

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

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

k122359

**B. Purpose for Submission:**

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

**C. Measurand:**

Ceftriaxone concentrations of 0.125, 0.25, 1, and 4 µg/mL. The MIC result range of the card is  $\leq 0.125 - \geq 8$  µg/mL.

**D. Type of Test:**

A qualitative growth based detection test using an algorithm with a predetermined growth threshold to determine the minimum inhibitory concentration (MIC).

**E. Applicant:**

bioMérieux, Inc.

**F. Proprietary and Established Names:**

VITEK<sup>®</sup> 2 Streptococcus Ceftriaxone

**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<sup>®</sup> 2 Streptococcus Ceftriaxone is designed for antimicrobial susceptibility testing of *Streptococcus* species. VITEK<sup>®</sup> 2 Streptococcus Ceftriaxone is a quantitative test 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. Ceftriaxone 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*, *Streptococcus agalactiae*, and viridans group streptococci.

2. Indication(s) for use:

VITEK<sup>®</sup> 2 Streptococcus Ceftriaxone is designed for antimicrobial susceptibility testing of *Streptococcus* species. VITEK<sup>®</sup> 2 Streptococcus Ceftriaxone is a quantitative test 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. Ceftriaxone 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*, *Streptococcus agalactiae*, and viridans group streptococci.

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

Due to the absence of resistant beta hemolytic *Streptococcus* isolates for Ceftriaxone, the following will be included in the package insert after the antibiotic name:

“Beta hemolytic streptococci: The current absence of resistant isolates precludes defining any results other than susceptible. Isolates yielding MIC results suggestive of non-susceptible category should be submitted to a reference laboratory for further testing.”

4. Special instrument requirements:

For use with the VITEK<sup>®</sup> 2 and VITEK<sup>®</sup> 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<sup>®</sup> 2 Streptococcus Ceftriaxone has the following concentrations in the card: 0.125, 0.25, 1, and 4 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<br>AST- ST | Equivalent<br>Standard Method<br>Concentration by<br>Efficacy in µg/mL | Organism<br>(Infection)                  | MIC Ranges and<br>FDA/CLSI Categories* |   |    |
|--------------------|--|--|--|---|----|
|                    |  |  | S                                      | I | R  |
| Ceftriaxone        | 0.125, 0.25, 1, 4  | <i>S. pneumoniae</i><br>(non-meningitis) | ≤ 1                                    | 2 | ≥4 |
|                    |  | <i>S. pneumoniae</i><br>(meningitis)     | ≤ 0.5                                  | 1 | ≥2 |
|                    |  | Beta hemolytic<br>streptococci           | ≤ 0.5**                                | - | -  |
|                    |  | Viridans group<br>streptococci           | ≤ 1                                    | 2 | ≥4 |

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

\*\* Currently only a “Susceptible” category is defined for Beta hemolytic streptococci

**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:

| <b>Similarities</b>           |   |                  |
|-------------------------------|---|------------------|
| <b>Item</b>                   | <b>Device</b>   | <b>Predicate</b> |
| Intended Use                  | Determining quantitative and qualitative susceptibility to antimicrobial agents   | Same             |
| Inoculation and test organism | Isolated colonies of <i>Streptococcus pneumoniae</i>  | Same             |
| Instrument                    | Test are run on both the VITEK 2 and VITEK 2 Compact Systems  | Same             |
| Test Card                     | The VITEK 2 card, including base broth  | Same             |
| Test Method                   | Automated quantitative Antimicrobial susceptibility test to determine the <i>in vitro</i> susceptibility of <i>Streptococcus pneumoniae</i> | Same             |

| <b>Differences</b> |   |                                     |
|--------------------|---|-------------------------------------|
| <b>Item</b>        | <b>Device</b>   | <b>Predicate</b>                    |
| Antibiotic         | Ceftriaxone-specific concentrations   | Amoxicillin-specific concentrations |
| Reading algorithm  | Unique to Ceftriaxone   | Unique to Amoxicillin               |
| Test organisms     | <i>Streptococcus pyogenes</i> , <i>Streptococcus agalactiae</i> , and viridans group streptococci in addition to <i>S. pneumoniae</i> | <i>S. pneumoniae</i>                |

