BIOMÉRIEUX

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VITEK® 2 AST-P592

Rx only IVD

INTENDED USE

The VITEK® 2 Gram-positive Susceptibility Card is intended for use with the VITEK® 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Staphylococcus* spp., *Enterococcus* spp., and *S. agalactiae* to antimicrobial agents when used as instructed.

SUMMARY AND EXPLANATION

Susceptibility testing is indicated for any organism that contributes to an infectious process warranting antimicrobial chemotherapy. Susceptibility tests are most often indicated when the causative organism is thought to belong to a species capable of exhibiting resistance to commonly used agents. Isolated colonies of each type of organism that may play a pathogenic role are selected from an agar plate and tested for susceptibility. These tests are then examined and the Minimum Inhibitory Concentration (MIC) is determined. The MIC obtained using a dilution test may tell the physician the concentration of an antimicrobial agent needed at the site of infection to inhibit the infecting organism.

MICs have traditionally been determined using antimicrobial concentrations derived from serial twofold dilutions.[2] The MIC is then determined from the lowest concentration that exhibits inhibition of growth. An interpretive criterion (Susceptible, Intermediate, or Resistant) can then be assigned to MIC results to aid in the direction of therapy.

For some antimicrobials (e.g., high-level gentamicin, high-level streptomycin) a qualitative result is generated.

The standard and reference procedures are based on susceptibility tests requiring 16 to 24 hours of incubation for bacteria. Various manufacturers have now developed automated procedures designed to generate results more rapidly by using shortened incubation times. Laboratories worldwide use either variations of the standard reference procedure or a commercially available product to determine the MICs of infectious organisms.

Methicillin-Resistant Staphylococci (MRS)

Resistance to oxacillin is used to detect the presence of MRS. Most MRS are also usually resistant to multiple antimicrobials, including other beta-lactams, aminoglycosides, macrolides, clindamycin, and tetracycline. However, a “community-acquired methicillin-resistant *S. aureus*” phenotype has been described. These are not multi-drug resistant strains, but are typically resistant to penicillin and oxacillin, susceptible or resistant to erythromycin, and susceptible to gentamicin, clindamycin, and tetracycline.

Oxacillin (OX1)

This test provides an MIC determination and category interpretation for oxacillin. Interpretive results for MRS are reported as resistant to all beta-lactams (except anti-MRSA beta-lactams) when the instrument is operating in the CLSI® mode or the User-Defined (based on CLSI®) mode. The results from this test correlate to results that would be obtained from standard dilution testing of oxacillin. The calling range is 0.25 µg/mL to 4.0 µg/mL.

Cefoxitin Screen

This test may be used to predict *mec*A-mediated oxacillin resistance, and it is based on the cefoxitin disk screen test. The cefoxitin screen and oxacillin work in combination to determine the final interpretation reported for oxacillin.

Synergy Screen

Since the use of penicillin or ampicillin alone often results in treatment failure of serious enterococcal endocarditis, combination therapy is usually indicated to enhance bactericidal activity. The synergy between a cell wall active agent (such as penicillin, ampicillin, or vancomycin) and an aminoglycoside (such as gentamicin, kanamycin or streptomycin) is best predicted for enterococci by screening for high-level resistance to the aminoglycoside. When enterococci are susceptible *in vitro* to the high-level aminoglycoside and a cell wall active agent, this is predictive of the effectiveness of this combination therapy. Results are reported as SYN-S (high-level synergy screen is susceptible) and SYN-R (high-level synergy screen is resistant).

Inducible Clindamycin Resistance Test (ICR)

A positive ICR test is indicative of inducible MLS_b resistance, which confers resistance to macrolides, lincosamides, and type B streptogramin. An isolate with a positive ICR test should be reported as resistant to clindamycin; however, clindamycin may

still be effective in some patients. If the ICR test is positive and the clindamycin result is susceptible or intermediate, the clindamycin result will be forced resistant by the ICR test (in CLSI® mode or User-defined based on CLSI®).

STORAGE CONDITIONS

Upon receipt, store VITEK® 2 AST cards unopened in their original package liner at 2°C to 8°C.

PRINCIPLE OF THE TEST

The AST card for VITEK® 2 Systems is an automated test methodology based on the MIC technique reported by MacLowry and Marsh and Gerlach.[15,16] The AST card is essentially a miniaturized and abbreviated version of the doubling dilution technique for MICs determined by the microdilution method.[1]

Each AST card contains a control well containing only microbiological culture medium. The remaining microwells contain premeasured amounts of specific antimicrobials combined with culture medium.

The organism suspension to be tested must be diluted to a standardized concentration in 0.45% saline before being used to rehydrate the antimicrobial medium within the card. The card is then filled, sealed, and placed into the instrument incubator/reader, either automatically (as with VITEK® 2 60 or VITEK® 2 XL) or manually (as with VITEK® 2 Compact). The instrument monitors the growth of each well in the card over a defined period of time (up to 18 hours for *Staphylococcus, Enterococcus* and *S. agalactiae*). At the completion of the incubation cycle, MIC values (or test results, as appropriate) are determined for each antimicrobial contained on the card.

REAGENTS

When used with VITEK® 2 instrumentation, the AST card is a complete system for routine susceptibility testing. Each AST card contains selected antimicrobials in varying concentrations, dried with a microbiological culture medium.

