

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k073406

B. Purpose for Submission:

Addition of the trimethoprim/sulfamethoxazole on the VITEK®2 and VITEK®2 Compact Systems Antimicrobial Susceptibility Test (AST) System

C. Measurand:

Trimethoprim/sulfamethoxazole $\leq 1/19$ - $\geq 16/304$ $\mu\text{g/mL}$

D. Type of Test:

Qualitative growth based detection algorithm using predetermined growth thresholds

E. Applicant:

bioMerieux, Inc.

F. Proprietary and Established Names:

VITEK®2 Gram Negative Trimethoprim/sulfamethoxazole

G. Regulatory Information:

1. Regulation section:

866.1645 Short-Term Antimicrobial Susceptibility Test System

2. Classification:

II

3. Product code:

LON System, Test, Automated, Antimicrobial Susceptibility, Short Incubation

4. Panel:

83 Microbiology

H. Intended Use:

1. Intended use(s):

Trimethoprim/sulfamethoxazole at concentrations of $\leq 1/19$ - $\geq 16/304$ $\mu\text{g/mL}$ on the Gram Negative Susceptibility Card is intended for use with the VITEK®2 Systems for the automated quantitative or qualitative susceptibility testing of isolated colonies for most clinically significant aerobic Gram-negative bacilli, *Staphylococcus* spp., *Enterococcus* spp., *Streptococcus agalactiae*, *S. pneumoniae*, and yeast.

2. Indication(s) for use:

This application is indicated for the addition of trimethoprim/sulfamethoxazole at concentrations of 1/19, 4/76, 16/304 for a calling range of ≤ 20 (1/19) - ≥ 320 (16/304) $\mu\text{g/mL}$ on the VITEK®2 Gram Negative Susceptibility Cards for use with the VITEK®2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Escherichia coli*, *Klebsiella* species, *Enterobacter* species, *Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Shigella flexneri*, and *Shigella sonnei* to antimicrobial agents when used as instructed in the Online Product Information.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

Not applicable

I. Device Description:

The VITEK® 2 AST card containing the test is inoculated with a standardized organism suspension. The card is incubated within the instrument and optically monitored throughout the incubation cycle. Results are automatically calculated once a predetermined growth threshold is reached and a report is generated that contains the final result.

J. Substantial Equivalence Information:

1. Predicate device name(s):

VITEK® 2 Gram Negative Ertapenem

2. Predicate K number(s):

k041982

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Same	Same
Test organism	Colonies of Gram-Negative bacilli	Same
Test Card	VITEK®2 card format with base broth	Same
Instrument	VITEK®2 System	VITEK®2 System
Differences		
Item	Device	Predicate
Antibiotic	trimethoprim/sulfamethoxazole at specific concentrations	Ertapenem at specific concentrations
Reading algorithm	Unique for trimethoprim/sulfamethoxazole	Unique for ertapenem

K. Standard/Guidance Document Referenced (if applicable):

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”; CLSI M7 (M100-S17) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard”.

L. Test Principle:

Each VITEK®2 test card contains 64 microwells. A control well, that contains only microbiological culture medium is resident on all cards, with the remaining wells containing premeasured amounts of a specific antibiotic combined with culture medium. A suspension of organism is made in 0.45-0.5% sterile saline from a pure culture and standardized to a McFarland 0.5 standard using the DensiChek. The desired cards are placed in the cassette along with an empty tube for the susceptibility card. The cassette is placed in the VITEK®2 instrument where a susceptibility test will be automatically diluted from the ID suspension by the VITEK®2. The cards are then automatically vacuum filled; the tubes are cut and the cards sealed prior to proceeding to the Incubator Loading Station. Cards are then transferred from the cassette into the carousel for incubation at 35.5° C, and optical scanning during testing. Readings are performed every 15 minutes.

In addition to the automatic dilution, there is also a manual inoculation dilution

procedure described in the packager insert. VITEK®2 results for trimethoprim/sulfamethoxazole is reported as the sum of the concentrations of the two antibiotics.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Ten gram-negative on-scale organisms were tested at three sites in triplicate in three days with >95% reproducibility. This testing was performed using both the manual dilution and the automatic dilution method.

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The recommended QC isolates, *E. coli*, and *P. aeruginosa* were tested on every test occasion with the reference method and the VITEK®2. The reference method QC results were in range for every day tested. The VITEK®2 was tested a sufficient number of times to demonstrate that the system can produce QC results in the recommended range.

Quality Control was performed during the studies using both the auto-dilution and the manual method of diluting the organisms. Results demonstrated that methods were comparable.

QC Table

ORGANISM	Reference Expected Range (ug/mL)	Reference	VITEK®2 Expected Range (ug/mL)	VITEK®2 AUTO-DIL	VITEK®2 MAN-DIL
<i>E. coli</i> ATCC 25922 Expected Range: ≤10 µg/mL	≤10	100	≤20	100	
<i>P. aeruginosa</i> ATCC 27853 Exp. Range 160 – 640 µg/mL I	20		20	2	3
	40		40		
	80		80		
	160	20	160	37	40
	320	41	320	57	43
	640	32	640		
	>640	3	>640		
n					

Inoculum density control was monitored using the DensiChek instrument. This was standardized weekly with all results recorded and in the expected range. Verification was performed during internal testing.

d. *Detection limit:*

Not applicable

e. *Analytical specificity:*

Not applicable

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

A clinical study was conducted at three sites using the VITEK®2 cards with trimethoprim/sulfamethoxazole and the CLSI reference agar dilution method prepared as recommended by CLSI. Inoculum was prepared with direct colony suspension. Two methods of inoculation, manual and automated, were evaluated. Clinical testing was performed using the automated method of inoculation and the challenge set was tested using both the manual and the automated method.

Greater than 90% of the isolates grew in the VITEK®2 cards in less than 16 hours. Essential agreement was not calculated because the VITEK®2 card contained <5 dilutions of trimethoprim/sulfamethoxazole. A comparison was provided to the reference method with the following agreement.

Summary Table for Gram Negative Organisms (Automated Dilution)

	CA Total	CA	%CA	#R	Min	maj	vmj
Clinical	284	284	100	49	-	0	0
Challenged	89	89	100	10	-	0	0
Combined	373	373	100	59	-	0	0

CA-Category Agreement

maj-major discrepancies

R-resistant isolates

vmj-very major discrepancies

Category Agreement is when the interpretation (SIR) of the reference method agrees exactly with the interpretation (SIR) of the VITEK®2 results. Minor errors are not possible since there is no intermediate category.

Manual Dilution:

The challenge set of organisms was also tested at one site using the manual method of inoculation with the following performance that demonstrated that there is no difference between the two inoculation methods.

Summary Table for Gram Negative Organisms (Manual Dilution)

	CA Total	CA	%CA	#R	Min	maj	vmj
Clinical	89	89	100	10	-	0	0

b. *Matrix comparison:*

Not applicable

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable

b. *Clinical specificity:*

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Enterobacteriaceae $\leq 2/38$ (S), $\geq 4/76$ (R)

N. Proposed Labeling:

The expected value range, interpretive criteria and QC are included in the package insert. The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The information submitted in this premarket notification is complete and supports a substantial equivalence decision.