# Evaluation of a New System, VITEK 2, for Identification and Antimicrobial Susceptibility Testing of Enterococci

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We evaluated the new automated VITEK 2 system (bioMérieux) for the identification and antimicrobial susceptibility testing of enterococci. The results obtained with the VITEK 2 system were compared to those obtained by reference methods: standard identification by the scheme of Facklam and Sahm [R. R. Facklam and D. F. Sahm, p. 308-314, in P. R. Murray et al., ed., Manual of Clinical Microbiology, 6th ed., 1995] and with the API 20 STREP system and, for antimicrobial susceptibility testing, broth microdilution and agar dilution methods by the procedures of the National Committee for Clinical Laboratory Standards. The presence of vanA and vanB genes was determined by PCR. A total of 150 clinical isolates were studied, corresponding to 60 Enterococcus faecalis, 55 Enterococcus faecium, 26 Enterococcus gallinarum, 5 Enterococcus avium, 2 Enterococcus durans, and 2 Enterococcus raffinosus isolates. Among those isolates, 131 (87%) were correctly identified to the species level with the VITEK 2 system. Approximately half of the misidentifications were for E. faecium with low-level resistance to vancomycin, identified as E. gallinarum or E. casseliflavus; however, a motility test solved the discrepancies and increased the agreement to 94%. Among the strains studied, 66% were vancomycin resistant (57 VanA, 16 VanB, and 26 VanC strains), 23% were ampicillin resistant (MICs, ≥16 µg/ml), 31% were high-level gentamicin resistant, and 45% were high-level streptomycin resistant. Percentages of agreement for susceptibility and resistance to ampicillin, vancomycin, and teicoplanin and for high-level gentamicin resistance and high-level streptomycin resistance were 93, 95, 97, 97, and 96%, respectively. The accuracy of identification and antimicrobial susceptibility testing of enterococci with the VITEK 2 system, together with the significant reduction in handling time, will have a positive impact on the work flow of the clinical microbiology laboratory.

Enterococci are part of the normal gastrointestinal flora of humans. Most clinical isolates of enterococci represent colonizing rather than infecting organisms; however, they can cause more serious infections and are sometimes responsible for cholecystitis, cholangitis, peritonitis, septicemia, endocarditis, and meningitis (9, 11). These infections are often difficult to treat because of the intrinsic and acquired resistance of enterococci to multiple antimicrobial agents (9, 12). Due to the increasing frequency with which multidrug-resistant enterococci are isolated from clinical specimens, there is a need for rapid reporting of results of identification tests and tests for susceptibility to antimicrobial agents. The contribution of rapid reporting of microbiology results must be recognized since it provides both clinical and financial benefits (2). The VITEK 2 system is a new automated system designed to provide rapid and accurate identification and susceptibility testing results for most clinical isolates including enterococci. Identification is made on the basis of biochemical reactions, and MIC determinations are made by applying an algorithm to the growth kinetics monitored by the VITEK 2 system (10; A. Bassel, R. Makkar, D. Freiner, J. L. Balzer, and D. Pincus, Abstr. 8th Eur. Congr. Clin. Microbiol. Infect. Dis., abstr. P255, p. 53, 1997; W. H. F. Goessens, H. J. A. Van Vliet, and H. A. Verbrugh, Abstr. 9th Eur. Congr. Clin. Microbiol. Infect. Dis., abstr. P822, p. 305, 1999).

In this study we evaluate the new automated VITEK 2 system (bioMérieux, Marcy l'Etoile, France) for the identification

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and antimicrobial susceptibility testing of enterococci and compare the results obtained with the VITEK 2 system with those obtained by reference methods.

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### MATERIALS AND METHODS

**Microorganisms.** We studied a total of 150 clinical isolates that belong to our laboratory collection of enterococci. Among those, 125 isolates were recovered in our clinical microbiology laboratory over a period of 10 years, and 25 were sent from other institutions in Spain. This collection studied included 60 *Enterococcus faecalis*, 55 *Enterococcus faecium*, 26 *Enterococcus gallinarum*, 5 *Enterococcus avium*, 2 *Enterococcus durans*, and 2 *Enterococcus rafinosus* isolates. None of the isolates were epidemiologically related. The *E. gallinarum* isolates were recovered from feces (24 isolates) and peritoneal fluid (2 isolates), and the origins of the remaining isolates were urine (30 isolates), wounds (30 isolates), abscesses (18 isolates), blod (17 isolates). Most of the isolates were chosen for the study for their specific mechanisms of resistance: 66% were vancomycin resistant (57 VanA, 16 VanB, and 26 VanC isolates), 23% were ampicillin resistant (MICs,  $\geq$ 16 µg/ml), 31% were high-level gentamicin resistant (HLGR), and 45%