Contents of the Card

Antimicrobic	Code	Concentration §	Calling Range ≤	Calling Range ≥	FDA Indications for Use
Ampicillin	am01n	0.5, 4, 8, 32	-	-	*Enterococcus* spp., *S. agalactiae*
Enterococcus spp.			2	32	
S. agalactiae			0.25	16	
Benzylpenicillin	p04n	0.125, 0.25, 1	0.03	0.5	*Staphylococcus* spp.
Cefoxitin Screen	oxsf01n	6	NEG	POS	*Staphylococcus* spp.
Ciprofloxacin	cip01n	1, 2, 4	0.5	8	*Staphylococcus* spp., *Enterococcus* spp.
Clindamycin	cm01n	0.5, 1, 2	0.25	8	*Staphylococcus* spp., *S. agalactiae*
Erythromycin	e02n❶	0.25, 0.5, 2	0.25	8	*Staphylococcus* spp., *Enterococcus* spp., *S. agalactiae*
Fosfomycin	fos01n	8, 32	8	128	**N/A
Fusidic Acid	fa01n	0.5, 1, 4	0.5	32	**N/A
Gentamicin	gm01n	8, 16, 64	0.5	16	*Staphylococcus* spp.
Gentamicin High Level (synergy)	hlg01n	500	S	R	*Enterococcus* spp.
Imipenem	ipm02n	2, 4, 8	1	16	**N/A
Inducible Clindamycin Resistance	icr02n❷	CM 0.5, CM/E 0.25/0.5	NEG	POS	*Staphylococcus* spp.
Linezolid	lnz02n	0.5, 1, 2	0.5	8	*S. agalactiae*, *E. faecalis*, *E. faecium*, *S. aureus*, *S. epidermidis*, *S. haemolyticus*
Moxifloxacin	mxf02n	0.25, 2, 8	0.25	8	**MSSA

Antimicrobic	Code	Concentration §	Calling Range ≤	Calling Range ≥	FDA Indications for Use
Oxacillin	ox101n	0.5, 1, 2	0.25	4	*Staphylococcus* spp.
Rifampicin	ra01n	0.25, 0.5, 2	0.5	32	*Staphylococcus* spp.
Streptomycin High Level (synergy)	hls01n	1000	S	R	*Enterococcus* spp.
Teicoplanin	tec01n	1, 4, 8, 16	0.5	32	**N/A
Tetracycline	te03n	0.5, 1, 2	1	16	*Staphylococcus* spp., *Enterococcus* spp., *S. agalactiae*
Tigecycline	tgc02n[NS]	0.25, 0.5, 1	0.12	2	*E. faecalis*, *E. faecium*, *S. aureus*, *S. epidermidis*, *S. haemolyticus*, *S. agalactiae*, *E. casseliflavus*
Trimethoprim/ Sulfamethoxazole	sxt02n❷	8/152, 16/304, 32/608	10 (0.5/9.5)	320 (16/304)	**N/A
Vancomycin	va04n❷	1, 2, 4, 8, 16	0.5	32	*Enterococcus* spp., *Staphylococcus* spp., *S. agalactiae*

Numerical values are expressed in µg/mL.

§ Equivalent standard method concentration by efficacy.

NEG = Negative

POS = Positive

❶, ❷ etc. = See performance characteristics identified by the drug code with this symbol.

**N/A = No specific FDA Indications for Use available

**MSSA = Methicillin-susceptible *S. aureus*

[NS] = The current absence of resistant isolates precludes defining any results other than susceptible. Isolates yielding MIC results suggestive of Nonsusceptible category should be submitted to a reference laboratory for further testing.

PRECAUTIONS

- For *In Vitro* Diagnostic Use Only.
- For US Only: Caution: US Federal Law restricts this device to sale by or on the order of a licensed practitioner.
- For professional use only.
- Suspensions not within the appropriate zone on the VITEK® 2 DensiCHEK™ Plus or VITEK® 2 DensiCHEK™ may compromise card performance.
- Do not use the card after the expiration date shown on the package liner.
- Store the card unopened in the package liner. Do not use the card if the protective package liner is damaged or if no desiccant is present.
- Allow the card to come to room temperature before opening the package liner.
- Do not use powdered gloves. Powder may interfere with the optics.
- Use of culture media other than the recommended types must be validated by the customer laboratory for acceptable performance.
- The card performs as intended only when used in conjunction with VITEK® 2 Systems, following the instructions contained in the Instructions for Use.
- It is highly recommended that Good Laboratory Practices (e.g., FDA, CLSI, ISO, etc.) also be followed, according to local guidelines or requirements.

- **Do not use glass test tubes**. Use clear plastic (polystyrene) tubes only. Variation exists among test tubes of standard diameter. Carefully place the tube into the cassette. If resistance is encountered, discard and try another tube that does not require pressure to insert.
- Prior to inoculation, inspect cards for tape tears or damage to the tape and discard any that are suspect. Check the saline level in the tubes after the cassette has been processed to ensure proper filling of card.
  - VITEK® 2 60 or VITEK® 2 XL: Eject improperly filled cards.
  - VITEK® 2 Compact: Do not load improperly filled cards.
- Give special consideration to specimen source and patient therapy regimen. AST cards may contain some antimicrobials that are not proven to be effective for treatment of infections due to all organisms that may be tested. For interpreting and reporting of antimicrobial results that have been shown to be active against organism groups both *in vitro* and in clinical infections, refer to the individual pharmaceutical antimicrobial labeling or local therapy guidelines.
- Interpretation of test results requires the judgment and skill of a person knowledgeable in AST. Additional testing may be required.[17]

Warning: All patient specimens, microbial cultures, and inoculated VITEK® 2 cards, along with associated materials, are potentially infectious and should be treated with universal precautions [18,20]

INSTRUMENT

The VITEK® 2 instruments are a family of *in vitro* diagnostic devices intended to rapidly assess the antimicrobial susceptibility of bacterial and yeast pathogens to available antimicrobial agents. For detailed information on the use and operation of these devices, refer to the appropriate Instrument User Manual.

