bioMérieux CONNECTION
JANUARY 2009 • VOL 6 NO 1

Message from bioMérieux

Welcome to the January 2009 issue of bioMérieux Connection newsletter.

The healthcare industry will experience significant changes this year, and we are here to help. Budget constraints and staff shortages will create challenges, and denial of payment will create even more work for laboratories already at full capacity.

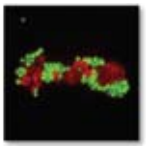
bioMérieux will spend 2009 adapting to these changes. In 2008, we made three acquisitions and forged three strategic alliances with industry leaders such as Sysmex, Wescor and Hitachi. We also continue to dedicate significant funding to research and development efforts.

We will continue these efforts with the goal of helping your laboratory overcome challenges. Additionally, bioMérieux will do more to reach out to you this year because we know you will have budget restraints for travel.

Our resolution is to provide you with education and solutions to help you create a lean laboratory. We look forward to working with you in 2009.

Happy New Year!

IN THIS ISSUE



from diagnosis,
the seeds of better health

BIOMÉRIEUX

A Flood of Blood Culture Orders at St. Luke's Hospital

The Midwest suffered a tremendous flood this past summer. Iowa, South Dakota, Minnesota, Wisconsin, Nebraska, Illinois, and Indiana were all affected by this natural disaster. As of June 20, 2008, a total of 22 levees were breached. Twenty-four people were killed, 148 other were injured and approximately 35,000 – 40,000 were evacuated from their homes.

In Iowa, a total of nine rivers crested at record levels, and 83 of 99 counties were declared disaster areas. On June 13, 2008, the Cedar River crested at over 32 feet, exceeding the historic flood record from 1929.

Cedar Rapids, IA was hit particularly hard. Water covered 1,300 city blocks, or 9.2 square miles. City Hall, the Linn County jail, the fire department, police communication equipment and the public library were flooded. The Cedar River flooded more than 4,000 homes and many businesses in Cedar Rapids, and damage costs were estimated at over $1.5 billion.

On June 11, officials began evacuating the area around the Cedar River. By the next day, Cedar Rapids lost power, the substation went out, and the levee broke. Citizens were told they needed to evacuate within 30 minutes. That afternoon, bridges began closing. The bridges that were still open had at least a 45-minute wait time to cross them.

At St. Luke's Hospital in Cedar Rapids, IA, a three story parking structure was completely flooded on the first floor, and floodwaters were rising to the second floor. The hospital was running on emergency back-up generators for 24 hours before a temporary substation could be brought in to serve the city. Fortunately, the computer system only went down for eight hours. But over the next several weeks, the city and the hospital lost power, causing the emergency generators to kick on. At times, staff had to work with flashlights and extension cords.

St. Luke's was inundated with patients because it became the city's only operating hospital. On June 13, Mercy Medical Center became flooded and needed to evacuate all patients to nearby hospitals and care centers. This left St. Luke's to care for all incoming flood victims and take on 52 patients from Mercy. On an average day, the hospital registered 150 patients. In June, that number jumped to 458. The emergency

department usually received 140 patients per day. In June, they received 280.

Mary Stanford is the microbiology instructor and key operator for BacT/ALERT® 3D, and Sue Smith is the supervisor of the microbiology department. Before the flood, Mary and Sue processed about 900 blood cultures every month using a BacT/ALERT incubator module with six drawers of 60-cells (for a total capacity of 360 cells). In June, however, they had orders for 1,243 blood cultures. To deal with the huge volume increase, they ordered a BacT/ALERT 3D combination module with two drawers of 60 cells (for a total of 120 cells).

When Mary placed the order with bioMérieux on June 20, she was told someone would deliver the combination module by the next morning despite the fact that interstate 80 and three area bridges were closed. Sure enough, a truck arrived at 8:30 a.m. the next day, and Mary's bioMérieux field service technician, Joe Steward, had all 120 drawers loaded by 11:00 a.m. The following morning, bioMérieux technical representative Mark Lewis called Mary to make sure the instrument was running smoothly.

With the addition of the combination module, they were able to load 480 bottles at a time. They used the combination module continuously for three weeks to keep up with the number of blood culture orders.

Since a nearby hospital had to close due to the flood, its staff came to St. Luke's to help. The combined hospital staffs learned to work together for the good of the patients.

On an average day, the hospital registered 150 patients. In June, that number jumped to 458.

