K121863

510(k) SUMMARY

AUG 16 2012

VITEK® 2 AST- ST Cefotaxime

510(k) Submission Information:

Submitter's Name:	bioMérieux, Inc.
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Date of Preparation:	June 25, 2012

A. 510(k) Number:

k121863

B. Purpose for Submission:

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

C. Measurand:

Cefotaxime concentrations of 0.25, 0.5, 1, and 2 µg/ml. The MIC result range of the card is ≤ 0.125 – ≥ 8 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:

bioMérieux, Inc.

F. Proprietary and Established Names:

VITEK® 2 AST - ST Cefotaxime

G. Regulatory Information:

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

H. Intended Use:

1. Intended use:

   VITEK® 2 AST - ST Cefotaxime is designed for antimicrobial susceptibility testing of *Streptococcus* species. VITEK® 2 AST - ST Cefotaxime 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. Cefotaxime 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:
   Streptococcus pneumoniae, Streptococcus pyogenes (Group A beta-hemolytic streptococci), *Streptococcus* spp.

2. Indication(s) for use:

   VITEK® 2 AST - ST Cefotaxime is designed for antimicrobial susceptibility testing of Streptococcus species. VITEK® 2 AST - ST Cefotaxime 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. Cefotaxime 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:
   Streptococcus pneumoniae, Streptococcus pyogenes (Group A beta-hemolytic streptococci), *Streptococcus* spp.

   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 - ST Cefotaxime for *Streptococcus* species has the following concentrations in the card: 0.25, 0.5, 1, and 2 µg/ml (equivalent standard method concentration by efficacy in µg/ml). The MIC result range for the VITEK 2 card is ≤ 0.125 – ≥ 8 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
Cefotaxime	0.25, 0.5, 1, and 2	*S. pneumoniae* (non-meningitis) CLSI	≤ 1	2	≥ 4
		S. pneumoniae (meningitis) FDA	≤ 0.5	1	≥ 2
		Streptococcus Species FDA	≤ 0.5	1	≥ 2

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

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VITEK® 2 AST - GP Amoxicillin for *S. pneumoniae*

2. Predicate K number(s):

   k063597

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 *Streptococcus pneumoniae*	Same
Instrument	Test are run on both the VITEK® 2 and VITEK® 2 Compact Systems	Same
Test Card	VITEK® 2 card, including base broth	Same
Test Method	Automated quantitative Antimicrobial susceptibility test to determine the *in vitro* susceptibility of *Streptococcus pneumoniae*	Same

Differences		
Item	Device	Predicate
Antibiotic	Cefotaxime-specific concentrations	Amoxicillin-specific concentrations
Reading algorithm	Unique to Cefotaxime	Unique to Amoxicillin
Test organisms	*Streptococcus pyogenes* (Group A beta-hemolytic streptococci), and *Streptococcus* spp. in addition to *S. pneumoniae*	*S. pneumoniae*

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 - ST Cefotaxime for *Streptococcus* species has the following concentrations in the card: 0.25, 0.5, 1, and 2 µg/ml (equivalent standard method concentration by efficacy in µg/ml). The MIC result range for the VITEK® 2 card is ≤ 0.125 - ≥ 8 µg/ml.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

      A reproducibility study was conducted at three external clinical sites. Nine isolates of *Streptococcus pneumoniae* and one isolate of *Streptococcus mitis* were tested at each site and testing was performed in triplicate over three days with the VITEK® 2 AST - ST Cefotaxime 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.

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	Auto Dilution	100%	100%
	Manual	100%	100%
VITEK® 2 Compact	Manual	100%	100%

b. *Linearity/assay reportable range:*

Not applicable

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

The recommended *Streptococcus pneumonia* QC organism was 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 Cefotaxime were as follows:

Organism	Cefotaxime Concentration (µg/ml)	Auto Dilution		Manual Dilution	
		Reference	VITEK® 2	Reference	VITEK® 2
Streptococcus pneumonia ATCC 49619 Acceptable MIC range: 0.06-0.25 (FDA)					
	0.016	1		1	
	0.03				
	0.06	128		126	
	0.12*	53	182	52	178
	0.25*				
	0.5*				1
	1*				
	2*				
	4*				
	8*				

* VITEK® Card Result Range is ≤ 0.125 – ≥ 8.

