

# Comparison of Phoenix to Vitek2 Antimicrobial Susceptibility Test Performance with a Diverse Group of Bacteria which are Found in Clinical Microbiology Labs.

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## REVISED ABSTRACT

■ **OBJECTIVES:** Two rapid automated identification and antimicrobial susceptibility test (AST) systems, Phoenix (BD Diagnostic Systems) and Vitek2 (bioMérieux), were evaluated for their AST performance using a challenge set of gram-negative bacilli and gram-positive cocci.

**METHODS:** Standard commercially available Phoenix panels and Vitek2 cards were used with an appropriate panel type for gram-negative and gram-positive organisms. A total of 165 gram-negative bacilli, 102 Enterococcus (34 VRE) and 339 Staphylococcal strains (168 *S. aureus* and 47 MRSA) were tested composing a sample of species that are commonly seen in clinical microbiology. All antibiotics evaluated were clinically relevant for organisms being tested and included 10 antibiotics for gram-negatives, 10 for Staphylococci, and 8 for Enterococcus. Isolates were tested in both systems following normal procedures recommended for each product. Individual MICs were interpreted following DIN standards, except for agents where there were no interpretive standards, in which case SFM or NCCLS standards were used. Phoenix and Vitek2 AST results were compared and major discrepancies were retested and the AST result arbitrated by microdilution MIC testing. Overall performance by organism group and by significant resistance mechanisms was compared.

**RESULTS:** Overall, Phoenix AST results were comparable to Vitek2 in 94% of the tests. The comparability by organism group was 92% for gram-negative bacillus, 96% for Staphylococcus, and 89% for Enterococcus. MRSA was detected in 49 strains in both systems, with two strains being resistant in Phoenix and susceptible in Vitek2, and 2 strains being susceptible in Phoenix and resistant in Vitek2. VRE was detected in both systems 32 times, and in Vitek but not Phoenix 2 times, and Phoenix but not Vitek 1 time. Arbitration testing was in favor of Phoenix in the two cases where Phoenix was susceptible and Vitek2 was resistant.

## INTRODUCTION

The Antimicrobial Susceptibility Testing (AST) of gram-negative and gram-positive bacteria represents a significant function of virtually all clinical microbiology laboratories. Over the years there have been a number of commercially available systems for performing these tests. These range from fully manual tests (Disk Diffusion, or Micro-broth dilution) to more automated tests such as Vitek (bioMérieux) or MicroScan (Dade) where incubation, reading, and interpretation are performed automatically by an instrument. Most of the automated systems combine bacterial identification and AST. In recent years two new automated systems have become available in the German arena. These include the Vitek2 (bioMérieux) and the BD Phoenix (BD) systems. These systems claim to offer more rapid test results and improvements to reduce workload of the laboratory (auto inoculation, Expert systems etc.). In this study, we evaluated the Phoenix system in comparison to the Vitek2 system for AST of some commonly isolated gram-negative and gram-positive bacteria.

## MATERIALS & METHODS

### Bacterial Isolates

A combination of fresh clinical isolates and frozen stock cultures was tested including 165 gram-negative organisms, 330 *Staphylococcus* strains, and 102 *Enterococcus* strains (Table 1). The gram-negative bacteria included a representative sample of *Enterobacteriaceae* and Non-fermentative species. For gram-positives a routine mix of 216 fresh strains of *Staphylococci* and *Enterococci* isolated from our routine clinical lab was tested. In addition, a set of 239 *Staphylococcus* challenge strains from a combination of our culture collection and BD culture collection was tested to include less routinely isolated species.