"We were so busy doing all the other microbiology work coming in, we wouldn't have been able to handle subbing or staining all those bottles," said Sue. "We were working 12-14 hour days."

During the day, St. Luke's has five full-time staff members working in the microbiology lab. At night, three technicians cover the entire hospital laboratory. When the flood hit, everyone came in early and left late to keep up with demand.

"We saw some highlights on television, but we didn't have time to process the damage because we were so busy working," said Sue. "We were working in a war zone with limited electricity and resources."

To learn more about St. Luke's Hospital and microbiology lab staff, please visit www.stlukescr.org. If you would like to make a donation to help the Midwest recover, please visit www.midwestfloodrelief.org.

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BacT/ALERT 3D™

Updated VITEK® 2 Card Menu

Continuous improvement of our products is a primary goal of bioMérieux, Inc.

Improvements to the Gram negative AST cards involve four antibiotics, including:

- Piperacillin/Tazobactam
- Piperacillin
- Levofloxacin
- Trimethoprim-Sulfamethoxazole (SXT)

Improvements to the Gram positive AST card for staphylococci, enterococci and Group B streptococci are:

- Inducible Clindamycin Resistance Test (ICR Test), commonly referred to as the D-test, approved for staphylococci
- Tigecycline (new antibiotic addition)
- Vancomycin with an enhanced calling range from ≤0.5 to ≥32 µg/ml. There are no FDA requirements for a vancomycin agar screen plate with this formulation.

Improvements to the Streptococcus pneumoniae AST card include the addition of two new antibiotics and improvements in an older antibiotic. These changes are:

- Amoxicillin (new antibiotic addition)
- Meropenem (new antibiotic addition)
- Erythromycin (no limitations for MIC's of 0.25 or 0.5 µg/ml)

The changes made to the VITEK 2 AST cards require that AIX software version 5.01 and PC software version 3.01 be installed on your VITEK 2 instrument.

Gram negative AST Cards

Piperacillin/tazobactam and piperacillin were originally developed to correlate with the agar dilution reference method. Published studies have shown that VITEK 2 results, based on a comparison to agar dilution, sometimes provide minimum inhibitory concentration (MIC) results that

Continuous improvement of our products is a primary goal of bioMérieux, Inc., as evidenced by the latest VITEK® 2 enhancements, involving improvements to Gram negative, Gram positive and *Streptococcus pneumoniae* antibiotic susceptibility test (AST) cards.

are one dilution lower than those obtained by reference broth microdilution (BMD) methods. Since these antibiotics do not have an Intermediate (I) category call, a one-dilution difference that occurs at or near the breakpoints can mean the difference between susceptible (64 µg/ml) or resistant (128 µg/ml). Since BMD is the methodology most often used as a reference method in the U.S., piperacillin/tazobactam and piperacillin were redeveloped to bring VITEK 2 MIC results into alignment with BMD results.

Levofloxacin was redeveloped to provide more stability at the very low range of the dilution spectrum. A small number of customers were experiencing quality control problems with levofloxacin against *Pseudomonas aeruginosa* at this low end of the dilution range and the redeveloped Levofloxacin eliminates this issue. SXT was redeveloped to resolve an issue with rare strains of *Escherichia coli* that demonstrated prolonged lag phases in their growth curve. The possibility for false susceptible results existed with these strains. Redevelopment of SXT incorporating these strains in clinical trials was undertaken to resolve this issue. All four antibiotics went through clinical trials and received 510(k) clearance from the U.S. Food and Drug Administration (FDA).

All four antibiotics went through clinical trials and received 510(k) clearance from the FDA.

All Gram negative VITEK 2 AST cards have been reconfigured with these new antibiotic formulations. A consequence of the redevelopment of piperacillin/tazobactam, piperacillin and levofloxacin is that these antibiotics now require four wells on the VITEK 2 card (as opposed to three wells in the past). To make room for these additional well, one antibiotic was deleted from cards with the previous antibiotic formulations.

Cards incorporating the new antibiotic formulations require new names and part numbers. Therefore, all GN cards with the previous formulations must be discontinued. These cards are:

- AST-GN04
- AST-GN05
- AST-GN07
- AST-GN09
- AST-GN10
- AST-GN13
- AST-GN14
- AST-GN15
- AST-GN16
- AST-GN17
- AST-GN18
- AST-EXN-6
- AST-GN20
- AST-GN21

Attached is a listing of all VITEK 2 Gram Negative Susceptibility Test cards with the antibiotic configurations as well as a list of which new card corresponds most closely with a previous card and the approximate availability date. Many of them are currently available and all will be available by the end of January 2009.

