bioMérieux CONNECTION

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Message From bioMérieux

As you may remember, bioMérieux conducted a survey during the American Association for Clinical Chemistry (AACC) Clinical Lab Expo last year to gauge need and interest in lab automation. We will conduct another survey on lab automation at this year's AACC show to see how your responses have shifted due to environmental and industry changes. Here is a re-cap of last year's findings:

More than 75 percent of respondents said they planned to add new microbiology lab automation solutions to their laboratories within the next year. Survey respondents included lab directors, managers and technicians, as well as other healthcare officials. Areas of focus included sample preparation (culture set up and gram staining), negative urine culture screening, identification and susceptibility testing, and reporting of statistical analysis, epidemiology, and connectivity.

Survey respondents indicated that the main reasons for looking at automated solutions include faster turn around time, labor savings, improved accuracy, and standardization. From a personnel standpoint, other factors such as staffing, employee satisfaction and retention are key factors in the purchasing decision.

Today's microbiologist is expected to do more work, faster, to increase profitability. We are committed to delivering automated solutions at the pre-analytical, analytical and informatics stages to streamline processes while delivering accurate results. A fully automated microbiology lab will better serve the patient, as well as be cost effective for your institution.

Join us at AACC 2009 to take our survey and learn more about taking your microbiology lab to full automation. We look forward to your survey feedback so we can continue to improve. While at the booth, take a look at our latest additions in automation, including the Previ™ Isola plate streaker, Previ™ Color Gram automated gram stainer, as well as the UF-1000i for automating urine microscopics.

from diagnosis,
the seeds of better health

BIOMÉRIEUX

Have You Heard The News?

bioMérieux Customer Support Services now fully supports PML Microbiologicals Prepared Media and LyfoCults® QC Organisms.

For assistance with Prepared Media or LyfoCults QC Organisms, and all other bioMérieux products, please refer to the new phone tree below. This new menu will quickly route your call to the appropriate specialist.

Orders for all bioMérieux clinical products may be placed online at biomerieux-usa.com/bioZone, faxed to 1-800-432-9682, or emailed to cscfax@na.biomerieux.com.

bioMérieux Customer Hotline
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PRESS 1: If you know your bioMérieux representative's extension

PRESS 2: To Place an Order

PRESS 3: For Reagent and User Software Technical Support

- **PRESS 1:** VITEK® Systems, API®, chromID™, and LyfoCults® Support
- **PRESS 2:** Molecular Systems and DiversiLab® Support
- **PRESS 3:** BacT/ALERT® Systems and PML Prepared Media Support
- **PRESS 4:** VIDAS® Systems Support
- **PRESS 5:** Previ™ Isola and Previ™ Color Gram Support
- **PRESS 6:** Etest™ Support

PRESS 4: For Instrument, Hardware and Computer Technical Support

- **PRESS 1:** VITEK Systems Support
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- **PRESS 4:** VIDAS Systems Support
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PRESS 5: For Credits and Collections

NucliSENS® easyMAG™

Now Labeled For Use In Front Of A New Nucleic Acid Test For Detection Of Toxigenic *Clostridium difficile*

Prodesse, Inc. received 510(k) clearance from the Food and Drug Administration for its ProGastro™ Cd Assay. The test is a real-time PCR assay where the easyMAG® is used in front as an automated extraction method. The easyMAG is the only extraction method claimed in the package insert.

The easyMAG makes easy work of the sample preparation, where clarified stool sample is placed directly on the instrument and lysed on board. Nucleic acid is extracted in only one hour, and the assay amplification and detection is two hours (result in three hours).

The easyMAG contributed to the excellent performance of the assay in that there were no inhibited samples reported by the three clinical trial sites. In addition, the assay detected 43 percent more positives that did the gold standard used in the trial, the cell cytotoxin assay. Genetic sequencing from an independent locus agreed with the results from ProGastro Cd for over 90 percent of these additional positives.

Customers interested in a molecular-based *C. difficile* toxin assay will greatly appreciate Prodesse's assay due to the extremely low inhibition rate (anticipated to remain one percent) enabled by easyMAG.

This is the fourth assay where easyMAG is specifically claimed for use for nucleic acid extraction. The other assays are:

- Luminex's xTAG® Respiratory Viral Panel – detection of 10 respiratory viruses
- Prodesse's ProFlu+™ – real-time detection of Influenza A, Influenza B and Respiratory Syncytial Viruses
- Prodesse's ProhMPV+™ – real-time detection of Human Metapneumovirus

NucliSENS™ easyMAG

WORKSMART

Submission

Edward Eiland earned an educational grant from bioMérieux for submitting the following article on sepsis syndrome. To earn your WorkSmart honorarium, share your thought leadership online at www.biomerieux-usa.com/worksmart.