Identification and susceptibility testing. (i) Standard procedures. All microorganisms had previously been identified by two standard procedures: by the scheme of Facklam and Sahm (8) and with the API 20 STREP system (bio-Mérieux) (6). Disagreements between the retrospective reference results and the VITEK 2 system results were solved by repeating the identification with the API 20 STREP system and a motility test. Susceptibility testing was previously performed by two methods: the broth microdilution method and the agar dilution method with Mueller-Hinton broth and agar, respectively, according to the recommendations of the National Committee for Clinical Laboratory Standards (14). The antimicrobial agents tested were ampicillin, teicoplanin, and vancomycin at twofold concentrations from 0.25 to 256  $\mu$ g/ml, gentamicin at 250 and 500  $\mu$ g/ml, and streptomycin at 1,000 and 2,000  $\mu$ g/ml. Discrepancies between these reference results and the VITEK 2 system results were solved by the microdilu-

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tion method. The presence of *vanA* and *vanB* genes was confirmed by PCR as described previously (4). Isolates were considered to have the VanC phenotype of resistance to glycopeptides according to biochemical characteristics, a positive motility test result, and low-level resistance to vancomycin and susceptibility to teicoplanin.

(ii) VITEK 2 system. The VITEK 2 system (bioMérieux) is an integrated modular system that consists of a filling-sealer unit, a reader-incubator, a computer control module, a data terminal, and a multicopy printer. The system detects bacterial growth and metabolic changes in the microwells of thin plastic cards by using a fluorescence-based technology. Different microwell cards contain antibiotics or biochemical substrates. We used the ID-GPC card of the VITEK 2 system for identification and the AST-P516 card of the VITEK 2 system for the antimicrobial susceptibility testing of enterococci. The ID-GPC card is a 64-well plastic card that contains 18 empty wells and 46 wells for fluorescent biochemical and inhibitory tests, as follows: 22 enzymatic tests for aminopeptidases and -osidases. Substrates used for the detection of aminopeptidases are coupled with 7-amino-methylcoumarin (7AMC): substrates for the detection of -osidases are usually coupled with 4-methylumbelliferone (4MU). The 22 test substrates are as follows: 4MU- $\alpha$ -L-arabinofuranoside, 4MU- $\alpha$ -Dgalactoside, 4MU-α-D-glucoside, 4MU-α-D-N-acetylneuraminic acid, 4MU-β-Dgalactoside, 4MU-β-D-glucoside, 4MU-β-D-glucuronide, 4MU-β-D-mannoside, 4MU-N-acetyl-β-D-glucosaminide, 4MU-phosphate, alanine-7AMC, arginine-7AMC, aurease (butiloxicarbonyl-Val-Pro-Arg-AMC), histidine-7AMC, a-glutamic acid-7AMC, threonine-7AMC, leucine-7AMC, lysine-7AMC, phenylala-nine-7AMC, proline-7AMC, pyroglutamic acid-7AMC, and tyrosine-7AMC. Furthermore, the ID-GPC card includes 16 fermentation tests (for D-raffinose, amygdaline, arbutine, D-galactose, glycerol, D-glucose, L-arabinose, lactose, Dmaltose, D-mannitol, N-acetylglucosamine, salicin, D-sorbitol, D-trehalose, D-melibiose, and D-xylose), 2 decarboxylase tests (for ornithine and arginine), and 6 miscellaneous tests (for urease, pyruvate, optochin, novobiocin, polymyxin B sulfate, and 6.5% NaCl). The AST-P516 card is a 64-well plastic card that contains the following 20 antimicrobial agents with different concentrations: ampicillin (0.5, 4, 8, and 32 µg/ml), ampicillin-sulbactam (4/2, 8/4, 16/8, and 64/16 µg/ml), benzylpenicillin (0.125, 0.25, 1, 2, 8, and 64 µg/ml), cefuroxime (4, and 8 µg/ml), ciprofloxacin (1, 2, and 4 µg/ml), clindamycin (0.5, 1, and 2 µg/ml), erythromycin (0.25, 0.5, and 2 µg/ml), gentamicin, high level (150 µg/ml), imipenem (8, 16, and 32  $\mu g/ml),$  kanamycin, high level (200  $\mu g/ml),$  levofloxacin (0.25, 2, and 8 µg/ml), nitrofurantoin (16, 32, and 64 µg/ml), norfloxacin (0.5, 1, and 4 µg/ml), ofloxacin (0.5, 2, and 4 µg/ml), quinupristin-dalfopristin (0.25, 0.5, and 2 µg/ml), streptomycin, high level (200 µg/ml), teicoplanin (1, 4, 8, and 16 µg/ml), tetracycline (0.5, 1, and 2 µg/ml), trimethoprim-sulfamethoxazole (160, 320, and 640 µg/ml), and vancomycin (2, 4, and 6 µg/ml). For this study we evaluated the performance of the VITEK 2 system for testing of susceptibility only to ampicillin, vancomycin, and teicoplanin and for testing for HLGR and HISR

