

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

A. 510(k) Number:

k122547

B. Purpose for Submission:

Substantial equivalence determination for the addition of Clindamycin to the VITEK 2 and VITEK 2 Compact Antimicrobial Susceptibility Test (AST) Systems for testing of *Streptococcus* species.

C. Measurand:

Clindamycin concentrations of 0.06, 0.25, and 1 µg/mL. The MIC result range for the card is ≤ 0.12 - ≥4 µg/mL.

D. Type of Test:

The minimum inhibitory concentration (MIC) is determined using qualitative growth based detection algorithm according to a predetermined growth threshold.

E. Applicant:

bioMerieux, Inc.

F. Proprietary and Established Names:

VITEK[®] 2 AST-GP Clindamycin

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LON	Class II	21 CFR 866.1645	Microbiology

H. Intended Use:

1. Intended use(s):

VITEK[®] 2 AST-GP Clindamycin is designed for antimicrobial susceptibility testing of *Staphylococcus aureus* and *Staphylococcus epidermidis*. VITEK[®] 2 AST-GP Clindamycin 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. Clindamycin has been shown to be active against most strains of the microorganism listed below, according to the FDA label for this antimicrobial.

Active *in vitro* and in clinical infections:

Staphylococcus aureus (methicillin-susceptible strains) and *Staphylococcus epidermidis* (methicillin-susceptible strains).

2. Indication(s) for use:

VITEK[®] 2 AST-GP Clindamycin is designed for antimicrobial susceptibility testing of *Staphylococcus aureus* and *Staphylococcus epidermidis*. VITEK[®] 2 AST-GP Clindamycin 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. Clindamycin has been shown to be active against most strains of the microorganism listed below, according to the FDA label for this antimicrobial.

Active *in vitro* and in clinical infections:

Staphylococcus aureus (methicillin-susceptible strains) and *Staphylococcus epidermidis* (methicillin-susceptible strains).

The VITEK[®] 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK[®] 2 and VITEK[®] 2 Compact 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 agalactiae*, and *S. pneumoniae*.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

For use with the VITEK[®] 2 and VITEK[®] 2 Compact Systems

I. Device Description:

The VITEK 2 AST card is essentially 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 wells. A control well which only contains microbiological culture media is resident on all cards. The remaining wells contain premeasured portions of a specific antibiotic combined with culture media. The bacterial or yeast isolate to be tested is diluted to a standardized

concentration with 0.45 – 0.5% saline before being used to rehydrate the antimicrobial medium within the card. The VITEK 2 System automatically fills, seals and places the card into the incubator/reader. The VITEK 2 Compact has a manual filling, sealing and loading operation. 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 that contains the MIC value along with the interpretive category result for each antibiotic contained on the card.

The VITEK[®] 2 AST-GP Clindamycin has the following concentrations in the card: 0.06, 0.25, and 1 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK 2 card is ≤ 0.12 - ≥4 µg/mL.

The MIC ranges, interpretive criteria and equivalent concentrations are as follows:

VITEK 2 AST- ST	Equivalent Standard Method Concentration by Efficacy in µg/mL	Organism (Infection)	MIC Ranges and FDA/CLSI Categories* MIC in µg/mL:		
			S	I	R
Clindamycin	0.06, 0.25, 1	Staphylococcus species	≤ 0.5	1-2	≥4

* S = Susceptible; I = Intermediate; R = Resistant

J. Substantial Equivalence Information:

1. Predicate device name(s):

VITEK 2 AST-GP Linezolid

2. Predicate K number(s):

k032766

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Determining quantitative and qualitative susceptibility to antimicrobial agents	Same
Inoculation and test organism	Isolated colonies of <i>Staphylococcus</i> species	Same
Instrument	Test are run on both the VITEK 2 and VITEK 2 Compact Systems	Same

Similarities		
Item	Device	Predicate
Test Card	The VITEK 2 card, including base broth	Same
Test Method	Automated quantitative antimicrobial susceptibility test for use with the VITEK® 2 and VITEK® 2 Compact Systems (VITEK® 2 Systems) to determine the in vitro susceptibility of <i>Staphylococcus</i> species.	Same

Differences		
Item	Device	Predicate
Antibiotic	Clindamycin-specific concentrations	Linezolid-specific concentrations
Reading algorithm	Unique to Clindamycin	Unique to Linezolid

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071462.pdf>

Clinical and Laboratory Standards Institute (CLSI) Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, Approved Standard -8th Edition, Document M7-A8.

