JULY 2005
Vol. 2 No. 3

bioMérieux connection

In this issue:

SXT testing on VITEK® 2 now FDA-cleared!

bioMérieux has received U. S. Food and Drug Administration (FDA) clearance to test SXT (Trimethoprim-sulfamethoxazole) against *Staphylococcus aureus* on the VITEK® 2 and VITEK 2 Compact ID/AST systems. A new Gram positive susceptibility card with SXT will be available in December, with a software update to run it.

Continued on page 5

Catch the "Innovation in Motion" bus tour!

bioMérieux is crossing the country to bring exciting innovations for the laboratory to 50 cities on our "Innovation in Motion" bus tour.

biomerieux-usa.com/innovation

You're invited to join us inside our Innovation in Motion laboratory and learn about important contributions to the fight against present and emerging microbial resistance — and learn new ways to improve patient outcomes.

You'll see a demonstration of the VITEK® 2 Compact, our new ID/AST system that provides fast, accurate, automated microbial identification and susceptibility testing in a compact space.

You'll also see the BacT/ALERT® 3D automated microbial detection system that integrates blood, sterile body fluid, platelet quality control testing and mycobacteria culturing into one compact unit.

innovation in motion

Both of these instruments can be combined with OBSERVA®, bioMérieux's newest data-management software. Now all you need is one platform, one PC — for ID/AST and blood culture result status, patient reports and epidemiology.

Continued on page 4

BIOMÉRIEUX

from diagnosis,
the seeds of better health

ECCMID posters show excellent performance of VITEK® 2 Colorimetric Cards

Two posters presented at the 15th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) conference in Copenhagen, Denmark, April 2-5, illustrate the excellent performance of the VITEK® 2 colorimetric identification cards. The abstracts below summarize the posters. They are reprinted with permission from IVD News.

Comparison of the identification performance of the VITEK 2 system to the PHOENIX® system under laboratory conditions

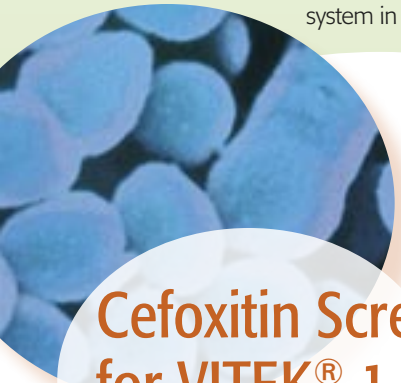
Authors: *T. Schulin, P. Cuppen, A. Voss (Nijmegen, NL)*

Study compared the performance of the VITEK® 2 system, equipped with the new colorimetric menu, and the Becton Dickinson PHOENIX® system in 501 clinical isolates. 247 were Gram positive and 254 Gram negative. 50% consisted of fresh clinical isolates and the rest, stock collection strains. All were subcultured on Columbia Blood Agar and tested in parallel. When there were result discrepancies the strains were retested on both systems. If the discrepancy persisted, supplemental tests were performed including molecular methods to define the reference identification. In the analysis, the repeats were also considered for the performance calculation. Overall, 81 (16%) strains were repeated due to discrepant results at the first test: 13 (16%) due to incorrect answer on both systems, 9 (11%) and 59 (73%) due to VITEK 2 and PHOENIX systems, respectively. The PHOENIX system had a higher level of discrepancies for the identification of Gram positive and stock collection isolates at the first test. Overall, the VITEK 2 system using the new colorimetric menu gives better correct identification than the PHOENIX system after the first test, and in particular, in Gram positive and stock collection isolates, its performance was found to be clearly superior to the Phoenix system in this study.