Each organism suspension was prepared from the growth of pure cultures of bacteria cultivated for 18 to 24 h on Columbia agar with 5% sheep blood. The handling time was very short: suspensions were prepared in sterile saline (0.45% NaCl) to a turbidity equivalent to that of a 0.5 McFarland standard. These suspensions were used for the inoculation of both cards (ID-GPC and AST-P516). The cards were manually situated, as were the suspensions, in plastic racks that were inserted in the VITEK 2 system's reader-incubator module (incubation temperature, 35.5°C). The cards were automatically filled by a vacuum device and were automatically sealed and subjected to a kinetic fluorescence measurement every 15 min. The results were interpreted by the ID-GPC database after an incubation period of 4 h, and final results were obtained automatically after a minimum of 4 h and a maximum of 15 h of incubation. All cards used were automatically discarded in a waste container. The ID-GPC database contained data on the following species of *Enterococcus: E. faecalis, E. faecium, E. durans, E. avium, E. hirae, and E. casseliflavus-E. gallinarum*.

**Quality control strains.** *E. faecalis* ATCC 29212, *Staphylococcus aureus* ATCC 29213, and *E. faecium* GE-1 (5) were used as quality control strains every day during the evaluation of the VITEK 2 system.

Analysis of results. (i) Agreement. The VITEK 2 system and the reference method were considered to be in agreement when the species identification of the VITEK 2 system agreed exactly with the species identification of the reference method.

(ii) Essential agreement. MICs obtained with the VITEK 2 system and by the reference methods were considered to be in essential agreement when the MIC obtained with the VITEK 2 system was within 1 twofold dilution of the reference MIC obtained by either the microdilution method or the agar dilution method. In the case of high-level resistance to aminoglycosides, "category agreement" occurred when the categorization of high-level resistance with the VITEK 2 system coincided with the results obtained by the reference methods.

(iii) MIC discrepancies. MIC discrepancies were considered "very major" (the VITEK 2 system indicated susceptible and the reference method indicated resistant), "major" (the VITEK 2 system indicated resistant and the reference method indicated susceptible), and "minor" (the VITEK 2 system indicated intermediate and the reference method indicated susceptible or resistant, or the VITEK 2 system indicated susceptible or resistant and the reference method indicated intermediate).

 TABLE 1. Discrepancies between identification with the VITEK 2 system and by the reference method

	Species identified:		
No. of isolates	By the reference method	With the VITEK 2 system	
2	E. faecium	E. faecalis	
10	E. faecium	E. gallinarum-E. casseliflavus	
1	E. faecalis	E. avium	
2	E. raffinosus	E. faecalis, E. avium <sup>a</sup>	
2	E. gallinarum	E. faecium, E. avium <sup>a</sup>	
1	E. durans	E. hirae	
1	E. faecium	E. hirae	

<sup>a</sup> The VITEK 2 system identified one of each species.

## RESULTS

**Identification.** Among the 150 isolates, 131 were correctly identified to the species level (agreement, 87%). For 19 strains (13%) the species identification with the VITEK 2 system was discrepant with the identification by the reference methods (Table 1). Approximately half of the misidentifications were due to *E. faecium* with low-level resistance to vancomycin, identified as *E. gallinarum-E. casseliflavus*, and a simple motility test solved the discrepancies and increased the agreement to 94%. However, although the system flagged these identifications as "low probability" or "acceptable," with type indices being between 0.25 and 0.66, the system nevertheless suggested complementary motility test results. In addition, two isolates of *E. raffinosus* were incorrectly identified, since the database of the system does not include data for this species.

