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

A. 510(k) Number:

K121546

B. Purpose for Submission:

The addition of Doxycycline to the VITEK® 2 and VITEK®2 Compact Systems Antimicrobial Susceptibility Test (AST) System.

C. Measurand

VITEK® 2 Gram Negative Doxycycline (≤ 0.5 - ≥ 16 µg/mL)

D. Type of Test:

Quantitative growth based detection algorithm using optics light detection for determination of the minimum inhibitory concentration (MIC).

E. Applicant:

bioMerieux, Inc.

F. Proprietary and Established Names:

Vitek®2 Gram Negative Doxycycline

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):

VITEK® 2 Gram Negative Doxycycline is designed for antimicrobial susceptibility testing of Gram negative bacilli. VITEK® 2 Gram Negative Doxycycline is a quantitative test intended for use with the VITEK® 2 and VITEK® 2 Compact Systems as a laboratory aid in the determination of in vitro susceptibility to antimicrobial agents. Doxycycline has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antimicrobial.

Active in vitro and in clinical infections

Acinetobacter species, *Enterobacter aerogines, Escherichia coli, Klebsiella* species, *and Shigella* species.

2. Indication(s) for use:

VITEK® 2 Gram Negative Doxycycline is designed for antimicrobial susceptibility testing of Gram negative bacilli. VITEK® 2 Gram Negative Doxycycline is a quantitative test intended for use with the VITEK® 2 and VITEK® 2 Compact Systems as a laboratory aid in the determination of in vitro susceptibility to antimicrobial agents. Doxycycline has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antimicrobial.

Active in vitro and in clinical infections

Acinetobacter species, *Enterobacter aerogines, Escherichia coli, Klebsiella* species, *and Shigella* species.

The VITEK® 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK® 2 Systems for the automated quantitative or qualitative susceptibility testing of isolated colonies for the most clinically significant aerobic gram-negative bacilli, Staphylococcus spp., Enterococcus spp., Streptococcus spp. and clinically significant yeast.

3. Special condition for use statement(s):

Prescription Use Only

4. Special instrument Requirements:

Not Applicable

I. Device Description:

The VITEK® 2 AST card is a miniaturized, abbreviated and automated version of the doubling dilution technique for determining the minimum inhibitory concentration (MIC). Each VITEK® 2 AST card contains 64 micro wells. A control well, which contains only microbiological culture media, is present on all cards. The remaining wells contain premeasured portions of specific antibiotics in a culture media base. The bacterial isolate to be tested is diluted to a standardized concentration with 0.45-0.5% saline before being used to rehydrate the antimicrobial medium in the wells in the card. The VITEK® 2 System automatically fills seals and places the card into the incubator/reader. With VITEK® 2 Compact the filling, sealing and loading of the card is done manually. The VITEK® 2 Systems monitor the growth of each well in the card over a defined period of time. At the completion of the incubation cycle, a report is generated which includes the MIC value and the result interpretation for each antibiotic.

The VITEK® 2 Gram Negative Doxycycline has the following concentrations in the card: 1, 4, and 16 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK® 2 cared is 0.5 – 16 µg/mL.

Vitek®2 AST-ST	Equivalent Standard Method Conc. By Efficacy in µg/mL	MIC Ranges and CLSI/FDA Categories (MIC in µg/mL)		
		S	I	R
Doxycycline	1, 4, 16	4	8	≥ 16

J. Substantial Equivalence Information:

1. Predicate device name(s):

VITEK® 2 Gram Negative Imipenem

2. Predicate K number(s):

K103752

3. Comparison with predicate

Similarities		
Item	**Device**	**Predicate**
Intended Use	Determine antimicrobial susceptibility to antimicrobial agents	Same
Test organism	Gram Negative Rods Colonies	Same
Test Card	VITEK® 2 card format with base broth	Same
Instrument	VITEK® 2 and VITEK ®2 Compact System	Same
Differences		
Item	**Device**	**Predicate**
Antibiotic	Doxycycline	Imipenem
Reading algorithm	Unique for Doxycycline (Discriminant analysis)	Unique for Imipenem (Growth pattern analysis)

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

1. Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA; August 28, 2009

2. CLSI M100-S19: Performance Standards for Antimicrobial Susceptibility Testing; Nineteenth Informational Supplement.

3. CLSI M07-A8: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.-Eighth edition.

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 card(s) 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 (35.5^{o} 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.

M. Performance Characteristics (if/when applicable):

Studies were conducted to evaluate a Doxycycline susceptibility panel.

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was demonstrated using 10 isolates at three sites on three separate days in triplicates. The study included the Auto-dilution and the Manual dilution for VITEK 2 and Manual dilution for VITEK 2 Compact. All results demonstrated >95% reproducibility.

b. Linearity/assay reportable range:
Not Applicable

c. Traceability (controls, calibrators, or method):

Organism	Conc in µg/mL	Auto-dilution		Manual dilution	
E. coli ATCC 25922 Range 0.5 - 2 µg/mL		**Ref.**	**Test**	**Ref.**	**Test**
	≤ 0.0625				
	0.125				
	0.25				
	0.5*	49	60	31	49
	1	55	44	41	23
	2				
	4				
	8				
	16				
	≥32				

*This value is ≤ 0.5 µg/mL for the VITEK

Inoculum density control:

A turbidity meter (VITEK 2 DensiChek) was used to adjust the inoculum to the turbidity of 0.5 McFarland. The VITEK 2 DensiChek instrument 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 performed at three external sites using the VITEK 2 AST-GN Doxycycline and broth microdilution panels containing Doxycycline. The study included 409 clinical isolates and a challenge set of 98 isolates. The vast majority of clinical isolates were fresh (stock isolates represented 2.2%). Clinical isolates were composed of 306 species included in the IFU and 103 other Enterobacteriaceae isolates within the spectrum of Doxycycline.

Testing of the clinical isolates was performed using the automated method of inoculation. Performance data comparing the VITEK 2 AST-GN Doxycycline and the reference method is illustrated in the tables below. Testing of challenge isolates was conducted at one external site and was performed using both auto-dilution and manual dilution method. As is illustrated in the tables below, no difference was noted in the device performance between the two types of dilution methods.

Combined Performance Summary for Indicated for Use species
(Auto Dilution)

	total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Clinical	306	295	96.4%	188	179	95.2%	298	97.4%	50	0	0	8
Challenge	98	98	100%	50	50	100%	92	93.9%	42	0	0	6
Combined	404	393	97.3%	238	229	96.2%	390	96.5%	92	0	0	14

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates
maj-major discrepancies
vmj-very major discrepancies
min- minor discrepancies

Combined Performance Summary for all species
(Auto Dilution)

	total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Clinical	409	397	97.1%	249	239	96.0%	390	95.4%	93	1	0	18
Challenge	98	98	100%	50	50	100%	92	93.9%	42	0	0	6
Combined	507	495	97.6%	299	289	96.7%	482	95.1%	135	1	0	24

Combined Performance Summary for Indicated for Use species
(Manual Dilution)

	total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Challenge	**98**	**98**	**100%**	**50**	**50**	**100%**	**92**	**93.9%**	**42**	**0**	**0**	**6**

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):

4. Clinical cut-off:
   Not Applicable

5. Expected values/Reference range

   The interpretative criteria and the recommended Quality Control ranges are the same as the FDA and CLSI and will appear in the Package Insert and software. Interpretative criteria used for the evaluation and that will appear in the Package Insert are as follows (values are expressed in µg/mL):

   Enterobacteriaceae and *Acinetobacter baumanii*
   ≤ 4 (S) 8 (I) ≥ 16 (R)

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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