Effective Management Of Sepsis Syndrome

Edward H. Eiland, III., Pharm.D., MBA, BCPS, CGP

Severe sepsis is the leading cause of death in non-coronary intensive care units, and it is the 11th leading cause of death overall.[1] In the United States, there are more than 750,000 cases of severe sepsis annually with more than 500 patient deaths daily from severe sepsis.[2] Sepsis-related mortality ranges from 30% to 50%, with advancing age increasing the risk. When septic patients die, it is most often secondary to the organ failure associated with sepsis.[3,4,5] Organ failure occurs from hypoperfusion of the organs due to maldistribution of the microvascular blood flow caused by the inflammatory mediators released by the underlying infection. In response to the infection, the body produces cytokines. These cytokines are then released into circulation where they recruit inflammatory cells and cause an acute phase response. Under normal circumstances, the inflammation process is kept in check by endogenous anti-inflammatory mediators. When the body fails to meet the demands of the inflammatory response, capillaries lose their integrity, nitric oxide production is stimulated, and the microvascular blood flow becomes impeded. This subsequently leads to organ injury and dysfunction.

Early recognition and early goal-directed therapy are the cornerstones of improving outcomes of patients who develop sepsis.[6,7] In order to achieve a positive outcome during sepsis management, it is imperative to make a timely diagnosis and identify the offending pathogen. Moreover, appropriate therapy should be initiated within six hours of presentation with sepsis. Goal-directed therapy includes monitoring, fluid resuscitation, and vasopressor or inotrope support. Patients should be monitored for hemodynamic stability and tissue perfusion. Sepsis-induced tissue hypoperfusion is defined as either septic shock, an elevated lactate, or oliguria. Blood lactate levels may lack precision as a measure of tissue metabolic status yet levels > 4 mmol/L with sepsis syndrome present support aggressive resuscitation. In the event the patient becomes

In the United States, there are more than 750,000 cases of severe sepsis annually with more than 500 patient deaths daily from severe sepsis.[2]

hemodynamically unstable, fluid resuscitation should be initiated with large volumes of either normal saline or albumin. A fundamental aspect of hemodynamic management of patients in septic shock is fluid resuscitation which should ideally be achieved prior to the initiation of vasopressors and intropes, however, early vasopressor utilization is often a necessary emergency measure in patients in severe shock.[7] In sepsis syndrome the initial vasopressors of choice are norepinephrine and dopamine, while in patients with myocardial dysfunction, dobutamine should be utilized. If the patient is still septic despite early intervention, other therapies can be utilized to regain control of the patient's compromised status. These include steroid replacement, infection source control, glycemic optimization, and nutritional support. Hydrocortisone can be administered to patients whose blood pressure responds poorly to initial efforts of fluid resuscitation and vasopressor/inotrope support. Appropriate antibiotics should be administered within the first hour of sepsis presentation in order to achieve source control. Treating the infection decreases the consequent inflammatory response. All infected lines should be removed and abscesses should be drained. Glycemic control should be targeted at maintaining the patient's blood glucose levels <150 mg/dL. Nutritional support should also be maintained to expedite the patient's recovery. Adjuncts to therapy may also be considered including stress ulcer prophylaxis, deep vein thrombosis prophylaxis, transfusion, sedation, analgesia, and organ replacement. In the appropriate situations, activated protein C (Xigris®) can be utilized. Activated protein C should only be used in patients at high risk of death with an APACHE II score ≥ 25. It should not be used in patients at low risk of death with an APACHE II score < 20 per the available medical literature.[7]

Evidence-Based Sepsis Guidelines

- Early Recognition
- Early Goal-Directed Therapy
  - Monitoring
  - Resuscitation
  - Pressor/Inotropic Support
- Steroid Replacement
- Source Control
- Glycemic Control
- Nutritional Support
- Adjuncts: Stress Ulcer Prophylaxis, DVT Prophylaxis, Transfusion, Sedation, and Analgesia
- Recombinant Activated Protein C (Xigris®)

In order to help meet these criteria, an "Adult Sepsis Order Set" should be developed and utilized within all acute care facilities. Past and present sepsis guidelines have always recommended the protocolized resuscitation of a patient with sepsis-induced shock, defined as tissue hypoperfusion.[7] These order sets or protocols should be implemented as soon as hypoperfusion is recognized and should not be delayed pending intensive care unit admission.