Evaluation of the new Gram negative identification card for the VITEK® 2

Authors: *C. Brosnikoff, R. Rennie, S. Shokoples, L. Turnbull, S. Graff, D.F. Sahm, S. Mirrett, L.B. Reller (Edmonton, CAN; Herndon, Durham, USA)*

Study evaluated the new Gram negative identification card (GN) for the VITEK® 2. The reference methods were API® 20E and API® 20NE. The three components of the study were reproducibility and QC testing, challenge testing, and clinical and stock isolate testing. The performance criteria for the challenge and clinical isolates with the GN card were set at >96% overall correct identification, <11% low discrimination, <2% incorrect identification, and <4% unidentified organisms within a >95% confidence interval. The evaluation was performed at three laboratory sites. The evaluation included 94 challenge and 562 clinical and stock isolates. The same challenge organisms were tested once at all three sites. Reproducibility testing included 7 different strains tested for 10 days, and QC for 20 days with 7 ATCC® species. All microorganisms were inoculated to the GN card and either an API 20E or API 20NE strip, depending on the suspected identification of the microorganism. Identification was deemed correct when the microorganism was identified by the GN card as the single first choice identification to the genus and species level, or to one of two closely related species of the same genus, or when the need for supplemental tests was specified due to low discrimination. The study found the challenge microorganism testing with the GN card showed 98% overall correct identification, 2.5% low discrimination ID, 2.0% incorrect ID and 0% unidentified organisms with the GN card. The clinical strains demonstrated 96.8% overall correct ID, 6.4% low discrimination ID, 3.0% incorrect ID and 0.2% unidentified microorganisms. Of the 3% (17/562) clinical isolates that were defined as giving incorrect ID only 3 strains were incorrect at the genus level. All QC testing yielded expected results within a 95% confidence interval except for three microorganism and biochemical combinations. The authors conclude that the reproducibility, challenge and clinical isolates tested indicate that the GN card meets all performance criteria within a > 95% confidence interval.



Cefoxitin Screen on the way for VITEK® 1 and VITEK® 2

The Cefoxitin Screen test is used to predict the presence or absence of the mecA gene that encodes for Methicillin resistance in *Staphylococcus* species. The combination of the Cefoxitin Screen test and the Oxacillin MIC is a more reliable method than Oxacillin testing alone. The Cefoxitin Screen test will be available on VITEK 1 and VITEK 2 Gram positive cards in late 2005 or early 2006. It will be available for the VITEK 2 Compact in mid-2006.

In the next edition of the *bioMérieux Connection*, we'll present an abstract from this year's ASM on the performance of this test.

Reducing upper-extremity strain: VITEK® 2 tops MicroScan® 96

In a past issue of the *bioMérieux Connection*, we brought you news about an ergonomics study that showed that the VITEK® 2 ID/AST system causes significantly less upper-extremity strain than another manufacturer's automated ID/AST system. In this issue, we reveal what you might already suspect -- that the other system is Dade Behring's MicroScan® 96. Below is an abstract of the study, which was performed by Worksite International, Inc.

Abstract

Objectives: Perform an ergonomic analysis of the biomechanical advantages and disadvantages of the processes of two ID/AST systems: the bioMérieux VITEK 2 system and the Dade Behring MicroScan 96 system. Compare and evaluate the risk of upper extremity strain by comparing the isolate set-up process of each system.

Methods: Two site visits were conducted to assess the use of the VITEK 2 in hospital laboratory environments by clinical laboratory scientists (CLS). Observations and video data were collected at each site to document how at least five CLSs utilized the system. The video was then analyzed using time and motion analysis techniques (MTM) of the card set-up processes (See Table 1). This data was then compared to data from other CLSs at a large laboratory using the MicroScan 96 system. All data was incorporated into the "Strain Index" (SI)[1] to determine which set-up process caused the least amount of upper extremity strain. A score of 5 or below on the Strain Index scale indicates less likelihood of strain.

Results: The Strain Index indicated that using the VITEK 2 for 1 hour or less for card set-up demonstrates the least likelihood of strain overall, with an SI score of 2.25. Next, using the VITEK 2 for 1-to-2 hours also shows relatively low strain with an SI of 4.5. By comparison, using the MicroScan 96 over the same time period earned an SI score of 6.75. For the VITEK 2 to score that high, the time period had to be doubled — to 2-to-4 hours. Finally, when the MicroScan was used for the same 2-to-4 hour time period, the SI Score was 60.75, indicating a significant risk of strain.

Table 1

	Strain Index Score		
	<1 hour	1-2 hours	2-4 hours
VITEK 2	2.25	4.5	6.75
MicroScan	N/A	6.75	60.75

Conclusion: The Strain Index for VITEK 2 card set-up process is significantly less than the panel set-up process for MicroScan. The VITEK 2 results indicate that there is less likelihood of strain than with the MicroScan system. Incorporating safe work practices, task rotation, proper workstation set up and other recommended ergonomic methods would further help to reduce the likelihood of strain to the user.

