

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

**A. 510(k) Number:**

k141149

**B. Purpose for Submission:**

To obtain clearance for the addition of Ceftaroline to the VITEK<sup>®</sup> 2 and VITEK<sup>®</sup> 2 Compact Antimicrobial Susceptibility Test (AST) Systems

**C. Measurand:**

VITEK<sup>®</sup> 2 AST-GP Ceftaroline concentrations of 0.25, 0.5, 1, 2µg/mL; the MIC result range for the card is  $\leq 0.06 - \geq 4\mu\text{g/mL}$

**D. Type of Test:**

Quantitative growth based detection algorithm using optics light detection

**E. Applicant:**

bioMérieux, Inc.

**F. Proprietary and Established Names:**

VITEK<sup>®</sup> 2 AST-GP Ceftaroline

**G. Regulatory Information:**

1. Regulation section:

866.1645 Short-Term Antimicrobial Susceptibility Test System

2. Classification:

Class II

3. Product code:

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

4. Panel:

83, Microbiology

**H. Intended Use:**

1. Intended use(s):

The VITEK<sup>®</sup> 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK<sup>®</sup> 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.

2. Indication(s) for use:

VITEK<sup>®</sup> 2 Gram Positive Ceftaroline is designed for antimicrobial susceptibility testing of Gram positive microorganisms and is intended for use with the VITEK<sup>®</sup> 2 and VITEK<sup>®</sup> 2 Compact Systems as a laboratory aid in the determination of in vitro susceptibility to antimicrobial agents. VITEK<sup>®</sup> 2 Gram Positive Ceftaroline is a quantitative test. Ceftaroline 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

*Staphylococcus aureus* (including methicillin-susceptible and -resistant isolates) The

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3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

VITEK<sup>®</sup> 2 and the VITEK<sup>®</sup> 2 Compact Systems  
VITEK<sup>®</sup> 2 Systems 7.01 (PC version) software

**I. Device Description:**

Each VITEK<sup>®</sup> 2 test card contains 64 micro-wells. A control well containing only 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<sup>®</sup> 2 System automatically fills, seals and places the card into the incubator/reader. The VITEK<sup>®</sup> 2 Compact has a manual filling, sealing and loading operation. The VITEK<sup>®</sup> 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<sup>®</sup> 2 AST-GP Ceftaroline has the following concentrations in the card: 0.25, 0.5, 1, and 2µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK<sup>®</sup>2 card is ≤0.06- ≥4µg/mL.

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

VITEK <sup>®</sup> 2 GP	Equivalent Standard Method Concentration by Efficacy in µg/mL	MIC Ranges and FDA/CLSI Categories, MIC in µg/mL		
		<i>S. aureus</i>		
		S	I	R
Ceftaroline	0.25, 0.5, 1, 2	≤1	2	≥4

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

VITEK<sup>®</sup> 2 AST-GP Clindamycin

2. Predicate 510(k) number(s):

k122547

3. Comparison with predicate:

<b>Similarities</b>		
Item	Device	Predicate
Intended Use	Determine antimicrobial susceptibility to antimicrobial agents	Same
Inoculation and test organism	Isolated colonies	Same
Test Card	VITEK <sup>®</sup> 2 card format with base broth	Same
Instrument	VITEK <sup>®</sup> 2 and VITEK <sup>®</sup> 2 Compact Systems	Same
<b>Differences</b>		
Item	Device	Predicate

Similarities		
Item	Device	Predicate
Antibiotic	Ceftaroline- specific concentrations	Clindamycin- specific concentrations
Reading algorithm	Unique for Ceftaroline	Unique for Clindamycin

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

Class II Special Controls Guidance Document: “Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”, August 28, 2009

CLSI M7-A8 “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard”, January 2009

CLSI M100-S20\* and S23 “Performance Standards for Antimicrobial Susceptibility; Twenty-First Information Supplement”, January, 2010, and 2013

\*Ceftaroline QC parameters

**L. Test Principle:**

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**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was demonstrated using ten *S. aureus* isolates at three sites on three separate days in triplicates. The study included the Auto-dilution and the Manual dilution with the VITEK<sup>®</sup>2, and the Manual dilution with the VITEK<sup>®</sup>2 Compact. All results were >95% reproducible.

b. *Linearity/assay reportable range:*

Not Applicable

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

The recommended QC isolates were tested on every test occasion with the reference method and the VITEK<sup>®</sup>2. The reference method QC results were in range for every day tested. The VITEK<sup>®</sup>2 was tested a sufficient number of times to demonstrate that the system can produce QC results in the recommended range. The ceftaroline test results demonstrate that the VITEK<sup>®</sup>2 can produce QC results within the expected 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<sup>®</sup>2, Auto and Manual dilution)