Most customers prefer to have a confirmatory ESßL test on their AST card, so this test was added to most of the newly configured cards. The ESßL test requires six wells on the card, so its inclusion necessitates the elimination of two antibiotics.

Decisions regarding which antibiotic to delete are always difficult. Deletion decisions were made in consultation with physicians and microbiologists. Cefoxitin has replaced cefotetan as the cephamycin on most of the AST-GN cards. Advisors tell us that cefotetan is used as prophylaxis in certain types of surgical cases but is rarely prescribed on the basis of an antibiotic susceptibility test. Cefoxitin, on the other hand, is used less often as a prophylactic agent but is a better indicator of the AmpC resistance mechanism. Detection of this important resistance mechanism and the lack of clinical utility of the cefotetan AST result is the reason cefoxitin most often represents the cephamycin class of antibiotics on the new AST-GN cards. [+]

(continued on page 6)

[-] *(continued from page 5)*

Gram positive AST Cards

The improvements to the Gram positive cards involve new antibiotics and tests on both the Gram positive AST card for staphylococci, enterococci and Group B Streptococci as well as new antibiotics on the *Streptococcus pneumoniae* AST card.

- The ICR Test replaces the need for laboratories to perform "off-line" D-tests. This important test alerts microbiologists and physicians to the presence of *Staphylococcus aureus* isolates that may test susceptible to clindamycin by MIC methodology but possess the mechanism to become resistant to clindamycin if exposed to this antibiotic.
- The reformulated vancomycin lowers the range of MIC results reported to 0.5 µg/ml. This is important as studies are showing that patients with MIC's this low have a better outcome than those infected with *S. aureus* isolates with MIC's of 1.0 µg/ml or higher. As a reminder, there is also no need to perform an off-line vancomycin agar screen with this formulation of vancomycin.
- Tigecycline is a relatively new antibiotic that provides physicians with another option in the treatment of Methicillin Resistant *Staphylococcus aureus* (MRSA) infections.

Discontinuation of GN04, GN07, GN09, GN10, GN11, GN13, GN14, GN15, GN16, GN17, GN18, EXN-6, GN20 GN21, GP61, GP63, GP65 and GP66 cards

We realize that changing susceptibility test cards involves work on our customer's part. Quality control must be performed on new antibiotics and changes to LIS configurations are necessary. It is necessary to discontinue the manufacturing of AST cards when improved versions of the antibiotics on those cards are available. For this reason, we will discontinue the manufacturing of the above cards on June 1, 2009. We would ask customers who plan to use the discontinued cards past March 1, 2009, to please place orders for these cards in advance. Orders can be placed through February for the discontinued cards that will be shipped as specified during the months of March, April and May. This will allow us to manufacture a sufficient number of cards and avoid backorder situations. Please contact your bioMérieux representative if you have any questions with regard to ordering cards that are being discontinued.

It is our hope that customers will use the card changes as an opportunity for microbiologists, pharmacists and physicians to meet and review their institutional needs. bioMérieux is making these changes in response to changes suggested by experts to continuously improve our product. Ultimately, we share your goals of providing laboratory results that financially benefit your institution, improve antibiotic stewardship and most importantly, provide optimal patient care.

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The introduction of the AST-GP67 card eliminates the need to continue manufacturing the AST-GP61, AST-GP63 and AST-GP66 cards. Further information on the schedule for the end of production of these cards is found below.

The new AST-GP68 card for *Streptococcus pneumoniae* includes antibiotics (listed above) that are not present on previous generations of this card. It also includes the redeveloped erythromycin that eliminates a limitation for *S. pneumoniae* with MICs of 0.25 or 0.5 µg/ml against erythromycin. The introduction of this new AST-GP68 card eliminates the need for continued production of the AST-GP65 card. Details of the end of production for this card follow.

