

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

A. 510(k) Number:

k062687

B. Purpose for Submission:

To add additional organism groups to ticarcillin/clavulanate on the BD Phoenix™ gram-negative ID/AST or AST only Phoenix panels and to remove limitations for *Pseudomonas* species (spp.) and *Stenotrophomonas maltophilia*

C. Measurand:

Ticarcillin/clavulanate 1/2 – 128/2 µg/mL

D. Type of Test:

Antimicrobial Susceptibility Test (AST) colorimetric oxidation-reduction, growth-based

E. Applicant:

Becton, Dickinson & Company

F. Proprietary and Established Names:

BD Phoenix™ Automated Microbiology System – Ticarcillin 1/2 – 128/2 µg/mL

G. Regulatory Information:

1. Regulation section:
21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility 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):
Ticarcillin/clavulanate at 1/2 – 128/2 µg/mL on the Gram Negative (GN) ID/AST or AST only Phoenix panels is intended for use with the BD Phoenix Automated Microbiology System for *in vitro* quantitative determination of antimicrobial

susceptibility by minimal inhibitory concentration (MIC) of most Gram-negative aerobic and facultative anaerobic bacteria isolates from pure culture for *Enterobacteriaceae* and non – *Enterobacteriaceae* and most Gram-positive bacteria isolates from pure culture belonging to the genera *Staphylococcus*, *Enterococcus*, and *Streptococcus*.

2. Indication(s) for use:

This application is indicated for ticarcillin/clavulanate with additional organism groups and removal of the limitations for *Pseudomonas* species (spp.) and *Stenotrophomonas maltophilia* from the original premarket notification (k033557).

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Not Applicable

I. Device Description:

This submission is for AST Panel only. The ID System was not reviewed.

The BD Phoenix™ Automated Microbiology System includes instrumentation and software, sealed and self-inoculating molded polystyrene trays with 136 micro-wells containing dried reagents, and specific inoculum broth formulations for ID and AST Indicator. The organism to be tested must be a pure culture and be preliminarily identified as gram positive or gram negative. Colonies are then suspended in broth, and equated to a 0.5 McFarland with the recommendation to use the BD CrystalSpec™ Nephelometer. A further dilution is made into an AST broth, which contains an AST indicator, prior to inoculating the panel. The AST broth is a cation-adjusted formulation of Mueller-Hinton broth containing 0.01% Tween 80. After adding the indicator solution to the AST inoculum the color is blue and after inoculation and incubation changes to pink then to colorless as reduction in the panel well proceeds. Inoculated panels are barcode scanned and loaded into the BD Phoenix™ Automated Microbiology System instrument where the panels are continuously incubated at 35°C. The AST has a final inoculum of 5×10^5 CFU/ml. The instrument incubates, reads and records the results of the biochemical substrates and antimicrobial agents and interprets the reactions to give an ID of the isolate and MIC value and category interpretation of the antimicrobial agents. Organisms growing in the presence of a given antimicrobial agent reduce the indicator, signaling organism growth and resistance to the antimicrobial agent. Organisms killed or inhibited by a given antimicrobial do not cause reduction of the indicator and therefore do not produce a color change. Additional interpretation is done using software driven “EXPERT” System using rules derived from the CLSI documentation.

Readings are taken every 20 minutes with an AST result available between 4-16 hours. This is only an autoread result; no manual readings are possible with this system.

J. Substantial Equivalence Information:

1. Predicate device name(s):
VITEK® System
2. Predicate 510(k) number(s):
N50510
3. Comparison with predicate:

| Similarities | | |
|--------------------|---|---|
| Item | Device | Predicate |
| 1. Intended Use | Intended for the <i>in vitro</i> rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria. | Same |
| 2. Isolates | Isolated colonies from culture used | Isolated colonies from culture used |
| 3. Result Reported | Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR) | Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR) |
| 4. Incubation Time | <16 hours | <16 hours |
| 5. Type of Test | Automated | Automated |

| Differences | | |
|-----------------------|---|---|
| Item | Device | Predicate |
| 1. Results achieved | Results are determined from serial twofold dilutions of antimicrobial agents | Results are determined from extrapolation of doubling dilutions |
| 2. Sample Preparation | Inoculum density equated to 0.5 McFarland standard | Inoculum density equated to 1.0 McFarland standard |
| 3. Technology | Automated growth based enhanced by use of a redox indicator (colorimetric oxidation-reduction) to detect organism growth. | Automated growth based with detection using an attenuation of light measured by an optical scanner. |

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA”; CLSI M7 (M100-S16) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.”