About Worksite International, Inc.

Worksite International, Inc., of Monterey, CA, provides office and technical ergonomic analysis and training to business and industry for the purpose of injury prevention and management as well as for improving employee productivity and comfort. Alison Heller-Ono CMC, Certified Industrial Ergonomist and President/CEO of Worksite International conducted the ergonomic study comparing the two ID/AST test kit set-up processes.

1. Moore, S. and Garg, A., "The Strain Index: A proposed method to analyze jobs for risk of distal upper extremity disorders," American Industrial Hygiene Assoc. Journal, 56:443-458, 1995.

BacT/ALERT® 3D wins key role in platelet collection system

Joint technology boosts shelf life of platelet products from five to seven days

The BacT/ALERT® 3D microbial detection system will play an integral role in a leading single-donor platelet technology system. Gambro BCT, Inc., recently received FDA clearance for apheresis platelets to be collected with its Trima® and COBE Spectra® Collection Systems for routine storage and patient transfusion for up to seven days. Clearance was obtained on the condition that the platelets are tested with the bioMérieux BacT/ALERT system and used as described in the Gambro BCT seven-day platelet protocol.

The FDA clearance will now allow blood banks that use the Gambro BCT system to store single-donor platelets for up to seven days. Previously, platelets had to be transfused within five days of collection because of concerns about bacterial contamination. The short shelf life of platelets creates continuing challenges for blood suppliers to meet transfusion needs. The two-day extension of platelet shelf life will have a positive impact on the United States platelet supply.

Safety is a key factor in blood platelet collection, because more than 70 percent of the annual 2.2 million platelet transfusions in the U.S. are done through apheresis and incorporate contaminant testing.

SXT Testing Continued from page 1

The new SXT card configuration for both instruments is found at the right. This card can be used for testing of staphyloccocci, entrococci and Group B streptolocus.

NOTE: bioMérieux has decided not to utilize valuable well space by including Cefazolin on these new cards. As all microbiologists are aware, these 1st-generation cephalosporins are deduced from Oxacillin. It is recommended that a comment be attached to the report indicating that Oxacillin-resistant *staphylococci* are resistant to all currently available ß-lactamase antibiotics. The CLSI recommends that only Penicillin and Oxacillin be reported for *staphylococci*. Routine testing of penicillins, ß-lactmase inhibitor combinations, cephems and carbapenems is not advised.[1]

NEW VITEK 2 and VITEK 2 Compact GP Card *Card name and ordering number to be determined
Ampicillin
Ciprofloxacin
Clindamycin
Erythromycin
Gatifloxacin
Gentamicin
Gentamicin High Level Synergy
Levofloxacin
Linezolid
Moxifloxacin
Nitrofurantoin
Oxacillin
Penicillin
Quinupristin/Dalfopristin (Synercid)
Rifampin
Streptomycin High Level Synergy
SXT (Trimethoprim-sulfamethoxazole)
Tetracycline
Vancomycin

1. Performance Standards for Antimicrobial Susceptibility Testing; Fifteenth Informational Supplement; M100-S15; Vol. 25 No. 1; p. 111. January 2005, Clinical Laboratory Standards Institute.

*Watch future issues of the *bioMérieux Connection* for card name and ordering number.

New VITEK® 1 antibiotic susceptibility test card for Ertapenem

bioMérieux is pleased to announce the availability of a new ertapenem susceptibility card for VITEK® 1 users.

Ertapenem is the newest of the carbapenem class of antibiotics and is manufactured by Merck & Co., Inc., under the brand name INVANZ®. Many hospitals have included ertapenem in their formularies, so you may want to check with your pharmacy to see if this card configuration would be of interest to your institution.

Ertapenem is a broad-spectrum antibiotic used for both Gram positive and Gram negative infections and *Streptococcus pneumoniae*.

The configuration of the new GNS-147 (V4649) card is shown at the right.