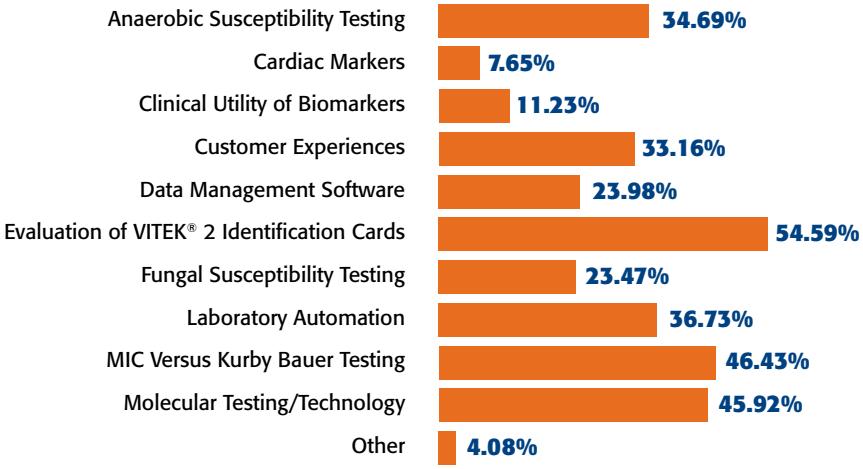
bioMérieux would like you to know that we appreciate your business. We will continue to work diligently to provide you with products that assist in the fight against infectious diseases.

bioMérieux CONNECTION

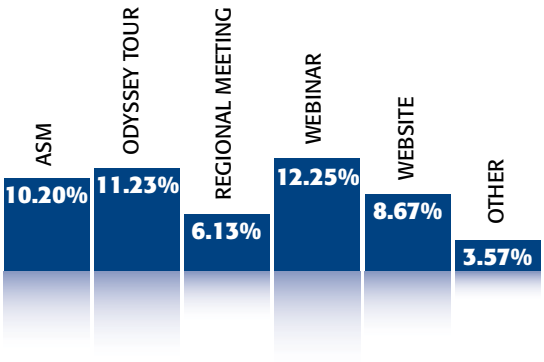
2008 Newsletter Survey Results

Thank you for participating in the November 2008 *bioMérieux Connection* newsletter survey, and congratulations to the PNA FISH laboratory timer winners. We are excited to present some key findings from the survey and look forward to better serving you in 2009.

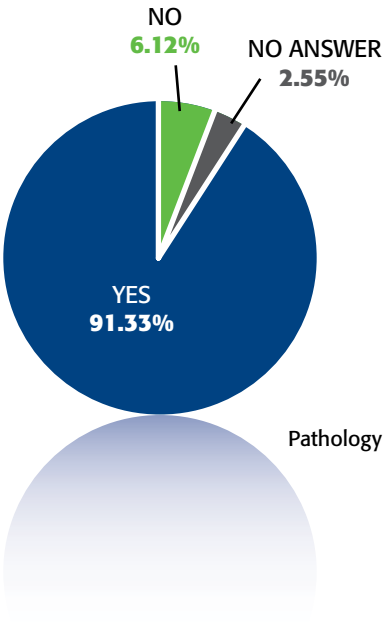
Which product highlights would you like to see more of in bioMérieux Connection newsletter? Select all that apply.



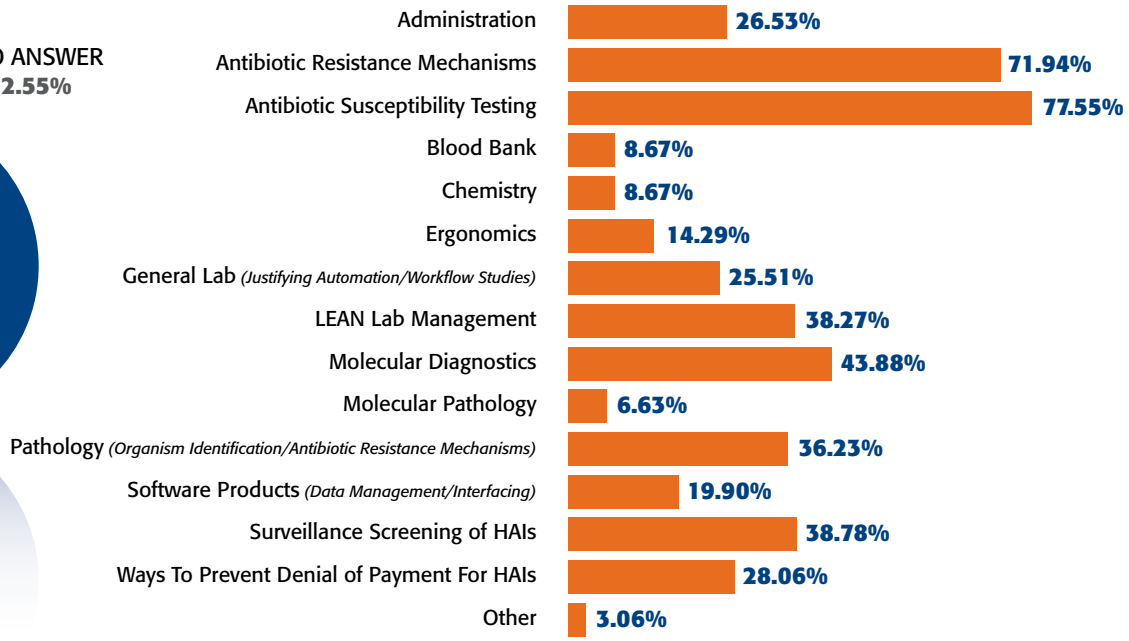
In which type of bioMérieux education segment have you participated? Select all that apply.



