

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

A. 510(k) Number:

k082538

B. Purpose for Submission:

Addition of the Phoenix Inducible Macrolide resistance (iMLSb) test to the BD Phoenix™ Automated Microbiology System

C. Measurand:

Inducible Macrolide resistance (iMLSb) test (Clindamycin/Erythromycin)

D. Type of Test:

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

E. Applicant:

Becton, Dickinson & Company

F. Proprietary and Established Names:

BD Phoenix™ Automated Microbiology System – Phoenix Inducible Macrolide resistance (iMLSb) in *Staphylococcus* species

G. Regulatory Information:

1. Regulation section:

21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System

2. Classification:

Class II

3. Product code:

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

4. Panel:

Microbiology

H. Intended Use:

1. Intended use(s):

The BD Phoenix™ Automated Microbiology System is intended for the *in vitro* rapid identification (ID) of gram positive bacteria from pure culture belonging to the genera *Staphylococcus*, *Enterococcus*, other gram positive *cocci* and gram positive bacilli. The BD Phoenix™ Automated Microbiology System is also intended for the quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most gram positive bacterial isolates from pure culture belonging to the genera *Staphylococcus* and *Enterococcus*.

2. Indication(s) for use:

This premarket notification is for the addition of the Phoenix Inducible Macrolide resistance (iMLSb) Test in *Staphylococcus* species to Gram-positive ID/AST or AST only Phoenix panels. The Phoenix Inducible Macrolide resistance Test is used to detect inducible macrolide-lincosamide-streptogramin B resistance in *Staphylococcus* species.

3. Special conditions for use statement(s):

Prescription use

Perform an alternate method when a positive result with Coagulase Negative *Staphylococcus* (CNS) specifically, *S. cohnii* ssp *cohnii*, *S. gallinarum*, and *S. hominis* and iMLSb is identified.

4. Special instrument requirements:

Not applicable

I. Device Description:

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 turns to blue. After inoculation and incubation, the color 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):

Sensititre® Dtest

2. Predicate K number(s):

k073653

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
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.	An <i>in vitro</i> diagnostic product for clinical susceptibility testing of gram negative and gram positive organisms.
Inoculum	Prepared from colonies using the direct inoculation method	Prepared from colonies using the direct inoculation method
Result Reported	Report results as minimum inhibitory concentration (MIC) and	Report results as minimum inhibitory concentration (MIC) and

Similarities		
Item	Device	Predicate
	categorical interpretation (SIR)	categorical interpretation (SIR)

Differences		
Item	Device	Predicate
Incubation	Rapid (<16 hours)	18-24 hours
Reading method	Automated	manually or automatically

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-S18) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.”

L. Test Principle:

The Phoenix Inducible Macrolide resistance (iMLSb) Test is used to detect inducible macrolide-lincosamide-streptogramin B (MLSb) resistance in *Staphylococcus* species. MLSb resistance, usually encoded by *ermA* or *ermC* genes, may be either constitutive (always expressed) or inducible after exposure to a macrolide antibiotic (e.g. erythromycin, clarithromycin, etc.). The Phoenix Inducible Macrolide Resistance Test is based on the same principle as the CLSI-recommended Disk Approximation test (D-Test) for the detection of inducible clindamycin resistance. When the Phoenix Inducible Macrolide Resistance Test result is positive, the categorical interpretation of clindamycin on the same Phoenix panel will be reported as resistant and accompanied by a separate BDxpert message. *Staphylococcus* isolates resistant to both erythromycin and clindamycin on initial testing will be reported as the MLSb phenotype to distinguish them from isolates that are resistant to macrolides alone by efflux mechanism.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility testing was performed on 10 *Staphylococcus* isolates. Acceptable reproducibility was demonstrated with only category agreement (Negative, Positive) since that is all that is detected.

b. *Linearity/assay reportable range:*

Not applicable

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

The CLSI recommended Quality Control (QC) isolates, *S. aureus* ATCC BAA-976 and *S. aureus* ATCC BAA-977 were tested on every test occasion with the reference method and the BD Phoenix™. The BD Phoenix™ was tested a sufficient number of times to demonstrate that the system can produce QC results in the recommended ranges.

Quality Control Table

ORGANISM	Conc ug/mL (Ery/Cli)	Reference	BD Phoenix™
<i>S. aureus</i> BAA-976	Neg	63	68
Expected Range: Neg	Pos	0	0
<i>S. aureus</i> BAA-977	Neg	2	1
Expected Range: Pos	Pos	60	68

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 CLSI recommended disk diffusion reference panel was prepared according to the CLSI recommendation. The disk diffusion reference panel was set up on a blood agar plate, inoculated with a direct colony suspension

and incubated in ambient air at 35°C for 16 – 18 hours as recommended by CLSI. Clinical testing was performed on 295 *Staphylococcus* species at three external sites which included fresh and stock clinical isolates, a set of challenge organisms, and CDC study isolates.

The Phoenix Inducible Macrolide resistance (iMLSb) Test is used to detect induction of clindamycin resistance by erythromycin. The test algorithm compares the growth rate observed in the test well to a predetermined threshold to determine the expression of the inducible resistance phenotype in the test isolate.

The comparison resulted in the following performance evaluations as reflected below. There are 3 maj errors with the CNS group, specifically *S. cohnii* ssp *cohnii*, *S. gallinarum*, and *S. hominis*.

Summary Table

	Total	CA	CA%	# Neg	# Pos	maj	vmj
<i>S. aureus</i>	214	210	98.1	94	120	1	3
<i>S. epidermidis</i>	39	39	100	23	16	0	0
Coagulase-negative <i>Staphylococcus</i> (CNS)	42	39	92.9	21	21	3	0

CA - Category Agreement

maj-major discrepancies

vmj-very major discrepancies

Category agreement (CA) is when the BD Phoenix™ panel result interpretation agrees exactly with the reference panel result interpretation.

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:

Staphylococcus species – Positive (inducible clindamycin resistance)
Negative (no inducible clindamycin resistance)

N. Proposed Labeling:

The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The information submitted in this premarket notification is complete and supports a substantial equivalence decision.