Organism	Ceftaroline (µg/ml)	Auto-dilution		Manual dilution	
		Ref.	Test	Ref.	Test
<i>S. aureus</i> ATCC 29213	≤0.03				
Expected Range	0.06				1
0.12- 0.5 µg/mL	0.12	66	4	61	4
	0.25	168	230	165	221
	0.5				

An additional QC study was performed with the VITEK<sup>®</sup>2 Compact, the secondary option, at three sites. VITEK<sup>®</sup>2 Compact does not have a functionality to support auto dilution to inoculate the card. Results were as follows:

Quality Control Summary (VITEK<sup>®</sup>2 Compact, Manual dilution)

Organism	Ceftaroline (µg/ml)	Manual-dilution	
		Ref.	Test
<i>S. aureus</i> ATCC 29213	≤0.03		
Expected Range	0.06		1
0.12- 0.5 µg/mL	0.12	61	8
	0.25	153	205
	0.5		

Inoculum density control was monitored using the DensiCHEK<sup>™</sup> Plus 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:

The reference method follows the CLSI approved broth microdilution testing conditions for ceftaroline:

- Medium: Mueller-Hinton broth with the appropriate dilutions of antimicrobial solution added.
- Inoculum: Direct colony suspension
- Incubation : 35°C, ambient air, 16 - 20 hours

It is noted in the FDA approved pharmaceutical labeling for ceftaroline that broth dilution MICs need to be read within 18 hours due to degradation of ceftaroline activity by 24 hours. The sponsor conducted a study with 52 *S. aureus* isolates to evaluate the 18hrs vs. 20hrs read for the reference method result. The 20hrs read and the 18hrs read were in agreement.

a. *Method comparison with predicate device:*

Clinical comparative study was performed at three external sites using the VITEK<sup>®</sup>2 AST- GP Ceftaroline card and the reference broth microdilution containing Ceftaroline. A total of 302 clinical isolates were tested by auto inoculation and 106 of the 302 isolates were stock isolates (35.1%, 106/302). All *Staphylococcus aureus* isolates grew in the study.

The clinical isolates were comprised of 48.8% of oxacillin resistant *S. aureus* (MRSA) and 51.2% of oxacillin susceptible *S. aureus* (MSSA); all 78 challenge isolates were MRSA and were tested at one external site. The VITEK<sup>®</sup>2 performance was presented in the table below:

Performance Summary Table (VITEK<sup>®</sup>2, Auto Dilution)

	Total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
<b>Clinical</b>												
MRSA	148	148	100	148	148	100	148	100	0	0	0	0
<b>Challenge (MRSA)</b>												
MSSA	78	77	98.7	78	77	98.7	76	97.4	0	2	0	0
<b>Combined</b>												
	380	372	97.9	371	363	97.8	377	99.2	0	3	0	0

EA-Essential Agreement  
CA-Category Agreement  
R-resistant isolates

maj-major discrepancies  
vmj-very major discrepancies  
min- minor discrepancies

MRSA (clinical+ challenge)

The majority of MIC values were at 0.5µg/mL; there were 14 isolates at the breakpoint of 1µg/mL, with one minor error, but within EA. The other minor error was two dilutions higher [reference: 0.5 (S), VITEK<sup>®</sup>2: 2 (I)].

MSSA

The MIC result ranges were 0.125- 0.25µg/mL, with 116 MSSA at 0.25µg/mL. There was one minor error [reference: 2 (I), VITEK<sup>®</sup>2: 0.25(S)].

The comparative study did not include any ceftaroline resistant *S. aureus* and a limitation is in place for the ceftaroline/*S. aureus* combination in the labeling.

**Manual Dilution:**

The challenge set of 78 *S. aureus* isolates were tested at one external site by manual inoculation method for VITEK<sup>®</sup>2 and VITEK<sup>®</sup>2 Compact with the following performance.

Comparison Challenge Data - VITEK<sup>®</sup>2, and VITEK<sup>®</sup>2 Compact (Manual dilution)

	Total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
<b>VITEK2</b>	78	77	98.7	78	77	98.7	78	100	0	0	0	0
<b>VITEK2 Compact</b>	78	78	100	78	78	100	78	100	0	0	0	0

The performance of the optional VITEK<sup>®</sup>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): None
- 4. Clinical cut-off: Not applicable
- 5. Expected values/Reference range:

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

*S. aureus* (including MRSA):            ≤1(S), 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.