GNS-147 V4649
Amikacin
Ampicillin
Aztreonam
Cefazolin
Cefepime
Ceftazidime
Ceftriaxone
Ciprofloxacin
Ertapenem
Gentamicin
Imipenem
Levofloxacin
Nitrofurantoin
Piperacillin/Tazobactam
Trimethoprim/Sulfamethaxazole
ESßL Confirmatory

OBSERVA® for VITEK® 2 Compact

bioMérieux's newest data-management software, OBSERVA®, connects VITEK® 2 Compact ID/AST and BacT/ALERT® 3D blood culture results with patient reports and epidemiology. In the future, OBSERVA will also connect VITEK 2 results with BacT/ALERT 3D. Ask your bioMérieux account manager for more information.

OBSERVA

Innovation in Motion continued from page 1

We'll demonstrate STELLARA™ HIPAA-compliant clinical intervention and advisory software that provides fully integrated communication among key hospital departments.

Tour stops are listed to the right. For more information, tour stop dates, and to sign up, please visit: www.biomerieux-usa.com/innovation or call 866-365-4204.

Baltimore, MD
Havre de Grace, MD
Doylestown, PA
Edison, NJ
Morris Plains, NJ
Hamilton, NJ
Long Island, NY
Norwalk, CT
Springfield, MA
Worcester, MA
Portland, ME
Concord, NH
Syracuse, NY
Pittsburgh, PA

Cleveland, OH
Columbus, OH
Ann Arbor, MI
Indianapolis, IN
Schaumburg, IL
Madison, WI
Minneapolis, MN
Des Moines, IA
Omaha, NE
Wichita, KS
Oklahoma City, OK
Denver, CO
Salt Lake City, UT
Bozeman, MT

Boise, ID
Spokane, WA
Seattle, WA
Tacoma, WA
Portland, OR
Sacramento, CA
Oakland, CA
Fresno, CA
Los Angeles, CA
Orange County, CA
Las Vegas, NV
Phoenix, AZ
Dallas, TX
New Orleans, LA

Normalization of PT and aPTT clot times

1. Concept

Prothrombin time (PT) and activated partial thromboplastin time (aPTT) clot times are specific for the combination of the instrument model and the reagent lot employed. Automation of these assays has resulted in a significant improvement of imprecision. At the same time, however, systematic errors are becoming more noticeable (Figure 1).

Systematic error, or bias, in the measurement of PT and aPTT clot times is primarily associated with variability in the instrument population and reagent lot-to-lot variability. The presence of systematic error results in shifts in the reference and therapeutic ranges. This bias can be minimized by normalizing the system to the "true mean" using appropriate reference materials. Such a normalization procedure (Figure 2) would result in stable reference and therapeutic intervals and allow direct inter- and intra-laboratory comparisons of PT and aPTT results.

This figure shows the effect on the PT assay. Automation has resulted in a significant reduction of imprecision, but the values tend to converge toward a "limiting mean," which may not be the "true value." Bias is the difference between the limiting mean and the true mean and is a systematic error inherent in a method caused by some artifact or idiosyncracy of the measurement system.

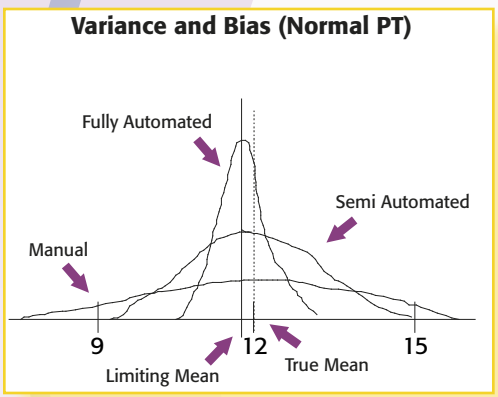


Figure 1. Impact of automation on precision and bias.

2. Implementation

The MDA®-180 and Coag-A-Mate® MTX systems can be normalized for PT and aPTT clot times using a set of lyophilized calibration plasmas (VeriCal®) and a built-in software program. The VeriCal set consists of three levels: VeriCal 1 is a buffered plasma containing protein stabilizers with characteristics similar to normal plasma; VeriCal 2 and VeriCal 3 are buffered plasmas containing protein stabilizers with factors II, VII, IX and X partially and selectively removed. Each of these VeriCal plasmas has a labeled value assigned to it for PT and aPTT clot times. The calibration values are assigned by the manufacturer using reference reagents and a reference instrument (Figure 2).

