential medical, surgical and specialty services.

Despite the hospital’s attractive architecture and prime location in South Texas (USA), the lab’s hematology efficiency used to be anything but picture-perfect.

**The Challenge**
Before January 2010, the hematology laboratory of Nix Medical Center was using a COULTER HmX analyzer with a COULTER MaxM analyzer for backup—both of which were aging gracefully, but beginning to require additional attention.

“Anytime there’s an R-flag or V-flag, a tech is required to make a manual blood smear and review the slide under the microscope to verify the results before releasing,” explains Monica Maza, hematology supervisor.

“So if you have to review five smears for every 10 patients, it can be time consuming.

“Each smear review adds about 10-20 minutes to the whole testing process,” she adds. “This is particularly hard on our second- and third-shift generalists, since they work in all areas of the lab. They may not be able to simply stop what they’re doing and stain a slide, which can delay the release of results.”

Without decision rules on the HmX or MaxM, techs had to either refer to hand-written notes, or continually reference the procedure manual, which takes additional time and is subjective.

**The Search for a Solution**
Maza soon began shopping for a new solution. After seeing an article about the DxH 800 in a trade journal, she decided to investigate further.

“I was really impressed with what I saw,” she states. “I knew the DxH 800 would be great for us. Beyond our previous systems, the DxH could do fully automated reticulocytes and body fluids, which would mean big labor savings—a big selling point for us.”

Maza also appreciated the fact that the DxH 800 offered extended decision rules, which would help the lab achieve more consistent quality while reducing post-analytical interpretation and review rates.

When Nix purchased its DxH 800 system in January 2010, it became Beckman Coulter’s first DxH 800 installation in Texas and, after a smooth transition, the lab began to see benefits right away.
Powerful Decision Rules Lead to Efficiency, Time Savings

"With the DxH 800, I'm able to create specific, customized decision rules that print directly on the reports, which is a huge improvement," said Maza. "Everybody pays attention to what is printed on the report and does what has to be done with each specimen."

"With our older systems, techs often had to make smears for about half of all specimens," she says. "But once we started using the DxH, that number was drastically reduced. In fact, one tech asked me once if I had changed anything, because he'd just run 10 patients and didn't get even one flag. That was an enormous benefit to our laboratory because it allowed techs to finish about 20 specimens in less than 15 minutes. Normal results are now automatically released into the computer, and the techs can go on to do more productive tasks."

"In addition, our review rate decreased from 23% with the HmX to 12% with the DxH 800," says Maza. "Plus, our STAT turnaround time for CBCs dropped from an average of 20 minutes to 15 minutes."

The decision rules are also helping the lab improve the confidence and quality in lab results—by helping technologists spot abnormal results quickly and easily.

"One big improvement came with variant lymphocytes," says Maza. "Our pathologist wants to see samples for any patient with normal white blood cell counts and high lymph absolute counts. Prior to the DxH 800 and the power and flexibility of decision rules, we had to manually review these cases. With the DxH 800, I've been able to create a specific decision rule to spot these cases."

Higher Confidence in Results

By helping the lab identify abnormal samples, the decision rules are also driving improved patient care.

"One patient, for example, had a normal CBC during a visit," says Maza. "When she came in again several months later—after the DxH had been implemented—there were enough slight changes in her WBC and absolute lymph count to trigger the decision rule and require a slide review. After seeing some abnormalities, the tech sent it to the pathologist, who talked to the doctor and requested flow cytometry on it. That test confirmed chronic lymphocytic leukemia (CLL). This demonstrates tremendous improvement to our ability to provide superior patient care."

With less time needed to process manual differentials and slide reviews, technologists now have more time to do other things in the lab, such as process blood bank specimens, assist with chemistry or urinalysis work—or even answer phones or process incoming specimens. It all contributes to higher lab efficiency.

"Today, I'm completely confident in our results," says Maza. "I really trust the DxH 800, and the more I work with it, the more I realize how accurate it is for differentials. We see quite a few leukemia patients and I've been very impressed with the accuracy of the system's monoblast and lymphoblast flags."

Maza is currently establishing a normal range for her patient population, so she can begin using cell population data (CPD) in her in-lab decision rules.

For Maza, the user-friendly software and PRO Service remote diagnostics feature are added bonuses.

"I recently had an issue with a flow cell laser and my service engineer used PRO Service to remotely dial in to the system to fix it," she says. "He made the necessary adjustments and fixed the problem without having to physically visit our lab. This saved us some potential downtime, which I thought was great."