SPECIMEN PREPARATION

Culture Requirements Table

VITEK® 2 Card	Media	Age of Culture	Incubation Conditions	McFarland Standards	Dilution for AST	Age of Suspension Before Loading Instrument
AST Gram-Positive	TSAB CBA CPS ID	18 to 24 hours	35°C to 37°C 5% to 10% CO_2 or aerobic, non-CO_2	0.50 to 0.63	280 µL in 3.0 mL 0.45% saline	VITEK® 2 Compact: ≤30 minutes VITEK® 2: ≤ 1 hour
GP and AST GP pair	TSAB[1] CBA[1] CPS ID	18 to 24 hours	35°C to 37°C 5% to 10% CO_2 or aerobic, non-CO_2	0.50 to 0.63	280 µL in 3.0 mL 0.45% saline	≤ 30 minutes

[1] These media were used in the identification product database developments and will give optimal performance.

Culture Requirements Table — Media Abbreviations

CBA = Columbia Sheep Blood Agar

CPS ID = chromID™ CPS (CPS ID Agar)

TSAB = Trypticase Soy Agar with 5% Sheep Blood

TEST PROCEDURE

Warning: Failure to properly follow instructions and recommendations provided in this section for performing laboratory tasks may cause erroneous or delayed results.

Materials

Materials provided are:

- VITEK® 2 DensiCHEK™ Plus Kit
- DensiCHEK™ Plus Standards Kit

- VITEK® 2 Cassette
- Adjustable volume saline dispenser
- 12 mm x 75 mm clear plastic (polystyrene) disposable test tubes
- VITEK® 2 60 or VITEK® 2 XL only: VITEK® 2 Pipettor/Diluter Accessory Kit (containing instrument pipette tips and saline hookup) and 0.45% saline bag

Materials required, but not provided are:

- Sterile saline (aqueous 0.45% to 0.50% NaCl, pH 4.5 to 7.0)
- Loops, sterile sticks or swabs
- Appropriate agar medium (See the Culture Requirements Table.)
- QC isolates
- VITEK® 2 AST Cards
- Micropipettors to deliver 280 µL
- Disposable pipette tips

Optional Accessories:

- Pre-dispensed saline test tubes (aqueous 0.45% to 0.50% NaCl, pH 4.5 to 7.0)
- Test tube caps
- Vortex

Test Card Setup Procedure

The following procedure contains general information applicable to all susceptibility products. (See the Culture Requirements Table for product-specific information.)

Note: Prepare the inoculum from a pure culture, according to good laboratory practices. In case of mixed cultures, a re-isolation step is required. It is recommended that a purity check plate be done to ensure that a pure culture was used for testing.

1. Do one of the following:
   - Select isolated colonies from a primary plate if culture requirements are met.
   - Subculture the organism to be tested to appropriate agar medium and incubate accordingly.
2. Aseptically transfer 3.0 mL of sterile saline (aqueous 0.45% to 0.50% NaCl, pH 4.5 to 7.0) into a clear plastic (polystyrene) test tube (12 mm x 75 mm).
3. Use a sterile stick or swab to transfer a sufficient number of morphologically similar colonies to the saline tube prepared in step 2. Prepare a homogenous organism suspension with a density equivalent to the appropriate McFarland standard using the VITEK® 2 DensiCHEK™ Plus (see the Culture Requirements Table). The inoculum density required for the GN, GP, ST, or YST can be diluted automatically for AST cards by the VITEK® 2 instrument (VITEK® 2 60 or VITEK® 2 XL). **Note:** The age of the suspension before loading the instrument for AST testing must be less than one hour when using VITEK® 2 60 or VITEK® 2 XL, and less than 30 minutes when using VITEK® 2 Compact.
4. Choose one of the following:
   - **For an automatic dilution (VITEK® 2 60 or VITEK® 2 XL only):** Place the suspension tube prepared in step 3 into the cassette with or without an identification card. In the next cassette slot, place an empty tube and an AST card. The instrument will automatically dilute the bacterial suspension to prepare an inoculum suitable for the susceptibility card.
   - **For a manual dilution (VITEK® 2 Compact, VITEK® 2 60 or VITEK® 2 XL):** In a second tube containing 3.0 mL of saline, transfer 280 µL of the suspension prepared in step 3. Then place this tube in the cassette with a susceptibility card. The tube with the initial bacterial suspension can also be used for inoculation of an identification card.

   Note: Check the saline level in the tubes after filling. When it is evident by the saline level in the tube that a card has been improperly filled, do not load the card if using VITEK® 2 Compact; **or**, eject the card if using VITEK® 2 60 or VITEK® 2 XL.