Protocol

The assigned values of each VeriCal plasma, specific for PT and aPTT reagents (Simplastin® and Platelin® range), are entered into the system's data base. The plasmas are analyzed on the system (n replicates of the three VeriCal's for PT and aPTT) and the mean of the obtained clot times are automatically correlated to the assigned values using linear least squares regression. This regression analysis also includes several steps to validate the calibration curve (test for CV, r2, and percent difference). After a successful calibration, each measured PT and aPTT clot time is automatically converted into a normalized result.

PT/aPTT calibration is recommended for new or reconditioned instruments and at each reagent lot change. Specific procedures are available to confirm that the "normalized" results lie within the expected standard deviation of the assigned values. These procedures are recommended immediately after the calibration (Calibration Verification) and monthly intervals (System Stability Check). Standard daily Quality Assurance procedures are used to verify whether the system is in statistical control (e.g., by running Verify® plasma controls at regular intervals; Figure 2).

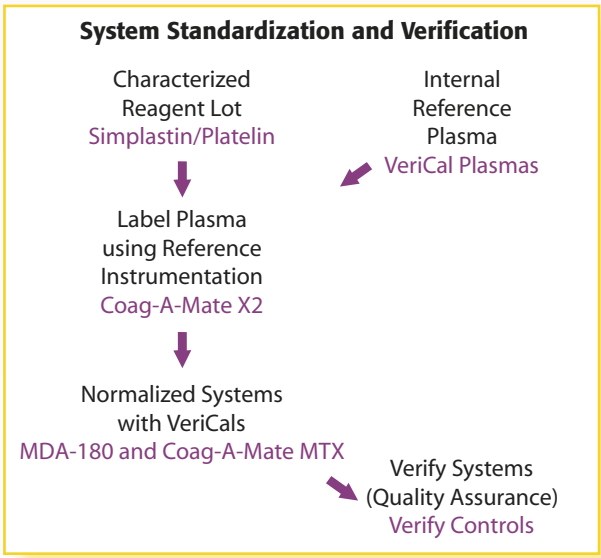


Figure 2. System standardization and verification.

MDA-180 and Coag-A-Mate MTX systems can be normalized for PT and aPTT clot times by using VeriCal, a set of lyophilized plasmas with values assigned by the manufacturer using reference reagents and instruments. A Quality Assurance procedure is used to verify whether the systems are maintained in statistical control.

3. Results

Variance analysis

A variance analysis model was used to demonstrate that a significant reduction in variance was obtained when the PT and aPTT assays were normalized. This variance analysis also showed that instrument and reagent variability are major contributing factors. Figure 3 shows the effect of calibration on the total variance.

