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

A. 510(k) Number:

k103752

B. Purpose for Submission:

To obtain clearance for the addition of Imipenem to the VITEK ® 2 and VITEK®2 Compact Systems Antimicrobial Susceptibility Test (AST) Systems using VITEK 2 Systems (PC) 5.02 Software.

C. Measurand

Imipenem concentrations (≤ 0.25- ≥ 16 µg/mL)

D. Type of Test:

Quantitative growth based detection algorithm using optics light detection

E. Applicant:

bioMérieux, Inc.

F. Proprietary and Established Names:

Vitek®2 Gram Negative Imipenem with VITEK 2 Systems (PC) 5.02 Software

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 GN Imipenem is designed for antimicrobial susceptibility testing of Gram Negative bacilli. VITEK® 2 GN Imipenem is a quantitative test intended for use with the VITEK® 2 and the VITEK® 2 Compact Systems using VITEK 2 Systems (PC) 5.02 Software as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. Imipenem has been shown to be active both *in vitro* and in clinical infections against most strains of the following microorganisms according to the FDA label for the antimicrobial.

Active *in vitro* and in clinical infections:
Acinetobacter spp
Citrobacter spp
Enterobacter aerogenes
Escherichia coli
Klebsiella spp
Morganella morganii
Proteus vulgaris
Providencia rettgeri
Pseudomonas aeruginosa
Serratia marcescens

Active *in vitro* but clinical significance unknown:
Providencia stuartii

The VITEK® 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK® 2 System 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 agalactiae, S. pneumoniae* and clinically significant yeast. The VITEK 2 Systems (PC) 5.02 Software is intended for use with VITEK 2 and VITEK 2 Compact Systems.

2. Indication(s) for use:

VITEK® 2 GN Imipenem is designed for antimicrobial susceptibility testing of Gram Negative bacilli. VITEK® 2 GN Imipenem is a quantitative test intended for use with the VITEK® 2 and the VITEK® 2 Compact Systems using VITEK 2 Systems (PC) 5.02 Software as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. Imipenem has been shown to be active both *in vitro* and in clinical infections against most

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3. Special condition for use statement(s):

   Prescription Use Only

4. Special instrument Requirements:

   VITEK® 2 and the VITEK® 2 Compact Systems

I. Device Description:

Each VITEK® 2 test card contains 64 micro-wells. A control well which contains only microbiological culture media 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 sterile saline from a pure culture and standardized to a 0.5 McFarland standard using the DensiChek2. The desired card(s) are placed in the cassette along with an empty tube for the susceptibility card. The VITEK® 2 System automatically vacuum fills, seals and places the card into the incubator/reader. The VITEK® 2 Compact has a manual filling, sealing and loading operation. Cards are then transferred from the cassette into the carousel for incubation (35.50 C) and optical scanning during testing.

Optics systems use visible light to directly measure organism growth. This transmittance optics is based on an initial light reading of a well before significant growth has begun. Periodic light transmittance samplings of the same well measure organism growth by how much light is prevented from going through the well. Readings are performed every 15 minutes. An interpretive call is made between 4 and 16 hours for a "rapid" read but may be extended to 18 hours in some instances. The VITEK® 2 Susceptibility Card test is based on the microdilution minimum inhibitory concentration (MIC) technique with concentrations equivalent to standard method concentrations. Several parameters based on the growth characteristics observed are used to provide appropriate input for the MIC calculations. Growth pattern analysis is used to develop the algorithm that determines the susceptibility result for all antimicrobials on the VITEK® 2 system. The MIC result must be linked to organism identification in order to determine a category interpretation. A category interpretation will be reported along with an MIC. This is only an auto-read result; manual readings are not possible.

The VITEK® 2 AST Gram Negative Imipenem has the following concentrations in the card: 1, 2, 6, 12 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK® 2 card is ≤0.25 - 16µg/mL.