   Note: Refer to the appropriate Instrument User Manual for detailed information regarding data entry, processing, etc.
5. Follow your local inspecting agency's guidelines for disposal of hazardous waste.

QUALITY CONTROL

Quality Control organisms should be processed according to the Test Card Setup Procedure.

Quality Control

CLSI® Quality Control Organisms VITEK® 2 Results									
Antimicrobic	Code	*E. faecalis* ATCC® 29212™	*S. aureus* ATCC® 29213™	*E. coli* ATCC® 35218™	*S. pneumoniae* ATCC® 49619™	*E. faecalis* ATCC® 51299™	*S. aureus* ATCC® BAA-1026™	*S. aureus* ATCC® BAA-976™	*S. aureus* ATCC® BAA-977™
Ampicillin	am01n	≤ 2	0.5 - 2	-	-	-	-	-	-
Benzylpenicillin	p04n	-	0.25 - ≥ 0.5	-	-	-	-	-	-
Cefoxitin Screen	oxsf01n	-	NEG	-	-	-	POS	-	-
Ciprofloxacin	cip01n	≤ 0.5 - 2	≤ 0.5	-	-	-	-	-	-
Clindamycin	cm01n	4 - ≥ 8	≤ 0.25	-	-	-	-	-	-
Erythromycin	e02n	1 - 4	≤ 0.25 - 1	-	-	-	-	-	-
Fosfomycin	fos01n	-	≤ 8	-	-	-	-	-	-
Fusidic Acid	fa01n	-	≤ 0.5	-	-	-	-	-	-
Gentamicin	gm01n	-	≤ 0.5 - 1	-	-	-	-	-	-
Gentamicin High Level (synergy)	hlg01n	S	-	-	-	R	-	-	-
Imipenem	ipm02n	≤ 1 - 2	≤ 1	-	-	-	-	-	-
Inducible Clindamycin Resistance	icr02n	-	-	-	-	-	-	NEG	POS
Linezolid	lnz02n	1 - 4	1 - 4	-	-	-	-	-	-
Moxifloxacin	mxf02n	≤ 0.25 - 0.5	≤ 0.25	-	-	-	-	-	-
Oxacillin	ox101n	-	≤ 0.25 - 0.5	-	-	-	-	-	-
Rifampicin	ra01n	-	≤ 0.5	-	-	-	-	-	-
Streptomycin High Level (synergy)	hls01n	S	-	-	-	R	-	-	-
Teicoplanin	tec01n	≤ 0.5	≤ 0.5 - 1	-	-	-	-	-	-
Tetracycline	te03n	8 - ≥ 16	≤ 1	-	-	-	-	-	-
Tigecycline[NS]	tgc02n	≤ 0.12	≤ 0.12 - 0.25	-	-	-	-	-	-
Trimethoprim/ Sulfamethoxazole	sxt02n	≤ 10 (0.5/9.5)	≤ 10 (0.5/9.5)	-	-	-	-	-	-
Vancomycin	va04n	1 - 4	≤ 0.5 - 2	-	-	-	-	-	-

Numerical values are expressed in µg/mL.

NEG = Negative

POS = Positive

[NS] = The current absence of resistant isolates precludes defining any results other than susceptible. Isolates yielding MIC results suggestive of Nonsusceptible category should be submitted to a reference laboratory for further testing.

Certification Statement

This is to certify that bioMérieux complies with ISO 13485 and FDA Quality System Regulation (QSR) requirements for design, development, and manufacture of antimicrobial susceptibility systems.

Frequency of QC Testing

Refer to *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically,* CLSI® and/or your local guidelines.[2]

Preparation of QC Organisms

1. Rehydrate the organism according to the manufacturer's instructions.
2. Subculture to Trypticase Soy Agar with 5% sheep blood (TSAB).
3. Incubate at 35°C for 24 hours.
   Note: Gram-positive organisms may require an atmosphere of CO_2. (Refer to the Culture Requirements Table).
4. Check for purity.
5. Subculture to a TSAB plate.
6. Incubate 16 to 18 hours at 35°C.

Short-Term Storage Conditions

1. Streak to a TSAB plate or slant.
2. Incubate for 24 hours.
3. Refrigerate at 2°C to 8°C for up to two weeks.
4. Subculture once as described above and use for QC.

Long-Term Storage Conditions

1. Make a heavy suspension in Tryptic Soy Broth (TSB) with 15% glycerol.
2. Freeze at -70°C.
3. Subculture to TSAB twice before running QC.
   Note: Avoid repeated thawing and refreezing by either freezing in single-use aliquots or removing a small portion of frozen organism preparation with a sterile applicator stick.

RESULTS

Susceptibility Analytical Techniques

The system evaluates each organism's growth pattern in the presence of the antimicrobial in relation to the growth control well. Several parameters based on the growth characteristics are used to determine the MIC or qualitative result (for example, ESBL POS/NEG). The MIC result must be linked to an organism identification to determine a category interpretation. Accurate identification is critical, especially with certain organism/antimicrobial combinations (e.g., *Staphylococcus aureus*/oxacillin).

In cases where the identification of an organism is in question, confirmatory testing is necessary to ensure correct interpretation of susceptibility results.

A category interpretation will be reported along with a MIC, according to the interpretations defined by the Food and Drug Administration (FDA), CLSI®, Comité de l'Antibiogramme de la Société Française de Microbiologie (CASFM), European Committee for Antimicrobial Susceptibility Testing (EUCAST), or to an adaptation of the global settings according to other local guidelines.