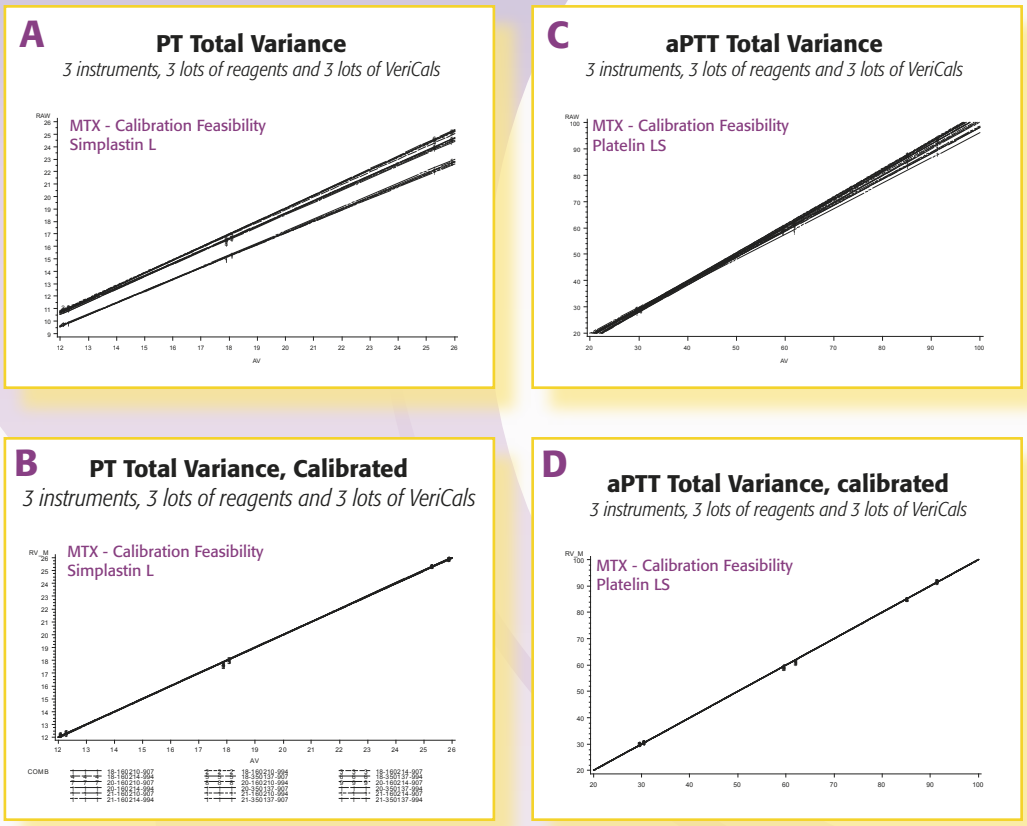


Figure 3. Reduced total variance by system calibration.
Calibration (normalization) of PT and aPTT: effect on variability using 3 different reagent lots, 3 VeriCal plasma lots and 3 different instruments, a total of 27 combinations. Observed values (y-axis) are plotted against assigned values (x-axis).

a. PT variance on a non-calibrated system
b. PT variance on a calibrated system
c. aPTT variance on a non-calibrated system
d. aPTT variance on a calibrated system

Peer consensus data

Peer consensus data over 3 months for 16 to 24 MDA-180 instruments with 3 to 6 lots of reagents had less than a 2% CV for the PT (n=22,075) and less than 3% CV for the aPTT assay (n=22,389). The mean values for 3 levels of control plasmas varied by less than 0.1 seconds for the PT assay and less than 0.4 seconds for the aPTT assay over this 3-month period. See Tables 2 and 3.

Table 1. Peer report PT.

			Verify 1			Verify 2			Verify 3		
month	instr.	lots	n	mean (sec)	CV%	n	mean (sec)	CV%	n	mean (sec)	CV%
12-96	24	6	3003	12.65	1.93	2802	17.78	1.62	3154	25.17	1.98
01-97	23	5	2728	12.64	2.06	2687	17.74	1.80	2661	25.11	1.72
02-97	16	6	1745	12.59	1.91	1608	17.67	1.54	1687	25.07	1.69

Table 2. Peer report aPTT.

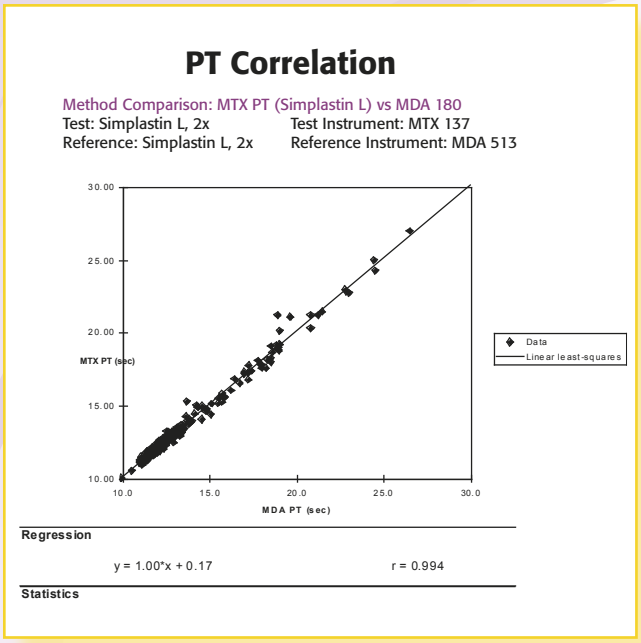
			Verify 1			Verify 2			Verify 3		
month	instr.	lots	n	mean (sec)	CV%	n	mean (sec)	CV%	n	mean (sec)	CV%
12-96	24	3	2912	29.06	2.01	2799	58.06	2.36	3172	83.33	2.40
01-97	23	3	2927	28.75	2.29	2686	57.80	3.66	2846	82.93	2.47
02-97	16	3	1743	29.09	1.96	1858	59.28	2.24	1546	82.96	2.17