Susceptibility testing. Percentages of agreement for susceptibility and resistance to ampicillin, vancomycin, teicoplanin, gentamicin (high level), and streptomycin (high level) (essential agreement) were 93, 95, 97, 97, and 96%, respectively (Table 2). Among the vancomycin-resistant strains, the essential agreement was 93%. The VITEK 2 system detected 93 of 99 resistant isolates, including 96% VanA, 81% VanB, and 96% VanC isolates. The discrepancies between the results obtained with the VITEK 2 system and the reference method are listed in Table 2. For two strains in which vancomycin resistance was not detected (one VanB strain and one VanC strain), the species identifications were also incorrect. The very major error rate ranged from 4% for vancomycin to 1.3% for ampicillin, teicoplanin, and gentamicin (high level). Nine ampicillin-susceptible E. faecalis isolates were categorized as ampicillin resistant by the VITEK 2 system. A beta-lactamasepositive E. faecalis strain (13) and an ampicillin-resistant betalactamase-negative E. faecalis strain (3) were not detected as resistant by the VITEK 2 system. Two isolates that presented

TABLE 2. Performance of the VITEK 2 system for susceptibility testing of enterococci compared to that of the reference method

Antimicrobial agant	% of strains (no. of isolates) <sup><i>a</i></sup>			
Antimicrobial agent	EA	mE	ME	VME
Ampicillin	92.6	0	6 (9)	1.3 (2)
Vancomycin	94.6	0	1.3(2)	4 (6)
Teicoplanin	97.3	1.3(2)	0	1.3 (2)
Gentamicin, high level	97.3	0	1.3(2)	1.3 (2)
Streptomycin, high level	96	0	4 (6)	0

<sup>a</sup> EA, essential agreement; mE, minor error; ME, major error; VME, very major error.

TABLE 3. Distribution of times needed to obtain the final results of susceptibility testing with the VITEK 2 system

Time (h)	No. of isolates <sup>a</sup>	% of isolates <sup>b</sup> 42	
6	63		
7	109	73	
8	125	83	
9	132	88	
10	140	93	
11	141	94	
12	145	97	
13	149	99	
14			
15	150	100	

<sup>*a*</sup> Cumulative number of isolates whose susceptibility testing results were available at the indicated incubation time.

<sup>b</sup> Cumulative percentage of isolates whose susceptibility testing results were available at the indicated incubation time.

with HLGR were incorrectly categorized with the system. Complete identification results were obtained after 4 h of incubation for all except two isolates, which required only 3 h, and complete susceptibility testing results were obtained after a minimum of 6 h and a maximum of 15 h of incubation. Results for 90% of isolates were complete after 10 h of incubation (Table 3).

## DISCUSSION

This evaluation of the VITEK 2 system for the identification and susceptibility testing of enterococci was performed with a collection of microorganisms that is not representative of the usual population encountered in general in clinical laboratories, since the majority of the microorganisms used for the evaluation of the system in this study presented with resistance to vancomycin. In our laboratory, the incidence of vancomycinresistant enterococci (VRE) in the last 10 years has ranged from 0.5 to 0.7% (1 to 11% among E. faecium isolates and 0 to 1% among E. faecalis isolates), and in a recent study of the prevalence of intestinal colonization in our institution, the rate of colonization with VRE was 4.5% (E. Cercenado, L. Alcalá, B. Padilla, F. García-Garrote, L. Torres, and E. Bouza, Abstr. 9th Eur. Congr. Clin. Microbiol. Infect. Dis., abstr. P147, p. 124, 1999). However, our data suggest that the VITEK 2 system performs equally well for susceptible and resistant isolates, and there is no evidence that the accuracy of the results differed significantly between the susceptible and resistant groups (Table 2). The enterococcal species included in the study (with the exception of E. raffinosus) are those most frequently encountered in a clinical laboratory, and the rate of accurate identification to the species level was 87%. This rate is only acceptable, and the performance of a simple supplementary motility test increased the agreement to 94%, which is, in our view, accurate, although for these isolates the identification time increased by 15 h. However, the system failed to suggest a complementary motility test, although it did flag these identifications as "low probability." So, in order to confirm the results, we recommend routine performance of the motility test whenever the VITEK 2 system reports E. gallinarum or E. casseliflavus as an identification, unless future upgrades of the database will be available. The system also needs upgrades concerning the enterococcal species data in the database, since data for very few species are included. When attempting to determine the performance of an automated identification system, one should consider the publications that have evaluated or compared the latest software, database, biochemical configuration, or other performance characteristics of the system. To our knowledge, very few studies have evaluated the VITEK 2 system for the identification of enterococci. Our results fell within the range obtained by others, who have demonstrated a correlation of between 83 and 95.3% for the results obtained with the VITEK 2 system compared with those obtained by the reference methods (Bassel et al., Abstr. 8th Eur. Congr. Clin. Microbiol. Infect. Dis.; E. Halle, I. Klare, and U. B. Göbel, Abstr. 9th Eur. Congr. Clin. Microbiol. Infect. Dis., abstr. P147A, addendum, 1999; K. Szczypa, M. Kawalec, A. Kuzimska, and T. Kaminska, Abstr. 9th Eur. Congr. Clin. Microbiol. Infect. Dis., abstr. P31, p. 92, 1999).