Note: When FDA and CLSI® breakpoints differ, VITEK® 2 Systems AST tests are cleared for use with FDA breakpoints applied.

Combination Antimicrobials

The MICs for the combination antimicrobials are listed on the laboratory and patient reports as the first concentration (e.g., ampicillin/sulbactam ≤ 8/4 µg/mL is reported as ≤ 8 µg/mL.). The actual concentrations for each value in the antimicrobial calling range are as follows:

- trimethoprim/sulfamethoxazole: **Note exception** — This drug is listed on the laboratory and patient reports as the sum of the two antimicrobial concentrations: 20 µg/mL = 1/19, 40 µg/mL = 2/38, 80 µg/mL = 4/76, 160 µg/mL = 8/152, 320 µg/mL = 16/304

Antimicrobial Deduction

Antimicrobials that have been deduced will only report an interpretive result and will be noted with a **+**.

Clinical Efficacy and Indications for Use

AST cards may contain some antimicrobials that are not proven to be effective for treatment of infections caused by all organisms that may be tested. For interpreting and reporting of antimicrobial results that have shown to be active against organism groups both *in vitro* and in clinical infections, refer to the individual pharmaceutical antimicrobial labeling or the local therapy guidelines.

Urinary Use Only Antimicrobials

Certain antimicrobial agents are limited to use in treating urinary tract infections. Accordingly, these agents should not be reported against pathogens recovered from infection sites other than the urinary tract (except as noted). Please refer to the current *CLSI Performance Standards for Susceptibility Testing, M100* and/or local guidelines for additional information.[3]

For urine only, per CLSI®:[3]

- *Staphylococcus* spp.: lomefloxacin, norfloxacin, nitrofurantoin, sulfisoxazole, trimethoprim
- *Enterococcus* spp.: ciprofloxacin, levofloxacin, norfloxacin, nitrofurantoin, tetracycline

LIMITATIONS

A VITEK® 2 AST card cannot be used with a direct clinical specimen or sample or other sources containing mixed flora. Any change or modification in the procedure may affect the results.

A result for an antibiotic/organism combination, which may have a limitation, may be suppressed from reporting. This can be accomplished through the use of bioART rules in the VITEK® 2 Systems software. Refer to the software user manual for instructions.

Perform an alternative method of testing prior to reporting of results for the following antibiotic/organism combination(s):

- Erythromycin (e02n): *Streptococcus agalactiae*
- Cefoxitin Screen (oxsf01n): *Staphylococcus pseudintermedius* (specific to VITEK® 2 Systems 8.01 software or higher)

Perform an alternative method of testing prior to reporting of results when a Positive (+) result is obtained with the following antibiotic/organism combination(s):

- Cefoxitin Screen (oxsf01n): *Staphylococcus saprophyticus*

The ability of the AST card to detect resistance with the following combination(s) is unknown because resistant strains were not available at the time of comparative testing:

- Ampicillin (am01n): *Streptococcus agalactiae*
- Linezolid (lnz02n): *Enterococcus* spp., *Staphylococcus* spp., *Streptococcus agalactiae*
- Tigecycline (tgc02n): *Enterococcus* spp., *Staphylococcus* spp., *Streptococcus* spp.

EUCAST Limitations

It is recommended that the existing bioART suppression rules be enabled, or new rules created and enabled, for these limitations if the EUCAST breakpoints are applied.

Perform an alternative method of testing prior to reporting of results for the following antibiotic/organism combination(s):

- Erythromycin (e02n): *Streptococcus agalactiae, Staphylococcus* spp.
- Teicoplanin (tec01n): *Staphylococcus epidermidis, Staphylococcus haemolyticus*
- Cefoxitin Screen (oxsf01n): *Staphylococcus pseudintermedius* (specific to VITEK® 2 Systems 8.01 software or higher)

Perform an alternative method of testing prior to reporting of results when a Positive (+) result is obtained with the following antibiotic/organism combination(s):

- Cefoxitin Screen (oxsf01n): *Staphylococcus saprophyticus*

The ability of the AST card to detect resistance with the following combination(s) is unknown because resistant strains were not available at the time of comparative testing:

- Linezolid (lnz02n): *Streptococcus agalactiae*
- Tigecycline (tgc02n): *Streptococcus agalactiae, Staphylococcus* spp.

EXPECTED VALUES

Expected results for susceptibility tests will vary based on location and institution. VITEK® 2 Systems were tested at several geographically diverse locations to ensure that trends that occurred by location were integrated into the performance

characteristics of the system. Organism resistance patterns will differ by institution; therefore, expected values will be directly related to the population of organisms at each site.

PERFORMANCE CHARACTERISTICS

The performance characteristics of the antimicrobial agents included in VITEK® 2 AST cards were established using the manual and autodilution modes (on a VITEK® 2 System) at multiple clinical laboratories. The VITEK® 2 AST card results were compared to results from a CLSI® reference method. Essential agreement (EA) represents VITEK® 2 results which agree exactly or are within a ± twofold dilution (± two doubling dilutions for antifungal) of the reference result.