Would you like to participate in online training?



If yes, which educational topics would be of most interest to you? Select all that apply.



Streamlining Quality Control Testing

Managing the quality control process for bacterial identification tests has traditionally been a long process due to the number of organisms required to ensure the proper reagent and technologist performance. A new CLSI standard M50-A entitled "Quality Control (QC) for Commercial Microbial Identification (ID) Systems; Approved Guideline" was published in July 2008. This new guideline has a significantly positive impact on simplification of your QC workflow for bioMérieux's ID products.

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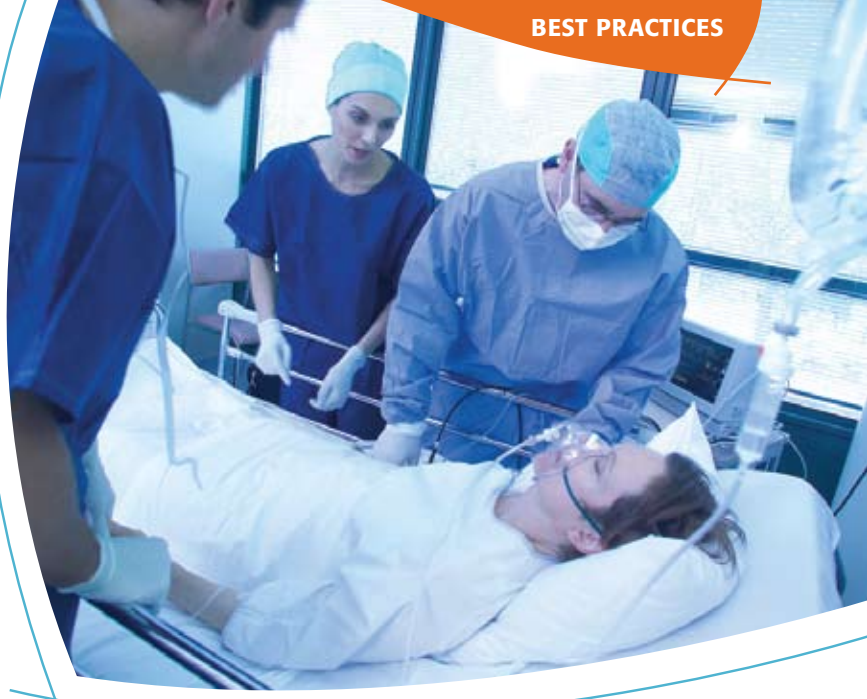
We have been working diligently to collect additional data on our VITEK® 2 ID products so that we are able to offer you the easiest QC indicators while meeting this guideline. We plan to introduce the new, streamlined quality control process for our VITEK 2 ID product line in early 2009. Initially, the testing procedure will be offered in printed format, and, soon afterward, it will also be integrated into our software platforms.

A similar evaluation of the QC testing process is being conducted with our API® identification products. Once the timeline for these products is completed, we will share the information for the API product line.

We would like to take this opportunity to thank you for using our identification products and we look forward to providing you with this new streamlined QC testing procedure in the near future.