**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<sup>®</sup> 2 Streptococcus Ceftriaxone has the following concentrations in the card: 0.125, 0.25, 1, and 4 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. Eight isolates of *Streptococcus pneumoniae*, and one isolate each of *Streptococcus mitis* and *Streptococcus anginosus* were tested at each site and testing was performed in triplicate over three days with the VITEK<sup>®</sup> 2 Streptococcus Ceftriaxone 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 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%      | 100%       |
|                 | Manual             | 100%      | 100%       |
| VITEK 2 Compact | Manual             | 99.3%     | 99.3%      |

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 Ceftriaxone were as follows:

| Organism   | Ceftriaxone Concentration (µg/mL) | Auto Dilution |         | Manual Dilution |         |
|--|-----------------------------------|---------------|---------|-----------------|---------|
|  |                                   | Reference     | VITEK 2 | Reference       | VITEK 2 |
| <i>Streptococcus pneumoniae</i> ATCC 49619<br><br>Acceptable MIC range:<br>0.03-0.12 µg/mL | 0.016                             |               |         |                 |         |
|  | 0.03                              |               |         |                 |         |
|  | 0.06                              | 163           |         | 161             |         |
|  | 0.12*                             | 19            |         | 18              |         |
|  | ≤ 0.12                            |               | 182     |                 | 178     |
|  | 0.25*                             |               |         |                 | 1       |
|  | 0.5*                              |               |         |                 |         |
|  | 1*                                |               |         |                 |         |
|  | 2*                                |               |         |                 |         |
|  | 4*                                |               |         |                 |         |
|  | 8*                                |               |         |                 |         |

\* VITEK Card Result Range is  $\leq 0.125 - \geq 8$ .

Results for the VITEK 2 AST-ST Ceftriaxone 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 four external study sites. A total of 1425 clinical isolates were tested by VITEK<sup>®</sup> 2 Ceftriaxone with the VITEK<sup>®</sup> 2 System. The majority of the isolates were recently recovered from clinical specimens. Four hundred fifty-nine of the 1425 clinical isolates tested were stock isolates (32.2%). 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 Ceftriaxone. 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 study was conducted using a set consisting of 200 *Streptococcus* species isolates (50 isolates each of *S. agalactiae*, *S. pneumoniae*, *S. pyogenes*, and viridans group streptococci). *S. pneumoniae* data was analyzed using the meningitis and non-meningitis breakpoints. The challenge set was tested with both of the VITEK<sup>®</sup> 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 *Streptococcus* Ceftriaxone 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 are different sets of breakpoints for *Streptococcus* spp in the FDA drug label for Ceftriaxone. The viridans group streptococci and *S. pneumoniae* (non-meningitis) data was analyzed using the same set of FDA breakpoints [ $\leq 1$  (S), 2 (I),  $\geq 4$  (R)]. In addition, *S. pneumoniae* data was analyzed using the FDA breakpoints for meningitis [ $\leq 0.5$  (S), 1 (I),  $\geq 2$  (R)].

The data was analyzed separately for the beta hemolytic streptococci because the breakpoint is different and there is a susceptible only category (S  $\leq 0.5$   $\mu\text{g/mL}$ ). A summary of the data is shown in the tables that follow.