Category agreement (CA) occurs when the VITEK® 2 and the reference interpretative results agree (Susceptible, Intermediate, and Resistant). There are instances when the category agreement for an antimicrobial falls below the essential agreement. This can occur when a significant number of MICs cluster around a category breakpoint during clinical trial testing, resulting in interpretative errors. For a description of interpretive errors, refer to the footnotes below the table that follows (Performance Characteristics). When the majority of the errors are of the minor type, a high corresponding essential agreement percentage demonstrates that the antimicrobial retains an acceptable overall performance.

There are instances when the performance is based solely on category agreement (CA) because at the time performance was established, less than five discrete twofold dilutions were evaluated. A minimum of five dilutions is necessary to calculate essential agreement (EA) based on ± one twofold dilution. These instances are designated by a "c" footnote in the Contents of the Card table. The following performance tables have values for CA only when EA was not established at the time of FDA clearance.

The reproducibility of the VITEK® 2 system was established by testing a set of on-scale organisms.*

*Data on file at bioMérieux, Inc

Performance Characteristics for Gram-Positive Antimicrobial Susceptibility Testing

Antimicrobial	Antimicrobial Code	Antibiotic Version	Bp[1]	Comment[2]	Essential Agreement				Category Agreement				% Reproducibility
					% Error				% Error				
					% EA	VME	ME	mE	% CA	VME	ME	mE	
Ampicillin	AM	am01n	CLSI	#, E	97.6	1.1	0.3	0.2	99.5	2.2	0.6	0.2	97
Benzylpenicillin (Penicillin)	P	p04n	CLSI	#, E	97.4	0.4	0.3	N/A	98.5	0.9	1.0	N/A	99.3
Cefoxitin Screen	OXSF	oxsf01n	CLSI	E, Ref. = CLSI Disk Diffusion	–	–	–	–	98.3	2.0	1.4	N/A	100
				E, Ref. = mecA PCR	–	–	–	–	97.2	2.3	3.2	N/A	
Oxacillin + Cefoxitin Screen			CLSI	#, Ref. = CLSI Cefoxitin Disk Diffusion	–	–	–	–	98.5	0.4	2.8	N/A	–
Oxacillin + Cefoxitin Screen			CLSI	E, Ref. = mecA PCR	–	–	–	–	97.8	1.2	3.2	N/A	–
Ciprofloxacin	CIP	cip01n	CLSI	#, E	99.3	1.4	0.0	0.2	96.7	1.4	0.0	2.9	100
			CA-SFM	E	99.3	1.4	0.0	0.2	96.7	1.4	0.0	2.9	
Clindamycin	CM	cm01n	CLSI	#, E	98.7	2.3	0.0	0.7	99.1	2.3	0.0	0.9	98.5
			CA-SFM	I	96.1	2.5	4.3	0.0	-	-	-	-	
Erythromycin	E	e02n	CLSI	#, E ❶	95.9	0.4	0.4	5.1	92.8	0.4	0.4	7.5	95.2
			CA-SFM	I ❶	94.7	9.4	0.0	0.3	95.0	9.4	0.0	0.3	
Fosfomycin	FOS	fos01n	CA-SFM	I, Staph	97.1	6.5	0.3	N/A	95.8	11.8	1.7	N/A	100
Fusidic Acid	FA	fa01n	CA-SFM	I, Staph	100	0.0	0.0	0.0	99.2	0.0	0.0	0.8	100
Gentamicin	GM	gm01n	CLSI	#, E, Staph	99.2	0.0	0.0	0.8	95.1	0.0	0.0	4.9	100
			CA-SFM	E, Staph	99.2	0.0	0.0	0.8	95.1	0.0	0.0	4.9	

Antimicrobial	Antimicrobial Code	Antibiotic Version	Bp[1]	Comment[2]	Essential Agreement				Category Agreement				% Reproducibility
					% Error				% Error				
					% EA	VME	ME	mE	% CA	VME	ME	mE	
Gentamicin High Level	HLG	hlg01n	CLSI	#, E	N/A	N/A	N/A	N/A	100	N/A	N/A	N/A	100
			CA-SFM	E, Enc	N/A	N/A	N/A	N/A	100	N/A	N/A	N/A	
Imipenem	IPM	ipm02n	CLSI	E	–	–	–	–	99.2	0.4	0.5	0.3	100
			CA-SFM	E	–	–	–	–	99.2	0.4	0.5	0.3	
Inducible Clindamycin Resistance	ICR	icr02n	CLSI	#, E	N/A	N/A	N/A	N/A	99.5	2.0	0.4	N/A	100
Linezolid	LNZ	lnz02n	CLSI	#, E	98.7	0.0	0.1	0.1	98.9	0.0	0.1	1.0	100
			CA-SFM	E	98.7	0.0	0.1	0.7	92.6	0.0	0.1	7.3	
Moxifloxacin	MXF	mxf02n	CLSI	#, E	99.2	0.0	0.0	0.0	83.3	0.0	0.0	16.7	100
			CA-SFM	E	98.5	0.0	0.0	0.1	92.4	0.0	0.0	7.6	
Oxacillin	OX1	ox101n	CLSI	#, E, Staph	97.4	1.6	1.1	0.0	97.1	2.2	3.4	0.0	98.1
Rifampicin (Rifampin)	RA	ra01n	CLSI	#, E	100	0.0	0.0	0.0	100	0.0	0.0	0.0	100
			CA-SFM	I, Staph	99.5	0.0	0.0	0.3	–	–	–	–	
Streptomycin High Level	HLS	hls01n	CLSI	#, E, Enc	N/A	N/A	N/A	N/A	100	N/A	N/A	N/A	100
			CA-SFM	E, Enc	–	–	–	–	100	0.0	0.0	–	
Teicoplanin	TEC	tec01n	CLSI	I	96.6	3.3	0.3	0.4	95.7	3.3	0.3	2.7	99.4
			CA-SFM	I	96.9	1.6	0.0	1.1	95.9	1.6	0.3	3.2	
Tetracycline	TE	te03n	CLSI	#, E	99.1	1.2	0.4	0.5	99.3	1.2	0.5	0.8	94.8
Tigecycline	TGC	tgc02n	CLSI	#, E	–	–	–	–	99.4	66.7†	0.4	N/A	100
Trimethoprim/ Sulfamethoxazole	SXT	sxt02n	CLSI	I ❷	97.3	1.6	1.5	0.0	–	–	–	–	97.6
			CA-SFM	I ❷	97.3	0.0	0.8	1.8	–	–	–	–	
Vancomycin	VA	va04n	CLSI[3]	#, E ❷	99.9	0.0	0.0	0.1	99.7	0.0	0.0	0.3	100
			CA-SFM	E ❷	99.9	0.0	0.0	0.1	99.7	0.0	0.0	0.3	

