Lifespan

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# Comparative Evaluation of the Sensititre® ARIS 2X® and the BD Phoenix Automated Identification and Antimicrobial Susceptibility Test Systems

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## ABSTRACT

**Background:** The objective of this study was to perform a prospective comparative evaluation of two automated identification (ID) and antimicrobial susceptibility test (AST) systems, the Sensititre® ARIS 2X® System (TREK Diagnostic Systems, Cleveland, OH) and the BD Phoenix (BD Diagnostics, Sparks, MD).
**Materials**: 639 organisms, including 242 gram positive (GP), 49 *S. pneumoniae* (SP) and 348 gram negative (GN), including *Pseudomonas* spp. were tested over 11 months (March 2005 through February 2006), for a total of 6374 antimicrobial-organism combinations. ID and AST panel inoculations were performed simultaneously and according to each of the manufacturer's instructions. Standard GP, GN and SP plates were used. Discrepant analysis included repeat of initial test, use of API identification systems, Kirby-Bauer and CLSI frozen reference panels.
**Results:** ID and AST results from the two systems were compared to each other and then to reference methods to resolve discrepancies. After discrepant analysis, identification agreement for all organisms to genus level was 98.8% and 99.0% and 99.2% and 97.4% to species level for Phoenix and ARIS 2X, respectively. Susceptibility Essential Agreement for 348 GN or 3453 antimicrobial-organism combinations after discrepant analysis was 99.1% for the Phoenix and 99.6% for ARIS 2X. Minor, major, and very major categorical errors were 0.5, 0.4%,and 0% for Phoenix and 0.3, 0 and 0% for ARIS 2X. Likewise, for 242 GP isolates or 2333 combinations, essential agreement was 99.6% for Phoenix and 99.9% for ARIS 2X. Categorical agreement showed 0.09, 0.05, and 0.2% and 0.04, 0 and 0.5% minor, major and very major errors for Phoenix and ARIS 2X, respectively. 49 SP isolates showed 99.8% AST categorical agreement between the 2 systems with no major or very major errors.
**Conclusion:** Overall both systems performed in an equivalent fashion but there were some slight differences. Phoenix trended to report higher MICs, and was unable to give an MIC for 25% of organism-antibiotic combinations due to current FDA restrictions and performance limitations. ARIS 2X trended to have lower MICs and was unable to provide genus/species ID for 3% of gram negative organisms.

## INTRODUCTION

The purpose of this study was to perform a prospective comparison of the Sensititre ARIS 2X and the BD Phoenix automated identification and susceptibility systems using a wide range of gram positive and gram negative unique patient isolates. Both components of a system are required to function extremely well given susceptibility determinations commonly relying on organism- identification based algorithms and changing trends in antimicrobial resistance.

## MATERIALS & METHODS

- Quality control and daily maintenance was performed according to the manufacturer's instructions.
- 348 gram negative, 242 Gram positive and 49 *Streptococcus pneumoniae* clinical isolates were tested. (Table 1)
- AST and ID inoculations for both systems were done simultaneously.
- Broths were adjusted to a 0.5 McFarland with a manufacturer specific nephelometer.
- Standard plates were used for identification and susceptibility testing; custom plates were not included. (Table 2)

BD plates
- One panel was used for both ID and AST.
- AST indicator was added to AST tube.
- 25 ul of ID broth was transferred to AST tube.
- Contents were poured into panel and placed in the instrument.
- Panels were read between 2-12 hours for ID and between 9-16 hours for AST

Trek plates
- Two separate plates were necessary for ID (3 IDs per plate) and AST.
- 10 ul was transferred to 10 ml broth for GP and GN, 1 ul for *Proteus* spp. and 100ul for *S. pneumoniae* and *S. viridans.*
- Plates were dosed with the autoinoculator.
- Plates were read at 18-24 hours via the ARIS 2X.

Data Analysis
- Neither method was considered a reference method. Agreement between the 2 systems was considered a correct result.
- Identifications were determined to genus and species level.
- AST results were determined for both categorical (S,I,R) and essential agreement (+/- one well )
  - Minor error: one method = I, one method = S or R
  - Major error: one method = S, one method = R
  - Very major error = determined after reference testing was performed

Discrepant Analysis
- Genus/species or susceptibility results were repeated with both systems and if in agreement no further testing was performed.
- Genus/Species disagreement remained:
  - API test systems for both gram positive and gram negative were performed.
- Susceptibility discrepant analysis was performed by frozen panels (PASCO and Sensititre) and Kirby-Bauer with investigator blinded to original results for the following unresolved isolates:
  - Minor errors with essential agreement greater than one dilution
  - Major errors
  - Essential agreement greater than one dilution