J. Substantial Equivalence Information:

1. Predicate device name(s)

VITEK® 2 Gram Negative Meropenem

2. Predicate K number(s):

k091899

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
Item	**Device**	**Predicate**
Antibiotic	Imipenem	Meropenem
Reading algorithm	Unique for Imipenem (growth pattern analysis)	Unique for Meropenem (discriminant analysis)

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 "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard"

CLSI M100-S19 "Performance Standards for Antimicrobial Susceptibility; Twenty-First Information Supplement"

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 DensiChek2. 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):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   Reproducibility was demonstrated using 10 isolates at 3 sites on 3 separate days in triplicates. The study included the Auto-dilution and the Manual dilution with the VITEK®2, and the Manual dilution with the VITEK®2 Compact. All results were >95% reproducible.

   b. Linearity/assay reportable range:

   Not Applicable

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

The recommended QC isolates 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 with the same mode.

Quality Control Summary (VITEK®2, Auto and Manual dilution)

Organism	Conc. in µg/ml	Auto-dilution		Manual dilution	
E. coli		**Ref.**	**Test**	**Ref.**	**Test**
ATCC 25922	0.06	1			
Expected Range	0.125	55		24	
0.06- 0.25 µg/ml	0.25	68	124	48	72
	0.5				
P. aeruginosa	1	30		9	
ATCC 27853	2	87	121	60	72
Expected Range	4	5		3	
1- 4 µg/ml	8				
	16		1		

An additional QC study was performed with the VITEK®2 Compact, the secondary option, at three sites, with the following results.

Quality Control Summary (VITEK®2 Compact, Manual dilution)

Organism	Conc. in µg/ml	Manual-dilution	
E. coli		**Ref.**	**Test**
ATCC 25922	0.06		
Expected Range	0.125	57	
0.06- 0.25 µg/ml	0.25	3	60
	0.5		
P. aeruginosa	1	40	
ATCC 27853	2	20	60
Expected Range	4		
1- 4 µg/ml	8		
	16		

Inoculum density control was monitored using the DensiChek2 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:

Clinical study was performed at four external sites using the VITEK 2 Gram Negative Imipenem and broth microdilution panels containing Imipenem. A total of 608 clinical isolates were tested at four external sites by auto inoculation. The no growth rate was 1.5% (9/608); fifteen of the 599 clinical isolates were from frozen stocks (2.5%, 15/599). For comparison of auto and manual dilution, the challenge set of 246 isolates was included.

Performance Summary Table (VITEK 2, Auto Dilution)

	total	**EA**	**%EA**	**Eval EA Total**	**Eval EA**	**Eval %EA**	**CA**	**%CA**	**#R**	**min**	**maj**	**vmj**
Clinical	599	576	96.2	202	194	96.0	569	95.0	154	26	2	2
Challenge	246	233	94.7	132	121	91.7	232	94.3	55	11	0	3
Combined	845	809	95.7	334	315	94.3	801	94.8	209	37	2	5

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

When analyzing the *Serratia marcescens* in the challenge study by manual method, it was noted that the EA by Compact was low at 61.5%; the CA was 100% because non-susceptible isolates are rare and might not be available for testing. However, the EA of the VITEK 2 manual dilution was high at 92.3%. An additional study was conducted with a total of 90 *Serratia marcescens* isolates with the following results:

Additional performance data summary for *S. marcescens*

S. marcescens	**total**	**EA**	**%EA**	**Eval EA Total**	**Eval EA**	**Eval %EA**	**CA**	**%CA**	**#R**	**min**	**maj**	**vmj**
VITEK2 Auto	90	81	90.0	70	63	90.0	89	98.9	1	1	0	0
VITEK2 Manual	90	68	75.6	82	61	74.4	87	96.7	1	3	0	0
Compact Manual	90	71	78.9	82	65	79.3	87	96.7	1	3	0	0

The EA of Imipenem/*Serratia marcescens* was low with manual dilutions, including the VITEK®2 Compact. A limitation was in place for Imipenem/*Serratia marcescens.*

The performance of the optional VITEK®2 Compact was evaluated in the QC, challenge, and reproducibility studies.

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

≤ 4 (S), 8(I), ≥ 16 (R)

N. Proposed Labeling:

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

O. Conclusion:

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