

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

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

k111909

**B. Purpose of Submission:**

To obtain clearance for the addition of Inducible Clindamycin Resistance (ICR) test to the VITEK®2 and VITEK®2 Compact Systems Antimicrobial Susceptibility Test (AST) System

**C. Measurand**

Clindamycin 0.5µg/mL  
Clindamycin/Erythromycin 0.25/0.5µg/mL

Positive: Inducible Resistance  
Negative: No Inducible Resistance

**D. Type of Test:**

Quantitative growth based detection algorithm using predetermined growth thresholds

**E. Applicant:**

bioMérieux, Inc.

**F. Proprietary and Established Names:**

VITEK®2 Gram Positive Inducible Clindamycin Resistance

**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 *Streptococcus* Inducible Clindamycin Resistance is designed for antimicrobial susceptibility testing of *Streptococcus agalactiae* and *Streptococcus pyogenes*. VITEK® 2 *Streptococcus* Inducible Clindamycin Resistance is a qualitative test. It is 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.

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 yeast.

2. Indication(s) for use:

VITEK® 2 *Streptococcus* Inducible Clindamycin Resistance is designed for antimicrobial susceptibility testing of *Streptococcus agalactiae* and *Streptococcus pyogenes*. VITEK® 2 *Streptococcus* Inducible Clindamycin Resistance is a qualitative test. It is 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.

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 yeast.

3. Special condition for use statement(s):

Prescription use only

4. Special instrument Requirements:

VITEK®2 Systems 5.01 Software  
VITEK®2 Compact is the secondary system

## **I. Device Description:**

Each VITEK® 2 test card contains 64 microwells. 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. Discriminant 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-ST Inducible Clindamycin Resistance consists of two wells at the following concentrations in the card: Clindamycin 0.5µg/mL and Clindamycin/Erythromycin at 0.25/0.5µg/mL (equivalent standard method concentration by efficacy in µg/mL). The CLSI Interpretive Criteria for the VITEK® 2 Inducible Clindamycin Resistance is Negative- Positive.

## **J. Substantial Equivalence Information:**

1. Predicate device name(s):

VITEK® 2 AST-GP Inducible Clindamycin Resistance

2. Predicate K number(s):

k080201

### 3. Comparison with predicate

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Intended Use	Determine qualitative antimicrobial susceptibility to antimicrobial agents	Same
Instrument	VITEK®2 and VITEK®2 Compact Systems	Same
Antibiotic	Clindamycin 0.5µg/mL Clindamycin/Erythromycin 0.25/0.5µg/mL	Same
<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Test organism	<i>Streptococcus agalactiae</i> and <i>Streptococcus pyogenes</i>	<i>Staphylococcus</i> spp.
Test Card	<i>Streptococcus</i> (AST-ST) Susceptibility Card	Gram positive (AST-GP) Susceptibility Card
Reading algorithm	Unique for <i>Streptococcus agalactiae</i> and <i>Streptococcus pyogenes</i>	Unique for <i>Staphylococcus</i> spp

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

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

CLSI M07-A8 “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard”

CLSI M100-S19 “Performance Standards for Antimicrobial Susceptibility Test”.

#### **L. Test Principle:**

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. 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 AST-ST Inducible Clindamycin Resistance consists of two wells at the following concentrations in the card: Clindamycin 0.5µg/mL and Clindamycin/Erythromycin 0.25/0.5µg/mL, with the following interpretation:

Clindamycin 0.5 µg/mL well	Clindamycin/Erythromycin 0.25/0.5 µg/mL well	VITEK 2 AST-ST ICR Interpretation
No Growth	No Growth	NEG
No Growth	Growth	POS
Growth	Growth	NEG
Growth	No Growth	NEG

Software forcing rules for *S. agalactiae* and *S. pyogenes* are applicable dependent on the AST-ST ICR test results.

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

#### 1. Analytical performance:

##### a. *Precision/Reproducibility:*

Five *S. agalactiae* and five *S. pyogenes* isolates were tested at three sites using both manual and automatic dilution methods. These same organisms were tested at one site three times to determine within site reproducibility. Acceptable reproducibility was demonstrated with only category agreement (Negative, Positive) since that is all that is detected.