Method comparisons

Normalized PT and aPTT results for method comparison studies using patient specimens showed excellent correlation (r>0.994) between the Coag-A-Mate MTX and the MDA-180, in the presence of minimal bias (Figure 4). This resulted in virtually identical PT and aPTT normal reference intervals (Table 3).

Table 3. Reference intervals on normalized systems.

System	n	Mean (sec)	SD (sec)	± 2 SD Range
PT				
MDA/Simplastin L	40	11.7	0.3	11.1 - 12.4
CAM MTX/Simplastin L	40	11.9	0.4	11.1 - 12.7
aPTT				
MDA/Platelin L	40	27.1	1.8	23.5 - 30.7
CAM MTX/Platelin L	40	27.8	2.7	22.4 - 33.2



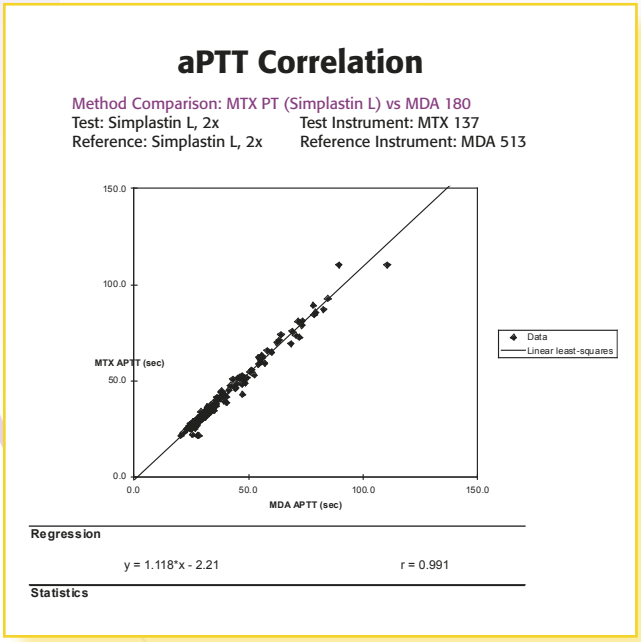


Figure 4. Comparison between systems.
Correlation of PT and aPTT clot times between two normalized systems, the MDA-180 (x-axis) and the Coag-A-Mate MTX (y-axis).

PT: y = 1.00x +0.17; r=0.994
aPTT: y = 1.118x -2.21; r=0.991

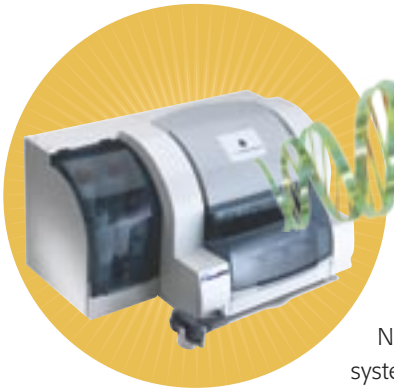
4. Conclusions

- Use of lyophilized plasmas to standardize the PT and aPTT assays normalizes the systematic bias associated with instrument and reagent variability.
- This process provides clotting times for direct reporting or for use in methods that standardize for reagent sensitivity (INR).
- Peer consensus data demonstrate that normalized systems allow for direct inter-laboratory comparisons.
- Also within a laboratory, using only one system, the calibration procedure has the advantage that normal and therapeutic intervals do not have to be adjusted when a change in reagent lot is required.

However, calibration does not compensate for compromised reagents, or adjust for unstable hardware or address improper specimen collection.