## RESULTS

- Performance parameters of organism identification and susceptibility results are shown in Tables 3-7.
- Reference testing utilizing frozen panels demonstrated trending as follows:
  - For the Phoenix 78% (27 total) of the discrepant isolates were at least one dilution higher than the reference method; 11% were lower. Of the isolates greater than the reference method 100% resulted in an error.
  - For the ARIS 2X 11%(27 total) were higher than the reference method and 44% were at least 1 dilution lower. For the isolates less than reference 26% resulted in an error.
  - Phoenix vancomycin MICs for MRSA were 2 and TREK MICs were 1 with 82% (60) of isolates tested. Further reference testing on these isolates is required.
- Phoenix MICs were at least 1 dilution higher than ARIS 2X MICs for greater than 90%(143) of gram negative/antibiotic combinations compared, including minor errors not repeated as well as discrepant results resolved.

## RESULTS cont.

**Table 1: Isolates Tested**

| Organism | No. tested | Organism | No. tested |
|---|---|---|---|
| **Gram-negative:** | | **Gram-positive:** | |
| *Escherichia coli* | 56 | *Staphylococcus aureus* (MSSA) | 33 |
| *Pseudomonas aeruginosa* | 53 | *Staphylococcus aureus* (MRSA) | 27 |
| Klebsiella spp. | 48 | *Enterococcus faecalis* (vancomycin S) | 33 |
| Enterobacter spp. | 46 | *Enterococcus faecalis* (vancomycin R) | 2 |
| Serratia spp. | 36 | *Enterococcus faecium* (vancomycin S) | 5 |
| Proteus spp. | 31 | *Enterococcus faecium* (vancomycin R) | 4 |
| *Stenotrophomonas maltophilia* | 18 | Coagulase-negative Staphylococcus | 52 |
| Acinetobacter spp. | 17 | *Streptococcus pneumoniae* | 49 |
| Citrobacter spp. | 12 | Beta-hemolytic Streptococcus (Group B) | 35 |
| *Morganella morganii* | 5 | Beta-hemolytic Streptococcus (Group A) | 30 |
| Providencia spp. | 3 | Streptococcus viridans | 21 |
| Misc. fermenters | 12 | **Total Gram-positive:** | **291** |
| Misc. nonfermenters | 11 | | |
| **Total Gram-negative:** | **348** | **Total isolates tested:** | **639** |

**Table 2: Antimicrobials Common to both Sensititre and Phoenix Panels**

| Gram Negative[a] | Gram Positive[b] | Streptococcus[c] |
|---|---|---|
| Amikacin | Ampicillin | Cefepime |
| Ampicillin | Clindamycin | Cefotaxime |
| Aztreonam | Erythromycin | Ceftriaxone |
| Cefepime | Gatifloxacin | Clindamycin |
| Cefoxitin | Gentamicin | Erythromycin |
| Ceftazidime | Gentamicin-Synergy | Gatifloxacin |
| Cefuroxime | Levofloxacin | Levofloxacin |
| Ciprofloxacin | Linezolid | Linezolid |
| Gatifloxacin | Oxacillin | Meropenem |
| Gentamicin | Penicillin | Penicillin |
| Imipenem | Quinupristin/Dalfopristin | Tetracycline |
| Meropenem | Rifampin | Trimethoprim/Sulfamethoxazole |
| Nitrofurantoin | Streptomycin-Synergy | Vancomycin |
| Piperacillin | Tetracycline | |
| Piperacillin/Tazobactam | Trimethoprim/Sulfamethoxazole | |
| Tobramycin | Vancomycin | |
| Trimethoprim/Sulfamethoxazole | | |

a Sensititre: GN2F(all GNR); Phoenix: NMIC/ID-107(GNR excluding *Pseudomonas* and misc.NF), NMIC/ID-108(*Pseudomonas* and misc.NF)
b Sensititre: GPN3F(*Staph* spp.,*Enterococcus*,BHS); Phoenix: PMIC/ID-100(*Staph* spp.,*Enterococcus*)
c Sensititre: STP3F(*S. pneumoniae* and S. viridans); Phoenix: SMIC-100(*S. pneumoniae*, *S. viridans* and BHS)

**Table 3: Performance of Organism Identfication**

| | Phoenix % correct (n[a]) | ARIS 2X % correct (n) |
|---|---|---|
| **Gram-negative (genus)** | 98.3(348) | 98.6(348) |
| **Gram-negative (species)** | 99.1(342) | 96.2(343) |
| **Gram-positive (genus)** | 100(160) | 100(160) |
| **Gram-positive (species)** | 99.4(160) | 100(160)[b] |
| **Overall (genus)** | 98.8%(508) | 99.0%(508) |
| **Overall (species)** | 99.2%(502) | 97.4%(503) |