PNA FISH®

Shown to Reduce Mortality by 42% for Patients with Healthcare-Associated Enterococcus faecium Bloodstream Infections

A new medical study demonstrated use of PNA FISH™ reduced mortality by 42 percent for patients with highly drug resistant healthcare-associated *Enterococcus faecium* bloodstream infections (BSIs). In addition, the study demonstrated that PNA FISH reduced the time to reporting of laboratory identification results for all enterococcal BSIs by 2.6 days and reduced time to appropriate antimicrobial therapy for *E. faecium* BSIs by 1.8 days. The study was undertaken by clinicians at the University of Maryland Medical Center (UMMC) in Baltimore, Maryland, and was published in the latest issue of Antimicrobial Agents and Chemotherapy.[1]

Bloodstream infections due to *Enterococcus* bacteria, predominantly *Enterococcus faecalis* and *E. faecium*, are often acquired while patients are in the hospital, and they can lead to increased mortality, longer hospital stays and increased healthcare costs. The infection is initially diagnosed when a culture of the patient's blood turns positive with Gram-positive cocci in pairs and chains (GPCPC), indicative of enterococci and/or streptococci.

Because conventional laboratory identification methods can take 48 hours or longer and early antimicrobial therapy is crucial to ensure positive patient outcomes, physicians often prescribe broad-spectrum antibiotics such as vancomycin to cover the patient. However, this may lead to the administration of inadequate or inappropriate antibiotic treatment, as *E. faecium* is often resistant to both vancomycin (VRE – vancomycin-resistant enterococci) and penicillin-based drugs such as ampicillin, while *E. faecalis* is often susceptible to ampicillin.

PNA FISH delivers rapid, molecular identification of *E. faecalis* and other enterococci, including *E. faecium*, directly from GPCPC positive blood cultures in hours instead of days. As a result, laboratories can provide faster information that enables clinicians to select effective antibiotic therapy sooner for patients afflicted with enterococcal bloodstream infections.[1] [+]

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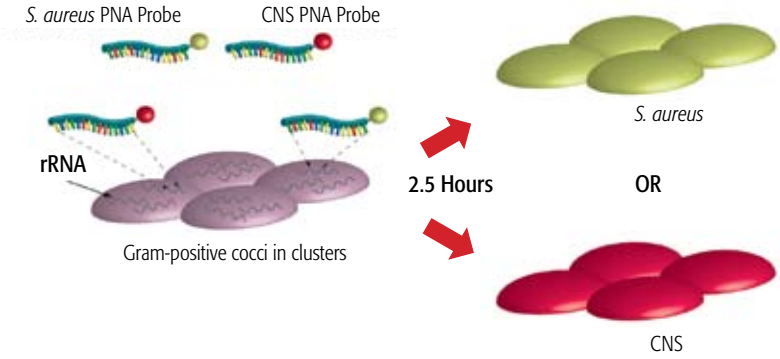

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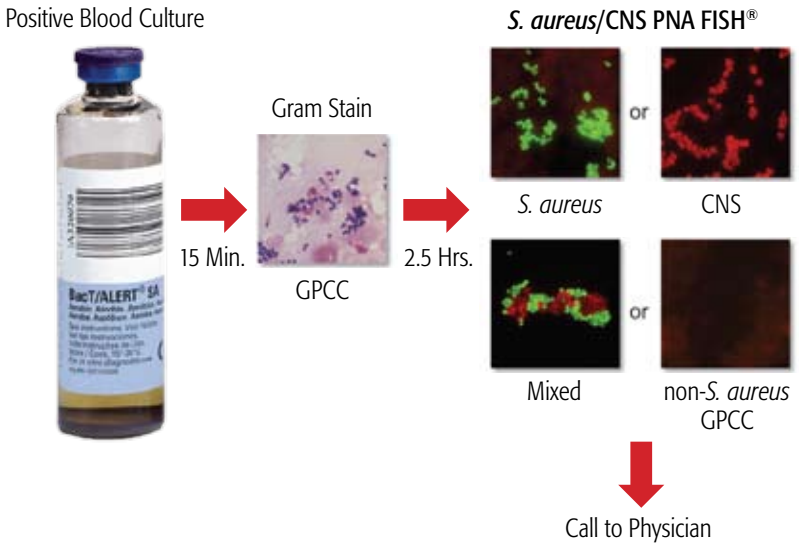
The study included 224 patients with hospital-acquired enterococcal bloodstream infections – 112 patients before the PNA FISH test was implemented (pre-PNA FISH group) and 112 after implementation (PNA FISH group). A treatment algorithm based on the rapid PNA FISH results was developed and implemented by the hospital's antimicrobial management team. Patients with *E. faecalis* by PNA FISH were to be given ampicillin, while patients with other enterococci, including *E. faecium*, and at "high risk" for VRE were to be given linezoid, a newer anti-VRE antibiotic. At the end of the study, data on characteristics, therapy and outcomes between the pre-PNA FISH and PNA FISH patients groups were compared.[1]