In order to achieve a positive outcome during sepsis management, it is imperative to make a timely diagnosis and identify the offending pathogen.

Therefore, it is often necessary for early goal-directed therapy to be practiced in the emergency department. Sepsis order sets and treatment protocols should be developed in accordance with the Surviving Sepsis Campaign and the International Guidelines for the Management of Severe Sepsis and Septic Shock. As these guidelines are updated, the order set or protocol should also be updated to reflect the most recent evidence. Use of the order set within the hospital setting will standardize therapy to ensure that all patients with sepsis receive the most appropriate treatment in a timely manner. ▮

References:

1. *National Center for Health Statistics. Deaths-leading causes. Available at: www.cdc.gov/nchs/fastats/lcod.htm. Accessed April 2009.*
2. *Angus DC, Linde-Zwirble WT, Lidicker J, et al. Epidemiology of severe sepsis in the United States: analysis of incidence outcome and associated costs of care. Crit Care Med. 2001;29:1303-1310.*
3. *Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348:1546-1554.*
4. *Angus DC, Wax RS. Epidemiology of sepsis: an update. Crit Care Med. 2001;29(suppl 7):S109-S116.*
5. *Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. N Engl J Med. 2003;348:138-150.*
6. *Rivers E, Nguyen B, Havstad S. Early-goal directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345(19):1368-1377.*
7. *Dellinger RP, Levy MM, Carlet JM, et al. Surviving sepsis campaign: international guidelines for management of sever sepsis and septic shock: 2008. Crit Care Med. 2008;36(1):296-327.*

Join bioMérieux At These Shows In 2009

American Association for Clinical Chemistry (AACC)
July 19-23
Chicago, IL
Booth #458

Ohio Signature Event
September 8
Medina, OH

Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)
September 11-14
San Francisco, CA
Booth #209

Southern California Symposium (SOCAL)
September 29
Huntington Beach, CA

American College of Emergency Physicians (ACEP)
October 5-8
Boston, MA

Association for Molecular Pathology (AMP)
November 19-22
Kissimmee, FL

bioMérieux HAI Educational Series:

Combining Knowledge And Education To Address The Challenges Of Healthcare-Associated Infections

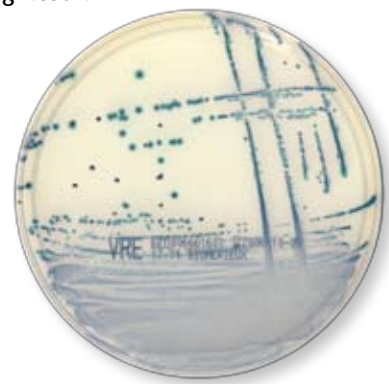
bioMérieux is sponsoring a series of educational workshops aimed at increasing awareness of aspects and challenges surrounding healthcare-associated infections and the implementation of processes that can assist in their overall reduction. Our main objective for these regional workshops is to sponsor local experts and enable them to communicate best practices implemented at their respective facilities so attendees can consider applying some presented elements at their own institutions. **Please visit www.biomerieux-usa.com/hai to learn more about the series.**