Today, with the implementation of the DxH 800 system, Nix Medical Center’s lab is now the picture of productivity and success—with hematology efficiency that's at an all-time high.
Around the globe, physicians rely on laboratories to provide rapid data in order to accurately and optimally diagnose and manage patients. However, from laboratory to laboratory, state to state, country to country, laboratory results can vary even when testing the same patient sample. As healthcare advances and becomes more complex, assay standardization becomes ever more essential to improving diagnostic and treatment accuracy and improving patient outcomes around the world.

A Win-Win-Win Proposition
The ultimate goal of assay standardization is to improve patient care. “Assay standardization and traceability to defined reference methods and materials provide the tools for clinical laboratories to assure the most accurate and meaningful test results to patients,” says Jack Zakowski, director, Scientific Affairs and Professional Relations for Beckman Coulter’s Chemistry Systems. “Standardization allows for best-in-class practices to improve patient care and outcomes.”

Standardization also makes interpreting laboratory results easier for the physicians providing patient care. Because each assay can have its own reference interval, physicians currently must be able to apply the correct reference interval to each test performed by a specific laboratory in order to accurately interpret that laboratory’s results. With standardization, analytical results would be similar across all testing methods so that only one reference interval would be needed, significantly decreasing the burden currently placed on physicians in interpreting laboratory results. Though geographic, ethnic or environmental differences may remain, physicians would be able to apply these necessary factors consistently to results received regardless of the laboratory.

Laboratories benefit as well, as do assay manufacturers. Standardization allows for common published processes and clearly defined requirements, removing the need for laboratories to reinvent best practices for each assay based on manufacturer. And, manufacturers would be able to provide consistent calibration and demonstrable good manufacturing practice (GMP) for customers. “Collaboration between laboratories, manufacturers and
standardization bodies creates the best possible healthcare,” says Zakowski. “But the only way to achieve standardization is through a real partnership between manufacturers and laboratories.”

Overcoming Challenges: Successes in Standardization

Standardization is not a one-size-fits-all proposition. It requires development of standard unit measurement definitions, consistent calibration points and standardized primary and secondary reference methods and/or materials for each analyte. Scientists must begin by isolating a pure substance to which an individual reference method can link back. For a simple molecule like glucose, the standardization process can be straightforward, but for many protein and nucleic acid analytes, reaching true standardization is far more daunting.

Standardization for immunoassays poses even more challenges. Some groups, including the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and American Association for Clinical Chemistry (AACC), have had successes reaching standardization for specific assays. However, because the essence of an immunoassay is a specific antigen-antibody interaction, both the antigen and antibody components require consideration. “One of the requirements for a successful standard is a stable antigen preparation,” says Bernard Cook, scientific manager, Strategic Marketing, Immunoassay and Molecular Diagnostics for Beckman Coulter. In some cases, this means being able to develop a stable preparation and qualify it as a reference material. An example is troponin. “The IFCC and AACC jointly worked to produce a reference preparation for troponin, and it was a great example of everything being done right, but in the end a commutable standard could not be achieved,” says Cook. “The resulting preparation did not produce equivalent results with all manufacturers’ assays.” On a positive note, the research advancements made through this collaborative effort were significant. “The project did teach us a great deal about how to approach standardization of troponin, and immunoassays in general,” says Cook.

Among the earliest standardization successes were formalized standardization guidelines for HbA1c (glycated hemoglobin) measurements. The AACC and the National Glycohemoglobin Standardization Program (NGSP) tackled standardization related to HbA1c measurement throughout the 1990s. As a result, there has been substantial progress in reducing method-to-method differences through standardization. For example, recent surveys conducted by the College of American Pathologists (CAP) and NGSP show significantly improved standardization between testing methods over the last 20 years as a result of NGSP standardization and certification guidelines coupled with CAP Proficiency Testing (PT) Survey specifications. In 2009, the International Diabetes Federation (IDF) and the European Association for the Study of Diabetes (EASD) recommended the use of the A1C testing to diagnose diabetes, and in 2010, the American Diabetes Association (ADA), IFCC, EASD and the International Society for Pediatric and Adolescent Diabetes (ISPAD) released a consensus statement regarding global standardization of HbA1c measurement. Today, the worldwide standard is that HbA1c be reported in both NGSP (%) and IFCC (mmol/mol) units, with a standardized crosswalk that ensures reporting is commutable from country to country.