CLSI Performance Standards for Antimicrobial Susceptibility Testing – Twenty-first Informational Supplement, M100-S21.

L. Test Principle:

Automated growth based detection using attenuation of light measured by an optical scanner. The optics used in the systems use visible light to directly measure organism growth. Transmittance optics are 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. The VITEK 2 System monitors the growth of each well in the card over a defined period of time. An interpretive call is made between 4 and 16 hours for a

“rapid” read but may be extended to 18 hours in some instances. At the completion of the incubation cycle, a report is generated that contains the MIC value along with the interpretive category result for each antibiotic on the card.

The VITEK[®] 2 AST-GP Clindamycin has the following concentrations in the card: 0.06, 0.25, and 1 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK 2 card is ≤ 0.12 - ≥4 µg/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

A reproducibility study was conducted at three external clinical sites. Six isolates of *Staphylococcus aureus* and four isolates of *Staphylococcus epidermidis* were tested at each site and testing was performed in triplicate over three days with the VITEK[®] 2 AST-GP Clindamycin card resulting in a total of 270 test results. The testing was performed using both the manual dilution method and the automated dilution method. Testing was conducted on the VITEK 2 instrument.

For the sake of reproducibility calculations, off-scale values are handled in two ways; “best case” and “worst case” scenarios. Best case calculation for reproducibility assumes the off-scale result is within one well from the mode MIC value. Worst case calculation for reproducibility assuming the off-scale result is greater than one well from the mode MIC value. All isolates tested by VITEK 2 gave on-scale MIC values but a few results were off-scale for isolates tested by the VITEK 2 Compact.

The overall reproducibility was >95% with +/- one dilution observation for the VITEK 2 and the VITEK 2 Compact system. Only Manual Dilution testing was conducted since the VITEK 2 Compact system does not have a functionality to support automatic dilution to inoculate the card. Results were as follows:

VITEK System	Inoculation Method	Best Case	Worst Case
VITEK 2	AutoDilution	100%	55.6%
	Manual	99.63%	51.1%
VITEK 2 Compact	Manual	100%	61.5%

b. *Linearity/assay reportable range:*

Not applicable

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

The recommended *Enterococcus faecalis* ATCC 29212 and *Staphylococcus aureus* ATCC 29213 QC organisms were tested on every test occasion with the reference method and the VITEK 2 System.

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 on the VITEK 2 System. Results demonstrated that methods were comparable.

Quality Control Results with the VITEK 2 System for Clindamycin were as follows:

Organism	Clindamycin Concentration (µg/mL)	Auto Dilution		Manual Dilution	
		Reference	VITEK 2	Reference	VITEK 2
<i>Staphylococcus aureus</i> ATCC 29213	0.016				
	0.03				
	0.06	1		1	
	0.12*	128	7	125	20
	0.25*	99	221	93	199
	0.5*				
	1*				
	2*				
	4*				
	≥4*				
	8				
	16				
	32				

* VITEK Card Result Range is $\leq 0.12 - \geq 4$.

For *S. aureus* ATCC 29213, results for the VITEK 2 AST-GP Clindamycin were within the expected QC results range > 95% of the time for both the automatic and manual dilution options of the VITEK 2.

A similar QC study was conducted to evaluate the VITEK 2 Compact System. Results were within the expected QC ranges.

Quality Control results for the VITEK 2 System using either inoculation dilution method demonstrated that the VITEK 2 System could produce the expected quality control results.

Inoculum density control was monitored using the DensiChek2 instrument. This was standardized weekly with all results recorded and in the expected range.

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:

Performance was established through a clinical study which was conducted at three external study sites. A total of 492 clinical isolates were tested by VITEK[®] 2 GP-Clindamycin with the VITEK[®] 2 System. The majority of the isolates were recently recovered from clinical specimens.