[a] n = total isolates tested
[b] 5% required Synercid susceptibility interpretation to distinguish between *E. faecalis* and *E. faecium.*

## RESULTS cont.

**Table 4: Gram-Negative Results of Arbitration for Minor and Major Errors**

| Antimicrobial | Organism | Phoenix | ARIS 2X | Reference MIC(ug/ml) | Reference Kirby-Bauer[a] | Resulting Error[b] Phoenix | Resulting Error[b] ARIS 2X |
|---|---|---|---|---|---|---|---|
| Aztreonam | *Klebsiella pneumoniae* | >16 R | <=8 S | | 17mm I | Minor | Minor |
| Cefepime | *Pseudomonas aeruginosa* | >16 R | <=4 S | 4 S | | Major | |
| | *Pseudomonas aeruginosa* | 16 I | <=4 S | 4 S | | Minor | |
| | *Serratia marcescens* | >16 R | <=4 S | 8 S | | Major | |
| Imipenem | *Serratia marcescens* | 8 I | <=2 S | 1S | | Minor | |
| | *Burkholderia cepacia* | >8 R | 4 S | 8 I | | Minor | Minor |
| Nitrofurantoin | *Enterobacter aerogenes* | >64 R | 32 S | 64 I | | Minor | Minor |
| | *Enterobacter aerogenes* | 64 I | <=16 S | 64 I | | | Minor |
| | *Enterobacter cloacae* | >64 R | 32 S | 64 I | | Minor | Minor |
| | *Enterobacter aerogenes* | 64 I | <=16 S | | 16mm I | | Minor |
| | *Klebsiella pneumoniae* | >64 R | 32 S | 32 S | | Major | |
| | *Klebsiella pneumoniae* | 64 I | <=16 S | 32 S | | Minor | |
| | *Klebsiella pneumoniae* | 64 I | <=16 S | 32 S | | Minor | |
| | *Klebsiella pneumoniae* | >64 R | 32 S | 64 I | | Minor | Minor |
| | *Klebsiella pneumoniae* | >64 R | 32 S | | 17mm S | Major | |
| | *Klebsiella pneumoniae* | >64 R | 32 S | | 17mm S | Major | |
| | *Klebsiella pneumoniae* | 64 I | <=16 S | | 17mm S | Minor | |
| | *Klebsiella pneumoniae* | 64 I | <=16 S | | 16mm I | | Minor |
| | *Klebsiella pneumoniae* | >64 R | 32 S | | 15mm I | Minor | Minor |
| Piperacillin | *Acinetobacter baumannii* | >64 R | <=16 S | 8 S | | Major | |
| | *Acinetobacter baumannii* | >64 R | <=16 S | 16 S | | Major | |
| | *Acinetobacter baumannii* | 64 I | <=16 S | | 21mm S | Minor | |
| | *Escherichia coli* | >64 R | 32 S | | 18mm I | Minor | Minor |
| Piperacillin/Tazobactam | *Serratia marcescens* | >64/4 R | 32 I | | 21mm S | Major | Minor |
| | *Escherichia coli* | >64/4 R | 32 I | | 18mm I | Minor | |
| | *Alcaligenes sp.* | 64/4 I | <=16 S | | 21mm S | Minor | |
| | *Klebsiella pneumoniae* | >64/4 R | 32 I | 32/4 I | | Minor | |
| Trimethoprim/Sulfamethoxazole | *Stenotrophomonas maltophilia* | >2/38 R | 2 S | 2/38 S | | Major | |
| | *Stenotrophomonas maltophilia* | >2/38 R | 2 S | 2/38 S | | Major | |
| | *Stenotrophomonas maltophilia* | >2/38 R | 1 S | 2/38 S | | Major | |
| | *Stenotrophomonas maltophilia* | >2/38 R | 1 S | 2/38 S | | Major | |

[a] Kirby-Bauer was utilized when frozen reference panels were not in agreement
[b] AST results were analyzed for:
Minor error: one method = I, one method = S or R
Major error: one method = S, one method = R
Very major error = reference testing = R, Phoenix or ARIS 2X = S (none noted)
(methods include: Phoenix, ARIS 2X or Reference result)