- More than 88 percent of all *E. faecium* were resistant to vancomycin (VRE), and 100 percent were resistant to ampicillin.
- Eighty four percent of initial empirical antimicrobial therapy for patients with *E. faecium* BSIs was inadequate
- There was a 2.6-day reduction in time to laboratory identification results in PNA FISH group
- There was a 1.8-day reduction in time to appropriate antimicrobial therapy for *E. faecium* in the PNA FISH group
- There was a 42 percent reduction in 30-day mortality rates for patients with *E. faecium* in the PNA FISH group
- PNA FISH sensitivity, specificity, positive predictive value, and negative predictive value were shown to be 100 percent compared to conventional methods.



Reference:
Forrest et al. Peptide nucleic acid fluorescent in situ hybridization for hospital-acquired enterococcal bacteremia: delivering earlier effective antimicrobial therapy. Antimicrob Agents Chemother. 2008 Oct;52(10):3558-63.

AdvanDx Receives FDA 510(k) Clearance for Yeast Traffic Light PNA FISH®

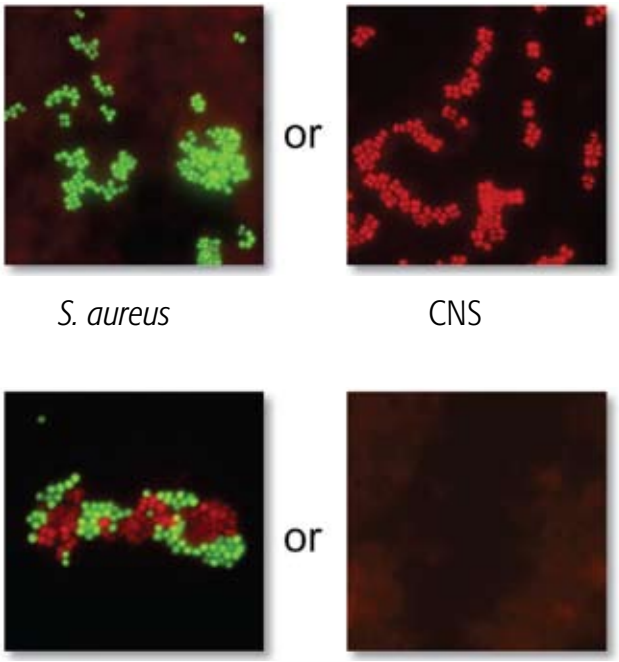
AdvanDx recently received FDA 510(k) clearance for Yeast Traffic Light PNA FISH® to identify *Candida* yeast species directly from positive blood cultures. The Yeast Traffic Light™ is the latest addition to AdvanDx's easy-to-use, molecular-based PNA FISH™ diagnostics platform that provides rapid identification of bloodstream pathogens in hours instead of days.

Candidemia, a bloodstream infection caused by *Candida* species is one of the most serious hospital acquired infections, afflicting over 24,000 patients in the U.S. every year. Immunocompromised transplantation, oncology and AIDS patients are especially at risk for contracting the infection with mortality rates as high as 50 percent.[1] While identification of the infecting *Candida* species is used to guide effective antifungal therapy, conventional laboratory methods can take up to five days or longer. For the first time, laboratories can identify, in a single Yeast Traffic Light test, up to five *Candida* species directly from positive blood cultures including *C. albicans* and/or *C. parapsilosis*, *C. tropicalis*, and *C. glabrata* and/or *C. krusei* in hours instead of days, enabling clinicians to provide early, effective and appropriate antifungal therapy for patients afflicted with candidemia.

Studies show that Candida species display varying resistance to commonly used antifungal agents. While *C. albicans* and *C. parapsilosis* are generally susceptible to the antifungal drug fluconazole, *C. tropicalis* may display intermediate resistance to the drug while *C. glabrata* and *C. krusei* display the highest level of fluconazole resistance.[2] At the same time, recent reports indicate that caspofungin, a newer and more expensive broad-spectrum antifungal drug, may be less potent against *C. parapsilosis*.[3] Yeast Traffic Light was designed to identify these *Candida* species as early as possible and provide rapid and actionable results to help clinicians guide appropriate antifungal therapy.