Jackson, WY • September 17
Intermountain States Seminar, Snow King Resort

Huntington Beach, CA • September 29
Southern California Symposium

Portland, OR • October 21

Greenville, SC • November 4
Annual SEACM Meeting



Odyssey™ Cities on Tour

Ft. Worth, TX • September 2-5 SWACM

Jackson Hole, WY • September 16-19 IMSS

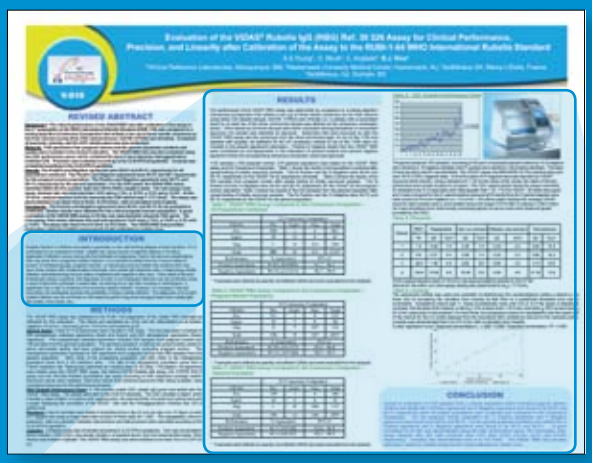
Seattle, WA • October 21-24 NWMLS

Greenville, SC • November 4-6 SEACM Fall Annual Meeting

bioMérieux Presented The Following Poster On

VIDAS® Rubella IgG (RBG) Assay

At The 2009 American Society Of Microbiology (ASM) General Meeting



INTRODUCTION

Rubella infection in children and adults is generally a mild, self-limiting disease of short duration. If it is contracted by an expectant mother, rubella may cause severe congenital defects in the fetus, especially if infection occurs during the first trimester of pregnancy. Due to the serious complications that may arise from congenital rubella infection, it is important to determine the immune status of women of childbearing age, pregnant women, or individuals such as health care workers who may have close contact with contaminated individuals. Anti-rubella IgG detection aids in diagnosing rubella infection and determining immune status of patients with regards to this virus. If the result of the anti-Rubella IgG assay is positive, the diagnosis (current or convalescent infection) can be confirmed using a second specimen collected 3 weeks later, by looking for an IgG titer increase or stabilization. A significant rise in IgG is evidence of an evolving rubella infection. However, no increase in the IgG level does not necessarily exclude the possibility of active rubella infection. The diagnostic of a current rubella infection can be confirmed or dismissed by performing other biological tests (anti-rubella IgM, IgG avidity, viral culture, etc.).

RESULTS

The performance of the VIDAS® RBG assay was determined by comparison to a testing algorithm (Consensus Comparator) that utilized a two out of three results consensus as the final outcome using three FDA cleared devices: AxSYM, VITROS and Immulite (i.e. a sample with a concordant result by at least two of the three commercial devices was defined as the consensus comparator result). If the results by the three devices were either discordant among themselves or concordant equivocal, the sample was classified as equivocal. Specimens that were equivocal by both the VIDAS® RBG assay and the consensus from the three commercial tests (12 out of the 1130) and samples with quantity not sufficient for the 2/3 consensus method (8 out of the 1130) were not included in the percent agreement calculation. Positive or negative results from the VIDAS® RBG were considered as non-agreements in the calculation of percent positive and percent negative agreement when the corresponding consensus comparator result was equivocal.

1130 samples (654 pregnant women, 476 general population) were tested on the VIDAS® RBG assay and the Consensus Comparator. Table 1 shows the results of all populations combined after repeat testing of initially equivocal samples. The % Positive and the % Negative were 95.0% and 99.1% respectively for the VIDAS® for all populations combined. Table 2 shows the results of the 654 samples from pregnant women after repeat testing of initially equivocal samples. The % Positive and the % Negative were 95.2% and 99.1% respectively for the VIDAS® for the pregnant women population. Table 3 shows the results of the 476 samples from the general population after repeat testing of initially equivocal samples. The % Positive and the % Negative were 94.7% and 99.1% respectively for the VIDAS® for the general population.

Table 1: VIDAS® RBG Assay Compared to the Consensus Comparator – All Populations Combined

	2/3 Consensus Comparator			
VIDAS	Pos	Equiv	Neg	Total
Pos	850	2	0	852
Equiv	29	12	0	41
Neg	1	15	213	229
Total	880	29	213	1122*
Performance	% Agreement		95% CI	
Positive Agreement	95.0% (850/895)		93.3 – 96.3	
Negative Agreement	99.1% (213/215)		96.7 – 99.9	

* 8 samples were defined as quantity not sufficient (QNS) and were excluded from the analysis.

Table 2: VIDAS® RBG Assay Compared to the Consensus Comparator – Pregnant Women Population

	2/3 Consensus Comparator			
VIDAS	Pos	Equiv	Neg	Total
Pos	511	1	0	512
Equiv	19	7	0	26
Neg	0	7	107	114
Total	530	15	107	652*
Performance	% Agreement		95% CI	
Positive Agreement	95.2% (511/537)		93.0 – 96.8	
Negative Agreement	99.1% (107/108)		94.9 – 99.9	

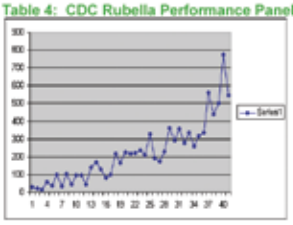
* 2 samples were defined as quantity not sufficient (QNS) and were excluded from the analysis.

Table 3: VIDAS® RBG Assay Compared to the Consensus Comparator – General Population

	2/3 Consensus Comparator			
VIDAS	Pos	Equiv	Neg	Total
Pos	339	1	0	340
Equiv	10	5	0	15
Neg	1	8	106	115
Total	350	14	106	470*
Performance	% Agreement		95% CI	
Positive Agreement	94.7 (339/358)		91.8 – 96.8	
Negative Agreement	99.1 (106/107)		94.9 – 99.9	

* 6 samples were defined as quantity not sufficient (QNS) and were excluded from the analysis.