Innovation@work
bioMérieux at ASM 2005

"Innovation@work: Integrating Solutions, Improving Outcomes" was bioMérieux's theme at the 105th American Society for Microbiology (ASM) General Meeting, June 5-9 in Atlanta, GA. We introduced attendees to key elements that integrate the laboratory and pharmacy – elements that can help institutions improve both patient and financial outcomes.



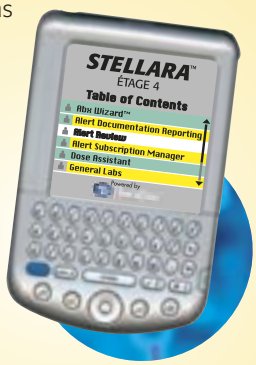
It's always easy – with NucliSens® EasyMAG™

bioMérieux unveiled the NucliSens® easyMAG™ system for automated nucleic acid isolation. The NucliSens easyMAG simplifies nucleic acid isolation and enhances laboratory productivity, providing pure, high-quality DNA and RNA ready for immediate use in downstream applications. Lysis, wash and elution buffers are continuously monitored and stay on-board the system for multiple runs. Set-up is quick and easy; disposables are minimal.

What's new?

VITEK® 2 Compact

bioMérieux demonstrated the new, now-FDA-cleared VITEK® 2 Compact ID/AST system. This new instrument brings to small and mid-sized labs many of the features of bioMérieux's market-leading VITEK 2 ID/AST system. The new VITEK 2 Compact uses the same 64-well Advanced Colorimetry™ bacterial identification and antimicrobial susceptibility test cards as the larger VITEK 2 system to provide the same reporting accuracy and rapid, same-day results interpretation. It also features the Advanced Expert™ System (AES) software, which was demonstrated to attendees. AES is the automated result validation tool that provides on-line review for bacterial resistance detection and result validation. The VITEK 2 Compact features bioMérieux's new OBSERVA® data-management software, with one platform for both ID/AST and blood culture data management.



Most extensive identification database

The new VITEK 2 Colorimetric ID cards also were featured at ASM. These new cards give laboratories using VITEK 2 and VITEK 2 Compact instruments the most extensive identification database of any rapid bacterial identification system. Watch for abstracts of ASM posters on the performance of these cards, in the next issue of the *bioMérieux Connection*.

SXT testing

bioMérieux was pleased to announce during the show that we have received FDA clearance for SXT testing for *Staphylococcus aureus* on VITEK 2 and VITEK 2 Compact instruments.

New level of clinical intervention software

bioMérieux launched the highest level of STELLARA™ clinical intervention software, Étage 4, and showed attendees how laboratory data can be transformed into clinician advisory information. Institutions using STELLARA can bring about a positive impact on challenges such as Pay-for-Performance, adverse drug events, and length of stay. This multi-tiered system brings BacT/ALERT® and VITEK 1/VITEK 2/VITEK 2 Compact test results together with patient antibiotic profiles for the pharmacist and clinician to review in real time. STELLARA, together with VITEK 1/VITEK 2/VITEK 2 Compact, and BacT/ALERT 3D with OBSERVA, forms the core of bioMérieux's integrated solutions. For more information visit www.biomerieux-usa.com/stellara.

Convenience and safety

Demonstrations of the compact BacT/ALERT 3D microbial detection system showed laboratorians just how easy microbial detection can be. The "TOUCH, WAND, LOAD" procedure saves time, facilitates cross-training and helps prevent errors.

BacT/ALERT features the world's only plastic blood culture bottles for added safety in the lab and hospital.

Knowledge forums and satellite symposium

Every year, bioMérieux sponsors Knowledge Forums in our booth and a special Satellite Symposium. These events feature expert speakers on topics that have an immediate impact on the microbiology laboratory. We will post these presentations on our web site later this summer in the Interactive Presentations section. You can view past presentations there now. Just visit www.biomerieux-usa.com/interactive/index.htm.

ASM posters on VITEK® 2 Colorimetric ID cards

Numerous posters presented at this year's ASM in Atlanta show the performance of VITEK® 2 Colorimetric ID cards. Look for abstracts of some of these posters in the next issue of the *bioMérieux Connection* — including the new NH (fastidious organisms) card. We'll also have an abstract from a poster on the Cefoxitin Screen test.

bioMérieux Connection

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