### Phoenix

(BD Diagnostic Systems, Sparks, MD): gram-negative (NMIC/ID-1 and NMIC/ID-5) and gram-positive (PMIC/ID-1 and PMIC/ID-4) combination panels were used. The gram-negative panels included a test for the presence of ESBL using a principle similar to the NCCLS confirmatory test. The gram-positive panels contained a test for *Staphylococcal* penicillinase ( $\beta$ -Lactamase). The results of these tests were integrated into the antibiogram through the BDXpert System. Phoenix panels were tested strictly following manufacturer's instructions. Briefly, blood agar plates were inoculated with the test cultures and were incubated for 18-24 hours at 35°C. Isolated colonies were used to prepare a suspension of the bacteria in the Phoenix ID broth to match a 0.5 MacFarland by the use of CrystalSpec. AST broth was supplemented with one drop of indicator dye and 25  $\mu$ L of the ID suspension. Panels were auto-inoculated by pouring the AST suspension into the AST port of the panel. After closing, the panels were logged and loaded into the instrument. The

instrument automatically incubated and optically scanned the panels at 20 min. intervals. Dedicated algorithms kinetically calculated the MICs after sufficient incubation time. These results were automatically interpreted, and additionally evaluated for consistency and resistance mechanisms with the on-board BDXpert system. The Phoenix software version was 1.06 and the system was configured to interpret MIC values following DIN recommendations, except for those antibiotics where there were no DIN breakpoints available. In these cases the NCCLS breakpoints, or in the case of teicoplanin SFM breakpoints, were used.

### Vitek2

Vitek2 AST-N010 cards were used for testing of gram-negative organisms, AST-P010 cards were used for testing of *Enterococcus*, and a combination of AST-P515, P523, and P526 cards was used for testing *Staphylococcus*. The Vitek2 instrument with the "Smart Carrier Station" and DensiCheck was used. All test procedures were performed according to manufacturer's recommendations. The software was configured to use DIN breakpoints (1998), except for antimicrobial agents where DIN breakpoints had not been defined. In these cases NCCLS breakpoints were used (1999).

### Arbitration

If the Phoenix *vs.* Vitek2 results exhibited a major or very major discrepancy, AST results were retested using a commercially available micro-broth dilution system (Biotest, Germany) following the DIN recommendations. The system that agreed with the arbitrator was considered the correct result.

Table 1  
Distribution of Organisms Tested

	Organism	n	
Gram-negative	<i>Acinetobacter baumannii</i> group	7	
	<i>Citrobacter braakii</i>	3	
	<i>Citrobacter freundii</i>	10	
	<i>Citrobacter koseri</i>	11	
	<i>Enterobacter amnigenus</i>	1	
	<i>Enterobacter aerogenes</i>	8	
	<i>Enterobacter cloacae</i>	16	
	<i>Escherichia coli</i>	19	
	<i>Hafnia alvei</i>	5	
	<i>Klebsiella oxytoca</i>	14	
	<i>Klebsiella pneumoniae</i>	21	
	<i>Morganella morganii</i>	10	
	<i>Proteus mirabilis</i>	11	
	<i>Pseudomonas aeruginosa</i>	19	
	<i>Serratia marcescens</i>	9	
	<i>Enteric spp.</i> Not identified	1	
	<b>Gram-negative total</b>		<b>165</b>
	Staphylococci	<i>Staphylococcus aureus</i>	169
		<i>Staphylococcus capitis</i>	8
		<i>Staphylococcus cohnii</i>	10
<i>Staphylococcus epidermidis</i>		50	
<i>Staphylococcus haemolyticus</i>		39	
<i>Staphylococcus hominis</i>		15	
<i>Staphylococcus hyicus</i>		1	
<i>Staphylococcus lugdunensis</i>		27	
<i>Staphylococcus saprophyticus</i>		12	
<i>Staphylococcus simulans</i>		1	
<i>Staphylococcus warneri</i>		7	
<b>Staphylococci total</b>		<b>339</b>	
Enterococci		<i>Enterococci casseliflavus/gallinarum</i>	10
		<i>Enterococci durans</i>	1
		<i>Enterococci faecalis</i>	48
	<i>Enterococci faecium</i>	54	
	<i>Enterococci raffinosus</i>	2	
	<i>Enterococci species</i>	1	
	<b>Enterococci total</b>		<b>116</b>
<b>Total</b>		<b>620</b>	

Table 2  
Gram-Negative Strain Comparison of Phoenix to Vitek2 Pre-Expert Interpretive SIR Results