The same study was conducted at three external sites; using the secondary VITEK®2 Compact by manual dilution with acceptable results.

##### b. *Linearity/assay reportable range:*

Not applicable

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

The CLSI recommended QC isolates, *S. aureus* ATCC BAA-977, and *S. aureus* ATCC 29213 were tested at each site by the VITEK®2 AST-ST ICR and the D test method. The reference method QC results were in range every day they were tested. The VITEK®2 was tested a sufficient number of times to demonstrate that the system produced QC results within the expected ranges (i.e. positive/negative) >95% of the time for both automatic and manual dilution methods.

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

ORGANISM	Test Results	Reference AUTO-DIL	VITEK®2 AUTO-DIL	Reference MAN-DIL	VITEK®2 MAN-DIL
<i>S. aureus</i> ATCC BAA-977 Expected Result: POS	Neg	0	3	0	2
	Pos	158	155	158	156
<i>S. aureus</i> ATCC 29213 Expected Result: Neg	Neg	146	146	147	147
	Pos	0	0	0	0

s

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

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

ORGANISM	Test Results	Reference	VITEK®2
<i>S. aureus</i> ATCC BAA-977 Expected Result: POS	Neg	0	0
	Pos	83	83
<i>S. aureus</i> ATCC 29213 Expected Result: Neg	Neg	83	83
	Pos	0	0

Inoculum density control was monitored using the DensiChek2 instrument. This was standardized weekly with all results recorded and within acceptable parameters. 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 was the CLSI standard disk diffusion (D test) procedure with a 15µg Erythromycin disk and placing a 2µg Clindamycin disk 12 mm away. The conditions were:

- Medium: Mueller-Hinton with 5% sheep blood
- Inoculum: Direct colony suspension
- Incubation : 35°C, in CO<sub>2</sub> for 20- 24 hours

### *a. Method comparison with predicate device:*

A clinical study was conducted at four external sites using the VITEK®2 AST-ST Streptococcus Inducible Clindamycin Resistance susceptibility test. Each isolate was tested by the VITEK®2 AST-ST Streptococcus Inducible Clindamycin Resistance (ICR) susceptibility test and the CLSI reference method. The ICR test wells are not supplemented with blood.

The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. A total of 538 clinical isolates were evaluated. There were 89 stock isolates (16.5%); all clinical isolates grew in the VITEK®2 AST-ST Inducible Clindamycin Resistance (ICR) test. The challenge set consisted of 100 isolates and all grew in the VITEK®2 AST-ST cards.

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. Software forcing rules for *S. agalactiae* and *S. pyogenes* are applicable dependent on the growth/no growth in the Clindamycin 0.5µg/mL, and the Clindamycin/Erythromycin 0.25/0.5µg/mL wells.

A comparison to the reference D test was provided with the following agreement:

Summary Table of Combined Clinical+ Challenge (Auto-dilution)

	Total	CA	%CA	Neg	Pos	maj	vmj
<b>Clinical</b>	538	538	100	504	34	0	0
<b>Challenge</b>	100	95	95	68	32	4	1
<b>Combined</b>	638	633	99.2	572	66	4	1

CA-Category Agreement

vmj-very major discrepancies

maj-major discrepancies

CA is when the interpretation of the reference D test agrees exactly with the interpretation of the VITEK®2 results.

A challenge study was performed utilizing auto-dilution and manual dilution at one site on 100 isolates. No differences observed between these two types of dilutions.

Summary Table of Challenge

	<b>Total</b>	<b>CA</b>	<b>%CA</b>	<b>Neg</b>	<b>Pos</b>	<b>maj</b>	<b>vmj</b>
<b>Auto</b>	100	95	95	68	32	4	1
<b>Manual</b>	100	95	95	68	32	4	1

The performance of the secondary VITEK®2 Compact Systems (manual dilutions) was demonstrated in the challenge studies at one external site, quality control, and reproducibility studies at three external sites with acceptable results.

*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:

Positive: Detection of inducible resistant clindamycin

Negative: No inducible resistance to clindamycin

**N. Labeling**

The labeling is sufficient and 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.