Results for the VITEK® 2 AST - ST Cefotaxime 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 FDA 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 four external study sites. A total of 1425 clinical isolates were tested by VITEK® 2 AST - ST Cefotaxime with the VITEK® 2 System. The majority of the isolates were recently recovered from clinical specimens. Four hundred sixty-five of the 1425 clinical isolates tested were stock isolates (32.6%). Nine of the isolates failed to grow in the VITEK® card giving a no growth rate of 0.6% (9/1425). Therefore, the total number of viable clinical isolates evaluated was 1416.

A total of 301 clinical isolates of *Streptococcus pneumoniae* were tested and the performance data was analyzed using the meningitis and non-meningitis breakpoints for Cefotaxime. None of the isolates failed to grow in the VITEK® 2 AST card. One hundred fifty one of the 301 clinical isolates tested were stock isolates (50.2%).

A challenge set consisting of 207 isolates (*Streptococcus* species) and 50 isolates for *Streptococcus pneumonia* (non-meningitis breakpoint) was also evaluated with VITEK® 2 AST - ST Cefotaxime at one external site. 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 - ST Cefotaxime 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.

There is only one set of breakpoints [≤ 0.5 (S), 1 (I), ≥ 2 (R)] for *Streptococcus* spp in the FDA drug label for Cefotaxime. The performance data for *Streptococcus* species and *S. pneumoniae* were analyzed using the FDA breakpoints for *Streptococcus* spp.

Another analysis was conducted using CLSI breakpoints for S. *pneumoniae*. As stated in CLSI M100-S22, Vol 32, No. 3, January 2012, *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Second Informational Supplement,* CLSI breakpoints for S. *pneumoniae* meningitis are the same as FDA breakpoints for

Streptococcus species [≤ 0.5 (S), 1 (I), ≥ 2 (R)]. Therefore, the clinical trial performance data was analyzed by combining *Streptococcus* species and the CLSI S. *pneumoniae* meningitis breakpoint. Because the CLSI breakpoints the S. *pneumoniae* non-meningitis ([≤ 1 (S), 2 (I), ≥ 4 (R)] are different, this performance data is presented separately.

A summary of the data is shown in the tables that follow.

Auto Dilution (*S. pneumonia* and *Streptococcus* species)

Organism Group	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	# vmj	# maj	# min
***Streptococcus pneumoniae* (non-meningitis breakpoint)**												
CLINICAL	301	296	98.3	83	79	95.2	270	89.7	6	0	1	30
CHALLENGE	50	50	100	35	35	100	45	90.0	17	0	0	5
COMBINED (CLINICAL AND CHALLENGE)	351	346	98.6	118	114	96.6	315	89.7	23	0	1	35
***Streptococcus pneumoniae* (meningitis breakpoint)**												
CLINICAL	301	296	98.3	83	79	95.2	270	89.7	29	0	2	29
CHALLENGE	50	50	100	35	35	100	44	88.0	25	0	0	6
COMBINED (CLINICAL AND CHALLENGE)	351	346	98.6	118	114	96.6	314	89.5	54	0	2	35
Streptococcus pyogenes												
CLINICAL	260	260	100	0	0	N/A	260	100	0	0	0	0
CHALLENGE	50	50	100	0	0	N/A	50	100	0	0	0	0
COMBINED (CLINICAL AND CHALLENGE)	310	310	100	0	0	N/A	310	100	0	0	0	0
All *Streptococcus* species including *S. pneumoniae* (meningitis breakpoint)												
CLINICAL	1416	1400	98.9	188	181	96.3	1367	96.5	50	0	3	46
CHALLENGE	207	207	100	55	55	100	199	96.1	31	0	0	8
COMBINED (CLINICAL AND CHALLENGE)	1623	1607	99.0	243	236	97.1	1566	96.5	81	0	3	54

EA-Essential Agreement; **CA**-Category Agreement; **maj**-major discrepancies **vmj**-very major discrepancies; **min**-minor discrepancies

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.