Gram-Negative	Antibiotic	Code	Total	Category Agreement Pre Expert	Agreement (Phoenix/Vitek2)			Major Discrepancies (Phoenix/Vitek2)		Minor Discrepancies (Phoenix/Vitek2)
					S/S	I/I	R/R	S/R	R/S	
	Ampicillin <sup>1</sup>	AM	165	87.3%	19	11	114	2	3	9.7%
	Piperacillin	PIP	163	85.9%	93	33	14	0	0	14.1%
	Piperacillin/Tazobactam <sup>2</sup>	TZP	160	89.7%	131	14	3	0	1	9.7%
	Cefuroxime	CXM	165	86.3%	72	2	64	0	0	13.8%
	Ceftazidime	CAZ	165	97.0%	153	1	6	0	0	3.0%
	Cefotaxime	CTX	164	95.1%	130	3	23	0	0	4.9%
	Cefepime	FEB	165	97.0%	153	6	1	0	0	3.0%
	Meropenem	MEM	165	97.0%	159	0	1	0	0	3.0%
	Ciprofloxacin	CIP	165	100.0%	161	2	2	0	0	0.0%
	Nitrofurantoin (NCCLS)	FM	161	78.9%	68	21	38	0	0	21.1%
	Amikacin	AN	165	95.8%	153	4	1	0	0	4.2%
	Gentamicin	GM	165	93.9%	140	13	2	0	0	6.1%
	<b>Total</b>		<b>1968</b>	<b>92.0%</b>	<b>1432</b>	<b>110</b>	<b>269</b>	<b>2</b>	<b>4</b>	<b>7.7%</b>

<sup>1</sup>AM - All were resolved by either Phoenix BDXpert (2 S to R), or Vitek2 AES (3 R to S) intrinsic resistance rules

<sup>2</sup>TZP - 1 strain of *K. pneumoniae* arbitration = 1

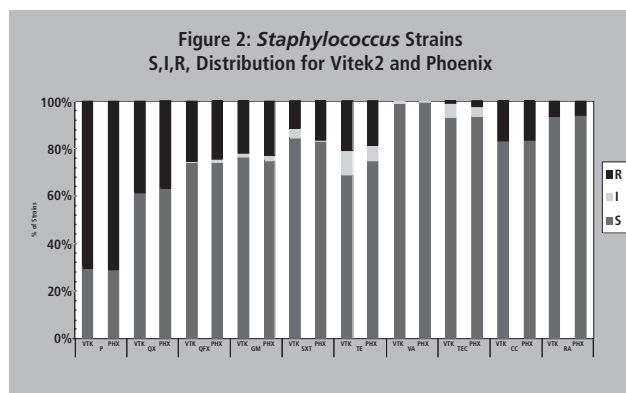
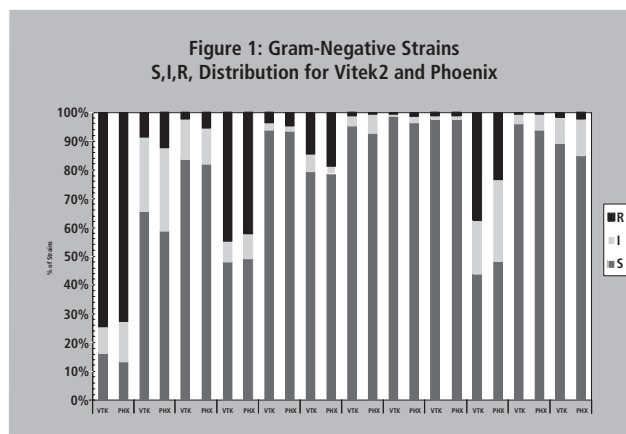
Table 3  
Staphylococcus Comparison of Phoenix to Vitek2 Pre-Expert Interpretive SIR Results