[1] Abbreviations — Bp = breakpoint committee; EA = essential agreement; CA = category agreement; VME = Very Major Error (susceptible result with resistant reference result); ME = Major Error (resistant result with susceptible reference result); mE = minor Error (susceptible or resistant result with an intermediate reference result, or an intermediate result with a susceptible or resistant reference result).

[2] Comment — Specific organism groups are designated as Staph for *staphylococci*, Enc for *enterococci*, S aga for Group B *streptococci*, Sau for *Staphylococcus aureus*.

[3] FDA breakpoints are used in the CLSI Interpretation Standard (breakpoint committee) in the VITEK® 2 Systems software.

For all gram-positive Beta-lactams with indications for *Staphylococcus* spp., with the exception of Benzylpenicillin (Penicillin), performance in this table represents forcing-resistance based on oxacillin resistance.

† Non-defined error; susceptible (S) breakpoints only, no I or R breakpoints exist.

Key:

= US Food and Drug Administration 510(k) cleared
CLSI® = Clinical and Laboratory Standards Institute
CA-SFM = Comité de l'Antibiogramme de la Société Française de Microbiologie
E = External performance data
I = Internal performance data
– = Not available
N/A = Not applicable

Ref. = Reference method for clinical performance study.

❶ ❷ = Symbol identifies the performance characteristics for a specific antimicrobial version.

EUCAST Performance Characteristics for Gram-Positive Antimicrobial Susceptibility Testing

Antimicrobial	Antimicrobial Code	Antibiotic Version	Comment[1]	Essential Agreement				Category Agreement			
				% Error				% Error			
				%EA[2]	VME	ME	mE	%CA	VME	ME	mE
Ampicillin	AM	am01n	*Enterococcus*	97.7	1.4	0.4	1.0	97.7	1.4	0.4	1.6
Benzylpenicillin	P	p04n	*Staphylococcus, S. agalactiae*	98.3	0.8	1.9	0.0	98.3	0.8	3.9	0.0
Ciprofloxacin	CIP	cip01n	*Staphylococcus*	99.0	0.0	0.0	0.0	100.0	0.0	0.0	0.0
Clindamycin	CM	cm01n	*Staphylococcus, S. agalactiae*	98.1	3.3	0.3	0.0	98.1	3.3	0.3	0.7
Erythromycin	E	e02n	*Staphylococcus* ❶	94.7	9.4	0.0	0.0	95.3	9.4	0.0	0.0
Fosfomycin	FOS	fos01n	*Staphylococcus*	97.1	6.5	0.3	N/A	95.8	11.8	1.7	N/A
Fusidic Acid	FA	fa01n	*Staphylococcus*	100.0	0.0	0.0	0.0	100.0	0.0	0.0	0.0
Gentamicin	GM	gm01n	*Staphylococcus*	99.2	0.0	0.0	0.0	99.7	0.0	0.4	0.0
Imipenem	IPM	ipm02n	*Enterococcus*	91.9	3.1	0.8	0.0	98.0	3.1	0.8	0.5
Linezolid	LNZ	lnz02n	N/A	98.7	0.0	0.1	0.0	99.5	0.0	0.5	0.0
Moxifloxacin	MXF	mxf02n	*Staphylococcus, S. agalactiae*	99.0	0.7	0.0	0.5	95.2	0.7	0.0	4.6
Rifampicin	RA	ra01n	*Staphylococcus*, *S. agalactiae*	96.0	0.0	0.0	3.5	88.4	0.0	0.0	11.6
Teicoplanin	TEC	tec01n	*S. agalactiae, S. aureus, Enterococcus*, coagulase-negative *Staphylococcus* except *S. epidermidis* and *S. haemolyticus*	98.9	4.8	0.2	0.0	99.4	4.8	0.2	0.0
Tetracycline	TE	te03n	*Staphylococcus, S. agalactiae*	98.5	1.0	1.4	0.3	96.0	1.0	1.4	2.8
Tigecycline	TGC	tgc02n	N/A	99.0	0.0	0.0	0.3	99.5	66.7	0.0	0.3
Trimethoprim/ Sulfamethoxazole	SXT	sxt02n	*Staphylococcus, S. agalactiae* ❷	92.9	6.7	4.1	2.2	89.8	6.7	4.1	6.2
Vancomycin	VA	va04n	*Staphylococcus, S. agalactiae, Enterococcus* ❷ (EUCAST v1.3 breakpoints)	99.8	2.0	0.0	0.0	99.7	4.1	0.1	0.0
			Staphylococcus, S. agalactiae, Enterococcus ❷ (EUCAST v2.0 breakpoints)	99.8	2.1	0.0	0.0	99.7	8.3	0.0	0.0

[1] Comment — Unless stated otherwise, performance is for *Staphylococcus*, *Enterococcus*, and *S. agalactiae*.