A recent study by Della-Latta et al. presented at the 2008 ECCMID meeting in Barcelona, Spain demonstrated that rapid identification of *Candida* species using PNA FISH can significantly impact antifungal selection and care for patients with candidemia. In the study, rapid identification of *C. albicans* led to a switch to fluconazole for 70 percent of the patients that had been on caspofungin. At the same time, rapid identification of *C. glabrata*, a *Candida* species with high levels of resistance to fluconazole, led to an 81 percent switch to caspofungin for those patients that had otherwise been given fluconazole. Based on the study results, the authors concluded that the PNA FISH test "can impact the appropriate selection of the most effective antifungal therapy, thereby making it a clinically relevant diagnostic assay."[4]

S. aureus/CNS PNA FISH®



S. aureus CNS

Mixed non-*S. aureus* GPCC

References:

[1] *Spellberg et al. Current Treatment Strategies for Disseminated Candidiasis. Clin. Infec. Dis. 42: 244-251. 2005*
[2] *Pfaller et al. Epidemiology of invasive candidiasis: a persistent public health problem. Clin Microbiol Rev. 2007 Jan;20(1):133-63.*
[3] *Aperis et al. Developments in the treatment of candidiasis: more choices and new challenges. Expert Opin Investig Drugs. 2006 Nov;15(11):1319-36.*
[4] *Della-Latta et al. Impact of Rapid Identification of C. albicans and C. glabrata Directly from Blood Cultures using PNA FISH Technology on Selection of Antifungal Therapy. Poster 1382. ECCMID 2008. Barcelona, Spain.*

2009 SHOWS AND CONFERENCES

First Coast Infectious Disease
January 30-31 • Ponte Vedra Beach, FL

Society of Critical Care Medicine (SCCM)
January 31-February 4 • Nashville, TN

California League of Food Processors (CLFP)
February 3-4 • Sacramento, CA

Virginia College of Emergency Physicians
February 11-12 • Hot Springs, VA

NC ASM
March 13-14 • San Ramon, CA

South Central Association for Clinical Microbiology (SCACM)
March 19-21 • Indianapolis, IN

Society for Healthcare Epidemiology of America (SHEA)
March 19-22 • San Diego, CA

Society of Armed Forces Medical Laboratory Scientists (SAFMLS)
March 22-26 • Reno, NV

Texas College of Emergency Physicians (TCEP)
April 2-4 • San Antonio, TX

California Association of Public Health Laboratory Directors (CAPHLD)
April 13-16 • San Diego, CA

MedAssets Healthcare Business Summit
April 13-17 • Las Vegas, NV

Clinical Virology Symposium (CVS)
April 18-22 • Daytona Beach, FL

American Urological Association (AUA)
April 25-30 • Chicago, IL

Clinical Laboratory Management Association (CLMA)
May 2-5 • Tampa Bay, FL

Clinical Laboratory Scientists of Alaska (CLSA)
May 5-8 • Anchorage, AK

Association of Public Health Laboratories (APHL)
May 5-8 • Anchorage, AK

Clinical Lab Collaborative (CLCC)
May 13-15 • Denver, CO

Society of Hospital Medicine (SHM)
May 14-17 • Chicago, IL

American Thoracic Society (ATS)
May 15-20 • San Diego, CA

American Society for Microbiology (ASM)
May 17-21 • Philadelphia, PA

Association for Professionals in Infection Control (APIC)
June 6-11 • Fort Lauderdale, FL

American Society of Health-System Pharmacists (ASHP) Summer Meeting
June 14-17 • Chicago, IL

International Association for Food Protection (IAFP)
July 12-15 • Grapevine, TX

American Association for Clinical Chemistry (AACC)
July 19-23 • Chicago, IL

Health Industry Distributors Association (HIDA)
September 10-12 • Washington, DC

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

Association for Professionals in Infection Control and Epidemiology (APIC) Hawaii
October 3 • Honolulu, HI

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

American Society for Reproductive Medicine (ASRM)
October 17-21 • Atlanta, GA

Infectious Diseases Society of America (IDSA)
October 29-November 1 • Philadelphia, PA

CHEST
October 31-November 5 • San Diego, CA

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

American Society of Health-System Pharmacists (ASHP)
December 7-9 • Las Vegas, NV

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