Continuing Areas of Challenge

There is still a long way to go to achieve the Win-Win-Win world that assay standardization offers to laboratories, treatment providers and patients. Prostate specific antigen (PSA), for example, provided manufacturers, laboratories and physicians with an important lesson in assay standardization. Even though the World Health Organization (WHO) produced an International Reference Preparation (IRP) for total and free PSA (IRP 96/670 and 97/668, respectively), manufacturers who claim traceability to these preparations do not generate equivalent patient results. The reason may lie in the second player in immunoassay, the antibody. Manufacturers use different antibodies and their varying antigen specificities can yield different patient results. Unless manufacturers can use the same antibodies in their assays, patient results can be expected to differ more significantly between manufacturers for antibody-based assays.

“Collaboration between laboratories, manufacturers and standardization bodies creates the best possible healthcare.”

—Jack Zakowski, director, Scientific Affairs and Professional Relations for Beckman Coulter’s Chemistry Systems
Adding to these challenges is a lack of reference materials that have kept up with the advances in assay methodologies over the years. "Immunoassays for testosterone and thyroid function testing are just now the subject of standardization projects," says Cook. But positive changes are in process. "Manufacturers and laboratorians have recognized the need for standardization early in the life of new markers. For example, there are encouraging standardization projects for PAPP-A and the novel preeclampsia markers (sFlt-1 and PlGF) where early ground-setting work has begun." These collaborative efforts, he notes, hope to yield stable, commutable reference preparations that will allow equivalent patient results from all manufacturers’ assays.

As organizations work together to offer standardization guidelines for individual assays, they must tackle the challenge of traceability. The Clinical and Laboratory Standards Institute (CLSI) has taken on this challenge, publishing guidelines on a variety of laboratory practices and tools that can promote assay standardization. (See http://www.clsi.org.) CLSI has also been a key facilitator in development of ISO and other standards.

To support this process, manufacturers will need to consider standardization and harmonization early in the research and development process. Ensuring traceability and globally accepted measurement standards during the investigation stage of new assays and biomarkers will help to prevent future issues related to consistency across laboratories, and will thus ultimately improve patient care.

Equally important is the role of laboratories in the testing process. From sample handling to analytic processes, consistency and clarity are crucial to standardization efforts. For example, National Kidney Disease Education Program (NKDEP) guidelines for urine albumin (uALB) testing recommend that measurement units should be milligrams albumin/gram creatinine in order to normalize for fluid balance and urine output. Different units and measurements (e.g., mg/L, mg/day, µg/min, mg/gm or ug/mg creatinine) will produce different values and can contribute to confusion in interpreting results.

Standardization also requires involvement and active participation by laboratories and physicians in selection and standardization of collection devices, transport and storage, reporting units, reference intervals, etc. Finally, ongoing PT and external quality assessment (EQA) will also play an important role in assay standardization. With so many variables and changing technologies affecting testing methodologies, applications and results, PT/EQA schemes with demonstrated commutable materials will help ensure that standardization goals are met consistently.

"Assay standardization is crucial to ensuring positive outcomes for patients worldwide as well as to increasing the ability of physicians and researchers to take treatment of disease to the next level," says Zakowski. "There is a lot of progress being made, and we all have a role to play."

2 Miller, W.G., et al., Clinical Chemistry, 2009 55:1; 24-38
Beckman Coulter recently advised customers of the closure of the UniCel DxC ISE Product Corrective Action (PCA). The United States Food and Drug Administration (FDA) has indicated that it supports the company’s recommendation to close the recall and eliminate the requirement to flag electrolyte results, effective immediately.

The closure is supported by a substantial body of data that includes:

- Trending of reported erroneous electrolyte results over the last 18 months
- Post-upgrade system performance data
- Surveillance study results

“Overall, we believe that these trends demonstrate we have identified and effectively addressed systemic root causes of erroneous electrolyte results on DxC systems.”

–Bob Hurley, President and CEO of Beckman Coulter

To explore helpful training and technical information provided for your Beckman Coulter Chemistry Systems, visit Beckman Coulter’s “Back to Basics” Program website at www.beckmancoulter.com/backtobasics. Customers are encouraged to visit regularly to view additional information updates.

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We're helping labs boost performance by collaborating with them to increase productivity, enhance workflow and cut the cost of patient care. Learn how other laboratories have become more efficient by joining us at booth #603 at the AACC/ASCLS Annual Meeting and Clinical Lab Expo (CLE) in Atlanta, Georgia (USA) from July 24-28, 2011.

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- AMH⁴ and reproductive-health testing
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- HbA1c and diabetes testing

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PREVIEW AU5820¹ Chemistry System

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PREVIEW Navios² Flow Cytometer

NEW ACL TOP³ 300 CTS⁹ Hemostasis Testing System

NEW Allegra X-30 Series General Purpose Centrifuge
Program highlights

Check out www.beckmancoulter.com/CLE for the very latest program information.