[2] Abbreviations — Bp = breakpoint committee; EA = essential agreement; CA = category agreement; VME = Very Major Error (susceptible result with resistant reference result); ME = Major Error (resistant result with susceptible reference result); mE = minor Error (susceptible or resistant result with an intermediate reference result, or an intermediate result with a susceptible or resistant reference result).

Key:

= EUCAST = European Committee on Antimicrobial Susceptibility

❶ ❷ = Symbol identifies the performance characteristics for a specific antimicrobial version.

LIST OF CLAIMS

Note: If the organism is not in the VITEK® 2 susceptibility database, results will not be reported.

Note: Organisms listed with an asterisk (*) indicate an AES claimed organism. No asterisk is displayed for a group; however, when an individual species (with an asterisk) is contained within a group, it is expertised.

Gram-Positive Organisms Claimed for AST-GP (keyID)

- *Coagulase-negative Staphylococcus**
- *Coagulase-positive Staphylococcus**
- *Enterococcus avium*
- *Enterococcus casseliflavus**
- *Enterococcus durans*
- *Enterococcus faecalis**
- *Enterococcus faecalis* ATCC® 29212™
- *Enterococcus faecalis* ATCC® 51299™
- *Enterococcus faecium**
- *Enterococcus gallinarum**
- *Enterococcus hirae*
- *Enterococcus malodoratus*
- *Enterococcus mundtii*
- *Enterococcus* spp.*
- *Escherichia coli* ATCC® 35218™
- *Staphylococcus aureus**
- *Staphylococcus aureus* ATCC® 29213™
- *Staphylococcus aureus* ATCC® BAA-976™
- *Staphylococcus aureus* ATCC® BAA-977™
- *Staphylococcus aureus* ATCC® BAA-1026™
- *Staphylococcus auricularis**
- *Staphylococcus capitis**
- *Staphylococcus chromogenes**
- *Staphylococcus cohnii**
- *Staphylococcus cohnii* ssp. *cohnii**
- *Staphylococcus cohnii* ssp. *urealyticus**
- *Staphylococcus epidermidis**
- *Staphylococcus haemolyticus**
- *Staphylococcus hominis**
- *Staphylococcus hominis* ssp. *hominis**
- *Staphylococcus hyicus**
- *Staphylococcus intermedius**
- *Staphylococcus kloosii**
- *Staphylococcus lentus**
- *Staphylococcus lugdunensis**
- *Staphylococcus pseudintermedius*
- *Staphylococcus saprophyticus**
- *Staphylococcus schleiferi**
- *Staphylococcus sciuri**
- *Staphylococcus simulans**
- *Staphylococcus warneri**
- *Staphylococcus xylosus**
- *Streptococcus agalactiae**
- *Streptococcus pneumoniae**
- *Streptococcus pneumoniae* ATCC® 49619™

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Permission to incorporate portions of M100 (Performance Standards for Antimicrobial Susceptibility Testing: Informational Supplement) in the bioMérieux clinical microbiology instrumentation and System has been granted by CLSI®. The current standard and supplements to it may be obtained from CLSI, 940 West Valley Road, Suite 1400, Wayne, PA 19087, USA.

BARCODES

User MUST enter the following barcodes into "Flex Panel Entry" program before first use of this Susceptibility Card.

01 

02 

03 

04 

05 

06 

07 

08 

09 

INDEX OF SYMBOLS

Symbol	Meaning
REF	Catalog number
IVD	In Vitro Diagnostic Medical Device
	Legal Manufacturer
	Temperature limitation
	Use by date
LOT	Batch code
	Consult Instructions for Use
	Date of manufacture

Symbol	Meaning
	Contains sufficient for <n> tests
EC REP	Authorized representative in the European Community
Rx only	For US Only : Caution : US Federal Law restricts this device to sale by or on the order of a licensed practitioner

Instructions for Use provided in the kit or downloadable from www.biomerieux.com/techlib

LIMITED WARRANTY

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WASTE DISPOSAL

All hazardous waste must be disposed of by following your local inspecting agency's guidelines.

REVISION HISTORY TABLE

Change type categories	
N/A	Not applicable (First publication)
Correction	Correction of documentation anomalies
Technical change	Addition, revision and/or removal of information related to the product
Administrative	Implementation of non-technical changes noticeable to the user
Note:	Minor typographical, grammar, and formatting changes are not included in the revision history.

Release Date	Part Number	Change Type	Change Summary
2018-01	045610-01	Administrative	• Formatting changes do not affect the fit, form, or function of the product
		Technical change	• Combined product package insert content with VITEK® 2 Product Information Manual AST content • Updated Limited Warranty section • Updated with RX only information • Updated with EUCAST limitations

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