Staphylococci	Antibiotic	Code	Total	Category Agreement	Agreement (Phoenix/Vitek2)			Major Discrepancies (Phoenix/Vitek2)		Minor Discrepancies (Phoenix/Vitek2)
					Pre Expert	S/S	I/I	R/R	S/R	R/S
Penicillin <sup>1</sup>	P	218	99.1%	62	0	154	1	1	0.0%	
Oxacillin <sup>2</sup>	OX	328	97.9%	202	0	119	4	3	0.0%	
<i>S. aureus</i>		168	98.8%	119	0	47	0	2	0.0%	
<i>S. epidermidis</i>		48	97.9%	6	0	41	1	0	0.0%	
other CNS		112	96.4%	77	0	31	3	1	0.0%	
Ofloxacin	OFX	309	99.4%	230	1	76	0	0	0.6%	
Gentamicin <sup>3</sup>	GM	333	98.2%	249	5	73	0	3	0.9%	
		298	98.7%	204	1	89	0	2	0.7%	
Trimethoprim/Sulfa.	SXT	323	95.4%	271	0	37	0	0	4.6%	
Tetracycline	TE	326	91.7%	224	14	61	0	0	8.3%	
Vancomycin	VA	336	98.8%	332	0	0	0	0	1.2%	
Teicoplanin	TEC	333	93.7%	304	6	2	0	0	6.3%	
Clindamycin	CC	330	100.0%	276	0	54	0	0	0.0%	
Rifampin	RA	333	99.7%	311	0	21	0	0	0.3%	
<b>Total</b>		<b>3467</b>	<b>97.4%</b>	<b>2665</b>	<b>27</b>	<b>686</b>	<b>5</b>	<b>9</b>	<b>2.0%</b>	

<sup>1</sup>P - Smaller n because Phoenix does not report results for penicillin for CNS other than *S. epidermidis*. With one *S. epidermidis* strain, the Phoenix BDxpert corrected "S" to "R" due to a positive  $\beta$ -lactamase test. One strain of *S. aureus* Phoenix = R, Vitek2 = S, Arbitration agrees with Vitek2.

<sup>2</sup>OX - 2 *S. aureus* strains Phoenix "R" and Vitek2 = "S" arbitrated in favor of Vitek2. One *S. epidermidis* Phoenix "S" and Vitek2 "R" arbitrated in favor of Phoenix. 4 other coagulase negative Staph arbitrated in favor of Phoenix.

<sup>3</sup>GM - 3 major discrepancies all with *S. aureus*. Arbitration: 2 were in favor of Phoenix, 1 in favor of Vitek2



## RESULTS

■ The distribution of interpretive results in both Phoenix and Vitek2 for gram-negative, *Staphylococcus*, and *Enterococcus* strains are presented in Figures 1, 2 and 3, respectively. The results of the performance of the Phoenix system in comparison to Vitek2 for clinical routine isolates and stock cultures of gram-negative and gram-positive bacteria are shown in Tables 2 to 4.

### Gram-negatives

The overall interpretive comparability between Vitek2 and Phoenix was good (92%). Most major discrepancies were seen with ampicillin. All of these discrepant results were resolved through the action of either systems expert algorithms (2 with Phoenix and 3 with Vitek2). One piperacillin/tazobactam discrepancy was arbitrated in favor of Phoenix.

Minor disagreements were most often observed with piperacillin, piperacillin/tazobactam, cefuroxime, and nitrofurantoin. These minor discrepancies were not arbitrated; however there was a tendency with piperacillin and piperacillin/tazobactam for Phoenix to give more resistant results than Vitek2, but the reverse trend was observed with cefuroxime and nitrofurantoin.

### Staphylococci

Phoenix and Vitek2 were highly comparable with most antibiotics with category agreement > 90% for all antibiotics and 9/11 antibiotics having greater than 95% category agreement.

In spite of this high category agreement there were more frequent

major disagreements with oxacillin, a critical test antibiotic for Staphylococci. Many of the interpretive disagreements (4/7) were with coagulase negative Staphylococci other than *S. epidermidis*. Within this group most of the discrepancies (3/4) were with one species, *S. lugdunensis*. These strains were oxacillin resistant in Vitek2 (MIC>1) but susceptible in Phoenix (MIC<=1) and arbitration tests were all in favor of Phoenix.

There were two strains of *S. epidermidis* with a Phoenix "R" and Vitek2 "S" results; both were arbitrated in favor of Vitek2 suggesting Phoenix false resistance. There was one strain of *S. epidermidis* with a Phoenix "S" and Vitek "R" and this was arbitrated in favor of Phoenix suggesting a major error with Vitek2.