**Table 5: Gram-Positive Results of Arbitration for Minor, Major and Very Major Errors**

| Antimicrobial | Organism | Phoenix | ARIS 2X | Reference MIC(ug/ml) | Resulting Error[a] Phoenix | Resulting Error[a] ARIS 2X |
|---|---|---|---|---|---|---|
| Oxacillin | *Staphylococcus aureus* | 2S | 8R | >4R[b] | Very Major | |
| Gentamicin | *Coagulase-negative Staphylococcus* | >16R | 8I | 8I | Minor | |
| Streptomycin-Synergy | *Enterococcus faecium* | >1000R | <=1000S | 2000R | | Very Major |
| Gentamicin-Synergy | *Enterococcus faecium* | >500R | <=500S | 1000R | | Very Major |
| Streptomycin-Synergy | *Enterococcus faecium* | >1000R | <=1000S | <=1000S[a] | Major | |
| Linezolid | *Enterococcus faecalis* | 4I | 1S | <=0.5S | Minor | |
| Ceftriaxone | *Streptococcus viridans* | 0.25S | 2I | 0.5S | | Minor |
| Trimethoprim/Sulfamethoxazole | *Streptococcus pneumoniae* | <=0.25/4.75S | 1I | <=0.5S | | Minor |

[a] Enterococcus screen agar was utilized when frozen reference panels were not in agreement
[b] Oxacillin screen agar was utilized when frozen reference panels were not in agreement
[c] AST results were analyzed for:
Minor error: one method = I, one method = S or R
Major error: one method = S, one method = R
Very major error = reference testing = R, Phoenix or ARIS 2X = S

**Table 6: Performance of BD Phoenix after Discrepant Testing with Reference Method[a]**

| Organism | No. Tested | Error Rates: Essential agreement[b] | Minor[c] | Major[d] | Very Major[e] |
|---|---|---|---|---|---|
| Gram-negative | 348 | 99.1 | 0.5 | 0.4 | 0 |
| Gram-positive | 242 | 99.6 | 0.09 | 0.05 | 0.2 |
| *Streptococcus pneumoniae* | 49 | 99.8 | 0 | 0 | 0 |
| **Overall** | **639** | **99.5** | **0.2** | **0.2** | **0.1** |

[a]Reference method: Frozen reference panels or Kirby Bauer
[b]Results within one (1) two-fold dilution
[c]One method: intermediate; one method sensitive or resistant
[d]One method: resistant; one method sensitive
[e]Reference method: resistant; Phoenix sensitive

## CONCLUSION

Overall, both systems yielded equivalent results for both identification and susceptibility results for both gram positive and gram negative organisms

Specific issues related to *identification* were the following:
- Incorrect species identifications for gram negative rods with the ARIS 2X were 3% higher than Phoenix and were not concentrated with any particular organism
- Periodically, off-line testing (for example, spot indole or susceptibility result) was required for complete identification with the TREK panels
- Phoenix identification required a 90% or greater determination to provide an identification, otherwise no ID was available (0.6% of the isolates tested yielded no ID).
- QC organisms for TREK panels assessed each analyte according to CLIA regulations

Specific issues related to *susceptibility* were the following:
- The Phoenix was unable to provide MIC values and/or susceptibility results for 25% of all organisms tested. The inability to report MICs was greater for gram negative organisms compared to gram positive.
- BD is in the process of resubmitting to the FDA, approximately 15 to 20% of these gram negative and gram positive organism/antibiotic combinations to be unrestricted and subsequently able to be reported.
- The remaining 5 to10% of unreported susceptibilities are due to:
  - Phoenix performance limitations and
  - Determination that antibiotics clinically ineffective (organism intrinsically resistant) or for which medical relevance is not documented.
- Phoenix MICs trended higher and ARIS 2X MICs trended lower for both gram negative and gram positive organism/antibiotic combinations.

**Table 7: Performance of Sensititre Aris after Discrepant Testing with Reference Method[a]**

| Organism | No. Tested | Error Rates: Essential agreement[b] | Minor[c] | Major[d] | Very Major[e] |
|---|---|---|---|---|---|
| Gram-negative | 348 | 99.6 | 0.3 | 0 | 0 |
| Gram-positive | 242 | 99.9 | 0.04 | 0 | 0.5 |
| *Streptococcus pneumoniae* | 49 | 99.8 | 0.2 | 0 | 0 |
| **Overall** | **639** | **99.8** | **0.2** | **0** | **0.2** |

[a]Reference method: Frozen reference panels or Kirby Bauer
[b]Results within one (1) two-fold dilution
[c]One method: intermediate; one method sensitive or resistant
[d]One method: resistant; one method sensitive
[e]Reference method: resistant; ARIS 2X sensitive