AutoDilution  
(*S. pneumoniae*,  $\beta$ -hemolytic streptococci and viridans group streptococci)

| Organism Group   | EA Tot | EA N | EA % | Eval EA Tot | Eval EA N | Eval EA % | CA N | CA % | #R | # vmj | # maj | # min |
|--|--------|------|------|-------------|-----------|-----------|------|------|----|-------|-------|-------|
| <i>Streptococcus pneumoniae</i> (non-meningitis breakpoint)                                  |        |      |      |             |           |           |      |      |    |       |       |       |
| CLINICAL   | 301    | 293  | 97.3 | 89          | 83        | 93.3      | 283  | 94.0 | 5  | 0     | 3     | 15    |
| CHALLENGE  | 50     | 50   | 100  | 49          | 49        | 100       | 46   | 92.0 | 11 | 0     | 0     | 4     |
| COMBINED (CLINICAL AND CHALLENGE)  | 351    | 343  | 97.7 | 138         | 132       | 95.7      | 329  | 93.7 | 16 | 0     | 3     | 19    |
| <i>Streptococcus pyogenes</i>  |        |      |      |             |           |           |      |      |    |       |       |       |
| 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     |
| <i>Streptococcus agalactiae</i>  |        |      |      |             |           |           |      |      |    |       |       |       |
| CLINICAL   | 272    | 272  | 100  | 0           | 0         | N/A       | 272  | 100  | 0  | 0     | 0     | 0     |
| CHALLENGE  | 50     | 50   | 100  | 0           | 0         | N/A       | 50   | 100  | 0  | 0     | 0     | 0     |
| COMBINED (CLINICAL AND CHALLENGE)  | 322    | 322  | 100  | 0           | 0         | N/A       | 322  | 100  | 0  | 0     | 0     | 0     |
| Viridans group streptococci  |        |      |      |             |           |           |      |      |    |       |       |       |
| CLINICAL   | 358    | 349  | 97.5 | 170         | 167       | 98.2      | 343  | 95.8 | 9  | 0     | 0     | 15    |
| CHALLENGE  | 50     | 50   | 100  | 29          | 29        | 100       | 50   | 100  | 4  | 0     | 0     | 0     |
| COMBINED (CLINICAL AND CHALLENGE)  | 408    | 399  | 97.8 | 199         | 196       | 98.5      | 393  | 96.3 | 13 | 0     | 0     | 15    |
| All <i>Streptococcus</i> species (includes <i>S. pneumoniae</i> , non-meningitis breakpoint) |        |      |      |             |           |           |      |      |    |       |       |       |
| CLINICAL   | 1416   | 1399 | 98.8 | 260         | 251       | 96.5      | 1383 | 97.7 | 14 | 0     | 3     | 30    |
| CHALLENGE  | 200    | 200  | 100  | 78          | 78        | 100       | 196  | 98.0 | 15 | 0     | 0     | 4     |
| COMBINED (CLINICAL AND CHALLENGE)  | 1616   | 1599 | 98.9 | 338         | 329       | 97.3      | 1579 | 97.7 | 29 | 0     | 3     | 34    |

**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 combined streptococci including *S. pneumoniae* (non-meningitis breakpoint), 34 (2.1%) minor categorical errors were seen with 3 (0.2%) major errors and no very major errors. A high agreement was observed with a total EA of 98.9%, evaluable EA of 97.3% and a CA of 97.7%.

Of 759 total isolates of *S. pneumoniae* and viridans group streptococci, 29 isolates were considered resistant based on the ceftriaxone breakpoints of [ $\leq 1$ (S), 2 (I) ,  $\geq 4$ (R)], but no very major errors occurred.

For the non-meningitis breakpoint for *S. pneumoniae*, 19 (5.4%) minor categorical errors were seen with three (3/335, 0.9%) major errors. Of 351 total isolates of *S. pneumoniae*, 16 isolates were considered resistant based on the ceftriaxone breakpoint for non-meningitis but no very major errors occurred. A high agreement was observed with a total EA of 97.7%, evaluable EA of 95.7% and a CA of 93.7%.