### Enterococci

Phoenix and Vitek2 were observed to have good interpretive agreement with these organisms with the exception of the two fluoro-quinolones, ciprofloxacin and ofloxacin, where a large proportion of minor errors was seen. There was no trend for either system to give a more resistant result.

There were 2 major discrepancies with vancomycin where arbitration was in favor of the Phoenix system. There were also 2 additional major discrepancies, one each, with ciprofloxacin and ofloxacin. In both of these cases the major discrepancies were brought into a minor category through the action of a Vitek2 AES recommendation to report these agents as "I."

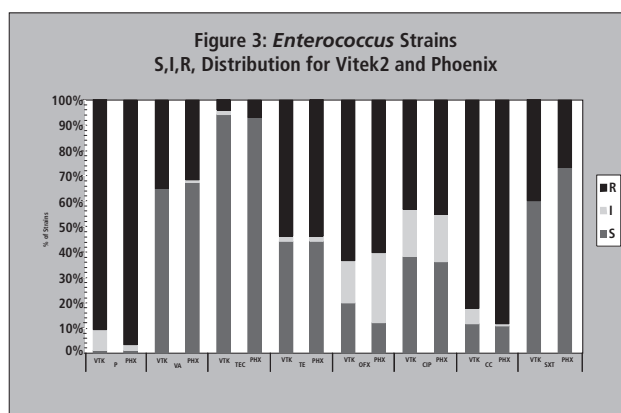
Table 4  
Enterococcus Comparison of Phoenix to Vitek2 Pre-Expert Interpretive SIR Results

Gram-Negative	Antibiotic	Code	Total	Category Agreement Pre Expert	Agreement (Phoenix/Vitek2)			Major Discrepancies (Phoenix/Vitek2)		Minor Discrepancies (Phoenix/Vitek2)
					S/S	I/I	R/R	S/R	R/S	
	Penicillin	P	87	92.0%	1	1	78	0	0	8.0%
	Vancomycin <sup>1</sup>	VA	101	97.0%	66	0	32	2	0	1.0%
	Gentamicin Synergy	GMS	90	97.8%	37	0	51	2	0	0.0%
	Streptomycin Synergy	STS	90	98.0%	34	0	54	1	1	0.0%
	Teicoplanin	TEC	102	98.0%	96	0	4	0	0	2.0%
	Tetracycline	TE	102	100.0%	45	2	55	0	0	0.0%
	Ofloxacin <sup>2</sup>	OFX	101	70.3%	11	8	52	0	1	28.7%
	Ciprofloxacin <sup>3</sup>	CIP	102	77.5%	29	8	42	0	1	21.6%
	<b>Total</b>		<b>595</b>	<b>89.1%</b>	<b>248</b>	<b>19</b>	<b>263</b>	<b>2</b>	<b>2</b>	<b>7.4%</b>

<sup>1</sup>VA - In two strains *E. faecium* arbitration indicates "S" in favor of Phoenix

<sup>2</sup>OFX - 1 strain Vitek2 AES suggests interpretive change to "I."

<sup>3</sup>CIP - 1 strain Vitek2 AES suggests interpretive change to "I."



## CONCLUSIONS

### For gram-negatives

Phoenix results were reasonably comparable to Vitek2. Discordant results were usually minor but suggested that Phoenix had a bias for higher MIC values with penicillins, with piperacillin and piperacillin/tazobactam; and Vitek2 had a bias for higher MIC values with cefuroxime and nitrofurantoin.

### For Staphylococcus

The performance of Phoenix was highly comparable. However, there were more major errors with the critical drug oxacillin. Arbitration of these major disagreements was most often in favor of Phoenix (5/7). *S. lugdunensis* was the species with most of the disagreements (3/5). In a recent report by Zafar Hussain *et. al.* (JCM 2000, Vol. 38, pp. 752-754) it is reported that most strains have MIC values >1 ("R" by DIN), but are *mecA* negative. Thus, we are unable to determine which system is more correct with these species.

### For Enterococcus

The Phoenix results were also fairly comparable to Vitek2. There were relatively few disagreements with antibiotics most critical with the organisms; i.e. ampicillin, vancomycin, aminoglycoside synergy.

**Phoenix and Vitek2 provide very comparable AST results.**