L. Test Principle:

The AST portion of the BD Phoenix™ Automated Microbiology System is a broth based microdilution method that utilizes a redox indicator (colorimetric oxidation-reduction) to enhance detection of organism growth. The MIC is determined by comparing growth in wells containing serial two-fold dilutions of an antibiotic to the growth in “growth control wells” which contains no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

The data included in this submission were acquired during the clinical studies performed at multiple sites. The accuracy performance data for limitation removal and additional organism report groups for clinical and challenge isolates are contained in this submission. The Reproducibility study was performed in the previous submission (k033557) and was not performed for this submission because the drug formulation has not changed. The QC performance was within the expected ranges as shown under the “Traceability, Stability.... Section.”

a. Precision/Reproducibility:

Intersite and Intrasite testing demonstrated >95% reproducibility. The ten isolate study described in the guidance document was used (10 organisms tested 3 times on 3 days at 3 sites).

b. Linearity/assay reportable range:

Not applicable

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

Quality Control was performed on every test occasion with the following results. BD Phoenix™ produced acceptable QC results as compared to the reference method results >95% of the time.

Ticarcillin/Clavulanate QC Table

| ORGANISM | conc. (µg/mL) | Reference | BD Phoenix™ | | |
|--|--------------------------|------------------|--------------------|--|--|
| | | | | | |
| <i>E. cloacae</i> ATCC 11061 Expected Range: ≥64 µg/mL | 16 | | 1 | | |
| | 32 | | 1 | | |
| | 64 | 11 | 45 | | |
| | 128 | 35 | 19 | | |
| | >128 | 3 | 3 | | |
| | | | | | |
| <i>E. coli</i> ATCC 25922 Expected Range: 4 - 16 µg/mL | 2 | 6 | | | |
| | 4 | 23 | 6 | | |
| | 8 | 17 | 59 | | |
| | 16 | 1 | 4 | | |
| | | | | | |
| <i>E. coli</i> ATCC 35218 Expected Range: 8 – 32 µg/mL | 2 | 1 | 1 | | |
| | 4 | | | | |
| | 8 | 3 | | | |
| | 16 | 39 | 58 | | |
| | 32 | 6 | 9 | | |
| | 64 | | | | |
| | 128 | | 1 | | |
| | | | | | |
| <i>P. aeruginosa</i> ATCC 27853 Expected Range : 8 - 32 µg/mL | 4 | | 1 | | |
| | 8 | 1 | | | |
| | 16 | 37 | 66 | | |
| | 32 | 9 | 1 | | |
| | 64 | 1 | | | |
| | | | | | |

Inoculum density control: The organism suspension density of the ID broth was equivalent to a 0.5 McFarland standard using the BBL™ CrystalSpec™ Nephelometer which was verified each day of testing. Internal data was used to demonstrate that the use of the BBL™ CrystalSpec™ Nephelometer would produce reproducible results. Five different instruments were used.

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:*

The broth dilution reference panel was prepared according to the CLSI recommendation and used to compare with the BD Phoenix™ results. Clinical testing was performed at several sites. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. Performance chart below includes all data, original with additional organisms, *Pseudomonas* spp. including *P. aeruginosa*, and *Stenotrophomonas maltophilia*.

GN Accuracy Summary Clinical and Challenge with Truncations Applied, Limitations Removed, and Additional Organisms Included

| | EA Tot | EA N | EA % | Eval EA Tot | Eval EA N | Eval EA % | CA N | CA % | #R | min | maj | vmj |
|--|--------|------|------|-------------|-----------|-----------|------|------|-----|-----|-----|-----|
| Combined (Original Data, Additional Org including <i>Pseudomonas</i> spp., and <i>S. maltophilia</i>) | 2114 | 1966 | 93 | 1379 | 1273 | 92.3 | 1890 | 89.4 | 566 | 203 | 6 | 15 |

EA-Essential Agreement

CA-Category Agreement

R-resistant isolates

vmj – very major discrepancies

maj - major discrepancies

min – minor discrepancies

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

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:

| | |
|---------------------------------|-------------------------------|
| <i>Enterobacteriaceae</i> | ≤16 (S); 32 – 64 (I); ≥128(R) |
| <i>Pseudomonas aeruginosa</i> | ≤64 (S); ≥128(R) |
| Non – <i>Enterobacteriaceae</i> | ≤16 (S); 32 – 64 (I); ≥128(R) |

N. Proposed Labeling:

The expected value range, interpretive criteria and QC for gram negative panels are included in the package insert. 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.