Two hundred and thirty-three of the 492 clinical isolates tested were stock isolates (47.4%). None of the isolates failed to grow in the VITEK card giving a no growth rate of 0.0%.

The clinical isolates were distributed as follows: 302 were *S. aureus* and 144 were *S. epidermidis*. The remainder 46 isolates were other coagulase negative species. A challenge study was conducted using a set consisting of 139 isolates (78 *S. aureus* and 61 *S. epidermidis*). The challenge set was tested with both of the VITEK[®] 2 System card inoculation options, automatic dilution and manual dilution. Testing of clinical isolates was performed using the automated method of inoculation and the challenge organisms were tested with both the manual dilution and automatic dilution. Each isolate was tested by the VITEK 2 AST-GP Clindamycin and the CLSI broth microdilution reference method. The inoculum was prepared with direct colony suspension. A comparison was provided to the reference method with the agreement shown in the following tables.

AutoDilution

Organism Group	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	# vmj	# maj	# min
<i>S. aureus</i>												
CLINICAL	302	293	97.0	136	129	94.9	301	99.7	54	1	0	0
CHALLENGE	78	76	97.4	37	35	94.6	78	100	6	0	0	0
COMBINED (CLINICAL AND CHALLENGE)	380	369	97.1	173	164	94.8	379	99.7	60	1	0	0
<i>S. epidermidis</i>												
CLINICAL	144	139	96.5	17	13	76.5	143	99.3	49	0	1	0
CHALLENGE	61	57	93.4	10	7	70	60	98.4	6	0	1	0
COMBINED (CLINICAL AND CHALLENGE)	205	196	95.6	27	20	74.1	203	99.0	55	0	2	0
All Staphylococci*												
CLINICAL	492	473	96.1	167	151	90.4	489	99.4	109	1	1	1**
CHALLENGE	139	133	95.7	47	42	89.4	138	99.3	12	0	1	0
COMBINED (CLINICAL AND CHALLENGE)	631	606	96.0	214	193	90.2	627	99.4	121	1	2	1

EA-Essential Agreement **CA**-Category Agreement **maj**-major discrepancies

vmj-very major discrepancies **min**-minor discrepancies

*Includes an additional 46 clinical isolates of other *Staphylococcus* species

** *Staphylococcus haemolyticus* strain

Essential agreement (EA) is when the VITEK 2 panels agree with the reference test panel results exactly or within one doubling dilution of the reference method. Category agreement (CA) is when the VITEK 2 panel result interpretation agrees exactly with the reference panel result interpretation. Evaluable EA is when the MIC result is on scale for both the VITEK 2 and the reference and have on-scale EA.

The VITEK 2 Manual dilution data showed similar performance as shown here:

Manual Dilution (VITEK 2)-Challenge

Organism Group (breakpoint)	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	# vmj	# maj	# min
<i>S. aureus</i>												
CHALLENGE	78	78	100	37	37	100	78	100	6	0	0	0
<i>S. epidermidis</i>												
CHALLENGE	61	57	93.4	14	10	71.4	61	100	6	0	0	0
All Staphylococci												
CHALLENGE	139	135	97.1	51	47	92.2	139	100	12	0	0	0

Performance of the VITEK[®] 2 Compact was evaluated as a secondary procedural option. The evaluation was conducted using the same 139 challenge set of *Staphylococcus aureus* and *Staphylococcus epidermidis* set tested in the VITEK[®] 2 system. A comparison was provided to the reference method with the following agreement as shown here:

Manual Dilution (VITEK 2 Compact)-Challenge

Organism Group (breakpoint)	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	# vmj	# maj	# min
<i>S. aureus</i>												
CHALLENGE	78	78	100	42	42	100	78	100	6	0	0	0
<i>S. epidermidis</i>												
CHALLENGE	61	57	93.4	16	12	75.0	61	100	6	0	0	0
All Staphylococci												
CHALLENGE	139	135	97.1	58	54	93.1	139	100	12	0	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:

The interpretive criteria and QC ranges are as recommended in the approved drug label.

For Staphylococci: ≤ 0.5 (S), 1-2 (I), ≥ 4 (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.