Table 4: CDC Rubella Performance Panel



The panel contained 100 samples, consisting of 50 pairs of duplicate samples titered by HI (9 negative sera resulting in 18 negative samples and 41 positive sera resulting in 82 positive samples). The pairs of sera served to test for reproducibility. The VIDAS® assay identified 80/82 (97.6%) positive tests and sera 18/18 (100%) negative tests. One of the pairs of HI negative sera was reported as VIDAS® equivocal (both results). Using a standard of >1.25 for the ratios of the values, the ratios of the two paired sera were scored as good or not good. The CDC reports typical results for assays submitted for evaluation are 5-10 sera pairs with ratios greater than 1.25. For the VIDAS®, 38 ratios were good and 3 were not good for the 41 paired positive sera and all 9 results from the 9 paired negative sera were scored as Immune negative (i.e. <10 IU/mL). The above graph displays the average VIDAS® result for each positive sera (y axis) plotted versus the lowest (1:8 HI titer) to highest (1:256 HI titer). No major deviations from continuously increasing signals for serum pairs were observed (graph provided by the CDC).

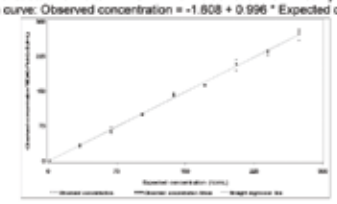
Table 5: Precision

Sample	Mean value IU/mL	Repeatability		Inter-run precision		Between site precision		Total precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	7.8	0.58	7.4	0.58	7.4	0.20	2.5	0.84	10.8
2	8.8	0.57	6.4	0.66	7.4	0.22	2.5	0.89	10.2
3	29.8	1.46	4.9	2.62	8.8	0.95	3.2	3.14	10.6
4	154.8	10.58	6.8	18.49	12.0	0.00	0.0	21.30	13.8

At the medical decision point of 10 IU/mL (as approximated by sample 2), the 3rd SD interval for the within-run (intra-assay) testing was determined to be ± 1.71 IU/mL.

Table 6: Linearity

The polynomial method was used and consisted of determining the concentration(s) where a device is not linear and of comparing the deviation from linearity at that level to a predefined allowable error due to nonlinearity. Acceptance criteria was 1) Assay is statistically linear (risk 5%) or 2) If the assay is statistically nonlinear, the deviation from linearity is within ± 12% at each level > 20 IU/mL and within ± 20% at each level ≤ 20 IU/mL (equivocal or low-positive). For each level, the acceptance criteria for repeatability was the upper limit of the interval for the CV profile deduced from the theoretical 95% confidence interval for the Variance profile. Linearity was demonstrated from 0 to 274 IU/mL with no deviation from linearity.
(Linear regression curve: Observed concentration = -1.808 + 0.996 * Expected concentration, R^2 = 0.99).



CONCLUSION

During an evaluation of 1130 samples from a clinical population which included pregnant women, children and adults the % Positive agreement and % Negative agreement were found to be 95.0% and 99.1% respectively when all patient populations were combined and compared to the Consensus Comparator. For the pregnant women population the % Positive agreement and % Negative agreement were found to be 95.2% and 99.1%. For the general population (children and adults) the % Positive agreement and % Negative agreement were found to be 94.7% and 99.1%. A good correlation to HI titer was demonstrated using the CDC performance panel. The intra-assay, inter-assay, between site, and total precision were %CV were ≤7.4%, ≤12.0%, ≤3.2% and ≤13.8% respectively. Linearity was demonstrated from 0 to 274 IU/mL. The VIDAS® RBG test provides automated, rapid and reliable measurement of IgG antibodies to rubella virus.

To view the entire poster online, go to www.biomerieux-usa.com/connection or contact your local bioMérieux representative.

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PRODUCT SPOTLIGHT

Product Spotlight: Etest™

Etest is used to determine the Minimum Inhibitory Concentration (MIC) of antibiotics, antifungal agents and antimycobacterial agents. Etest is valuable for the management of critical infections, including sepsis, when on-scale MICs are needed for treatment decisions.

Etest is a cost-effective tool for generating MICs across 15 dilutions. Over 100 antibiotics are now available in the product range for testing of aerobic bacteria and fastidious organisms such as pneumococci, haemophilus, *H. pylori*, meningococci, gonococci, anaerobes, fungi, and mycobacteria.

Etest provides MICs for slow-growing and fastidious organisms that have unique growth requirements and cannot be tested by automated methods. **To learn more, download our new Etest product brochure at www.biomerieux-usa.com/etest.**

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