AutoDilution  
(*S. pneumoniae*, meningitis breakpoint)

| Organism Group  | EA Tot | EA N | EA % | Eval EA Tot | Eval EA N | Eval EA % | CA N | CA % | #R | # vmj | # maj | # min |
|---|--------|------|------|-------------|-----------|-----------|------|------|----|-------|-------|-------|
| <i>Streptococcus pneumoniae</i> (meningitis breakpoint) |        |      |      |             |           |           |      |      |    |       |       |       |
| CLINICAL  | 301    | 293  | 97.3 | 89          | 83        | 93.3      | 275  | 91.4 | 20 | 0     | 0     | 26    |
| CHALLENGE   | 50     | 50   | 100  | 49          | 49        | 100       | 44   | 90.0 | 18 | 0     | 0     | 6     |
| COMBINED (CLINICAL AND CHALLENGE)                       | 351    | 343  | 97.7 | 138         | 132       | 95.7      | 319  | 90.9 | 38 | 0     | 0     | 32    |

For the meningitis breakpoint for *S. pneumoniae*, 32 (9.1%) minor categorical errors were seen along with no major or very major errors. An EA of 97.7%, evaluable EA of 95.7% and a CA of 90.95% were observed. Of 351 total isolates of *S. pneumoniae*, 38 isolates were considered resistant based on the ceftriaxone breakpoint for non-meningitis [ $\leq 0.5$  (S), 1 (I) ,  $\geq 2$ (R)] but no very major errors occurred.

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>Streptococcus pneumoniae</i> (non-meningitis breakpoint)                                  |        |      |      |             |           |           |      |      |    |       |       |       |
| CHALLENGE (non-meningitis)   | 50     | 50   | 100  | 49          | 49        | 100       | 45   | 88   | 11 | 0     | 0     | 6     |
| <i>Streptococcus pneumoniae</i> (meningitis breakpoint)                                      |        |      |      |             |           |           |      |      |    |       |       |       |
| CHALLENGE (meningitis)   | 50     | 50   | 100  | 49          | 49        | 100       | 45   | 90   | 18 | 0     | 0     | 5     |
| All <i>Streptococcus</i> species (includes <i>S. pneumoniae</i> , non-meningitis breakpoint) |        |      |      |             |           |           |      |      |    |       |       |       |
| CHALLENGE  | 200    | 200  | 100  | 78          | 78        | 100       | 194  | 97.0 | 15 | 0     | 0     | 6     |

Performance of the VITEK<sup>®</sup> 2 Compact was evaluated as a secondary procedural option. The evaluation was conducted using the same 200 isolate (*Streptococcus* species) which included 50 *Streptococcus pneumoniae* challenge set tested in the VITEK<sup>®</sup> 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>Streptococcus pneumoniae</i> (non-meningitis breakpoint)                                  |        |      |      |             |           |           |      |      |    |       |       |       |
| CHALLENGE (non-meningitis)   | 50     | 50   | 100  | 49          | 49        | 100       | 43   | 86   | 11 | 0     | 0     | 7     |
| <i>Streptococcus pneumoniae</i> (meningitis breakpoint)                                      |        |      |      |             |           |           |      |      |    |       |       |       |
| CHALLENGE (meningitis)   | 50     | 50   | 100  | 49          | 49        | 100       | 45   | 90   | 18 | 0     | 0     | 5     |
| All <i>Streptococcus</i> species (includes <i>S. pneumoniae</i> , non-meningitis breakpoint) |        |      |      |             |           |           |      |      |    |       |       |       |
| CHALLENGE  | 200    | 199  | 99.5 | 76          | 76        | 100       | 191  | 95.5 | 15 | 0     | 1     | 8     |

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* (meningitis):  $\leq 0.5$ (S), 1 (I),  $\geq 2$  (R)

*S. pneumoniae* (non-meningitis):  $\leq 1$ (S), 2 (I),  $\geq 4$  (R)

Viridans group streptococci:  $\leq 1$ (S), 2 (I),  $\geq 4$  (R)

Beta hemolytic streptococci:  $\leq 0.5$ (S only)

**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.