In-Booth Theater

KEYNOTE
Thursday, July 28, 2011
10:00am

It Is All About the Tests: The Clinicians Valuable Role in the Doctor/Patient Relationship
John Anderson, Advocate for Caregivers and Author of: Stand by Her: A Breast Cancer Guide for Men

• Automation in China
• HbA1c and the Management of Diabetes
• AU5800¹ Series: The High- to Ultra-High Throughput Chemistry Analyzer – First Experience
• Anti-Müllerian Hormone⁴ (AMH): A Novel Reproductive Endocrinology Assay with New Admirers
• The Next Generation of Prostate Cancer Detection: How to Make PSA a Better Marker
• MPV, An “Old New” Parameter
• Middleware: A User’s Perspective
• PROService: Supporting Your Uptime From Behind the Scenes
• Choosing the UniCel DxH 800 Hematology System: Realizing the Right Choice for Your Laboratory
• Lab Automation: Successful Installation Using Process Excellence
• Automating Molecular Diagnostics, A Sneak Peek at the Beckman Coulter DxNi² Molecular Diagnostic System
• Endocrinology & Longevity Medicine: Reducing Age-Related Disorders with Hormone Optimization
• Endocrinology & Longevity Medicine: Thyroid Management in a Wellness Practice
• Endocrinology & Longevity Medicine: The Impact of Adrenal Hormones
• Implementation of a Total Hematology Solution Using the DxH 800, ACL TOP® 500, CellaVision⁵ and REMISOL Advance⁶
• DxLab² Workflow Manager: Going Beyond Middleware

Industry Sponsored Workshop

• Beckman Coulter Innovations and Technology — 2011: Hematology in the Clinical Laboratory

Poster Sessions

• Performance Characteristics of a New Lactate Assay for the Synchron LX20 PRO and UniCel DxC 600/800 Clinical Systems from Beckman Coulter
• Comparison of Hybritech and WHO Calibrations for PSA and fPSA Used in the Beckman Coulter Prostate Health Index (phi)⁷ for Prostate Cancer Detection
• Value of the Prostate Health Index (phi)⁷ for Prostate Cancer Detection in Men Undergoing First or Repeat Biopsy. A Multi-Center Prospective Clinical Study
• The Effect of Age-Adjusted PSA Ranges on the Prostate Health Index (phi)⁷, a Mathematical Equation Combining PSA, fPSA, and [-2]proPSA on Prostate Cancer Detection. A Multi-Center Prospective Clinical Study

Scientific Sessions

Some events require registration. Please visit www.beckmancoulter.com/CLE for more information and the most current schedule.

• How to Fulfill the CLIA Requirements for Assay Calibration, Calibration Verification and Establishing the Reportable Range
• Novel Biomarkers in Prostate Cancer Research
• Knowledge and Awareness of Congenital Cytomegalovirus for the Laboratory
• Is That Normal? Reference Interval Studies Around the World
• Why One is Not Enough: Using Multi-analyte Panels in Cancer Detection and Monitoring
• False-Positive hCG Results: What Every Lab Should Know
• The Laboratory Evaluation of Ovarian Reserve
• Overview of Thyroglobulin and Thyroglobulin Antibody Tests Available for Monitoring Differentiated Thyroid Cancer and NACB Guidelines
• Testing for Chronic Kidney Disease (CKD): Creatinine, GFR, UAIB and More: Industry Responses to Clinical Needs
• Preeclampsia Diagnosis: What is the Future?
• Longevity Medicine and the Endocrine System
• Clinical Performance of Laboratory Tests (Sponsored Session at ASCLS)
• Challenges and Clinical Impacts of Standardization of Immunoassays
• The Central Role of the Sample: Lean Principles and Case Studies in Reducing Laboratory Errors (Sponsored Session at ASCLS)

¹ Currently available in limited geographies. Pending submission and clearance by the U.S. FDA.
² Not available in all countries.
³ In development.
⁴ In the U.S.: For Research Use Only; not for use in diagnostic procedures. IVD in some countries.
⁵ Products may not be available in all markets. CellaVision is a registered trademark of CellaVision AB.
⁶ REMISOL Advance is a trademark of Normand-Info SAS.
⁷ Not available in the U.S.
⁸ Pending clearance by the U.S. FDA. Not yet available in the U.S. for in vitro diagnostic use.
⁹ In development. Not currently saleable.
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Visit us at the 2011 AACC/ASCLS Annual Meeting & CLE, Booth #603 beckmancoulter.com/CLE