For the non-meningitis breakpoint for *S. pneumoniae*, 35 (10%) minor categorical errors were seen along with one major error. A high agreement was observed with a total EA of 98.6%, evaluable EA of 96.6%, and a CA of 89.7%. Of 351 total isolates of *S. pneumoniae*, 23 isolates were considered resistant based on the Cefotaxime breakpoint for non-meningitis, but no very major errors occurred.

For the meningitis breakpoint for *S. pneumoniae*, 35 (10%) minor categorical errors were seen along with two major errors. A high agreement was observed with a total EA of 98.6%, evaluable EA of 96.6%, and a CA of 89.5%. Of 351 total isolates of *S. pneumoniae*, 54 isolates were considered resistant based on the Cefotaxime breakpoint for non-meningitis, but no very major errors occurred.

For combined Streptococci species and *S. pneumoniae* (meningitis breakpoint), 54 (3.3%) minor categorical errors were seen along with three major errors. A high agreement was observed with a total EA of 99.0%, evaluable EA of 97.1%, and a CA of 96.5%. Of 1623 total isolates of Streptococci, 81 isolates were considered resistant based on the Cefotaxime breakpoints of [≤ 0.5(S), 1 (I) , ≥ 2(R)], but no very major errors occurred.

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
***Streptococcus pneumoniae* (non-meningitis breakpoint)**												
CHALLENGE (non-meningitis)	50	50	100	33	33	100	46	92.0	17	0	0	4
***Streptococcus pneumoniae* (meningitis breakpoint)**												
CHALLENGE (meningitis)	50	50	100	33	33	100	45	90.0	25	0	0	5
All *Streptococcus* species including *S. pneumoniae* (meningitis breakpoint)												
CHALLENGE	207	207	100	53	53	100	200	96.6	31	0	0	7

Performance of the VITEK® 2 Compact was evaluated as a secondary procedural option. The evaluation was conducted using the same 207 isolates (*Streptococcus* species), and 50 isolates of *Streptococcus pneumoniae* challenge 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
***Streptococcus pneumoniae* (non-meningitis breakpoint)**												
CHALLENGE (non-meningitis)	50	50	100	34	34	100	44	88.0	17	0	0	6
***Streptococcus pneumoniae* (meningitis breakpoint)**												
CHALLENGE (meningitis)	50	50	100	34	34	100	43	86.0	25	0	0	7
All *Streptococcus* species including *S. pneumoniae* (meningitis breakpoint)												
CHALLENGE	207	205	99.0	50	49	98.0	196	94.7	31	0	0	11

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. *S. pneumoniae* (non-meningitis) was also analyzed using CLSI interpretive criteria.

FDA: *Streptococcus* species and *S. pneumoniae* (meningitis): ≤ 0.5 (S), 1 (I), ≥ 2 (R)

CLSI: *S. pneumoniae* (non-meningitis): ≤ 1(S), 2 (I), ≥ 4 (R)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

bioMérieux, Inc.
c/o Elizabeth Landon
Staff Regulatory Affairs Specialist
100 Rodolphe Street
Durham, NC 27712

AUG 16 2012

Re: K121863
Trade Name: VITEK®2 AST- ST Cefotaxime
Regulation Number: 21 CFR §866.1645
Regulation Name: Fully automated short-term incubation cycle antimicrobial susceptibility system.
Regulatory Class: Class II
Product Code: LON
Dated: June 25, 2012
Received: July 13, 2012

Dear Ms. Landon:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-

510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K121863

Device Name: VITEK® 2 AST - ST Cefotaxime
(≤ 0.125 – ≥ 8 µg/ml)

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VITEK® 2 AST - ST Cefotaxime is designed for antimicrobial susceptibility testing of Streptococcus species. VITEK 2 AST - ST Cefotaxime 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. Cefotaxime 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
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Prescription Use ___X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Page 1 of 1

Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K121863