In our study, the VITEK 2 system correctly detected 94% of glycopeptide-resistant enterococci, including those with the VanA, VanB, and VanC phenotypes of resistance. The system failed to detect two VanA isolates, three VanB isolates, and one VanC isolate. A few studies have evaluated this system for the determination of the susceptibilities of enterococci to vancomycin and teicoplanin, and the results obtained were similar to ours (Halle et al., Abstr. 9th Eur. Congr. Clin. Microbiol. Infect. Dis.; B. König, A. Parkner, and A. König, Abstr. 9th Eur. Congr. Clin. Microbiol. Infect. Dis. abstr. P32, p. 92-93, 1999; J. Rader, C. Bradford, D. Leahart, M. Ullery, and J. Gerst, Abstr. 98th Gen. Meet. Am. Soc. Microbiol. 1998, abstr. C357, p. 113, 1998; Szczypa et al., Abstr. 9th Eur. Congr. Clin. Microbiol. Infect. Dis.), demonstrating that the VITEK 2 system accurately detects glycopeptide resistance. The results of the VITEK 2 system for the detection of HLGR and HLSR strains were highly correlated with those of the reference methods, with a very major error rate (false-susceptible result for a resistant isolate) of 1.3% for gentamicin and no very major errors for streptomycin. Previous studies have demonstrated similar results, with very major error rates between 0 and 1.5% (W. McLaughlin, C. Schubert, R. Griffith, M. Sanders, and M. Peyret, Abstr. 98th Gen. Meet. Am. Soc. Microbiol. 1998, abstr. C358, p. 113, 1998; L. A. Meeh, C. Schubert, S. Weber, P. Kim, and M. Peyret, Abstr. 98th Gen. Meet. Am. Soc. Microbiol. 1998, abstr. V66, p. 105, 1998). The detection of ampicillin-resistant enterococci with the VITEK 2 system was accurate. Of the two isolates with very major errors, one was a beta-lactamase-positive strain; however, the MIC determined by the system was correct. It is well known that betalactamase detection among enterococci is inoculum dependent and the error could be due to a low inoculum (16). On the other hand, the classification of nine ampicillin-susceptible E. faecalis strains as resistant indicates that the system needs further improvement. Other studies have demonstrated discrepant results concerning the detection of ampicillin-resistant enterococci with the VITEK 2 system, indicating that the algorithm for ampicillin must be adapted accordingly (Halle et al. and Szczypa et al., Abstr. 9th Eur. Congr. Clin. Microbiol. Infect. Dis.). In comparison with the AutoMicrobic system (1, 7, 15; N. Schiminsky and P. Ferrieri, Abstr. 87th Annu. Meet. Am. Soc. Microbiol. 1987, abstr. C94, p. 339, 1987), the old version of the VITEK 2 system, the new version has the advantage of a shorter handling time and the more rapid identification and susceptibility testing of enterococci.

In general, the VITEK 2 system is an easy-to-handle system that provides a rapid (4 to 15 h) and reasonably accurate means for the identification of most commonly isolated species of *Enterococcus* and accurately detects resistance to ampicillin and glycopeptides and high-level resistance to gentamicin and streptomycin among these species. However, the system needs further improvement in its accuracy of identification, interpretation of results, and database. One of the most important advantages of the VITEK 2 system is the significant reduction in handling time, which will have a positive impact on the work flow of the clinical microbiology laboratory.

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