

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

A. 510(k) Number:

K133847

B. Purpose for Submission:

To obtain clearance for the addition of DTEST broth microdilution test for detection of inducible clindamycin resistance to the Sensititre *Haemophilus/Streptococcus pneumoniae* (HP) Susceptibility Plates.

C. Measurand:

Erythromycin 1µg/mL and clindamycin 0.5µg/mL

Positive (growth): Inducible resistance

Negative (no growth): No inducible resistance

D. Type of Test:

Quantitative Antimicrobial Susceptibility Test (AST) growth based

E. Applicant:

ThermoFisher Scientific

F. Proprietary and Established Names:

Sensititre *Haemophilus/Streptococcus pneumoniae* (HP) Susceptibility Plate with Dtest (containing erythromycin at 1 µg/mL and clindamycin at 0.5 µg/mL)

G. Regulatory Information:

1. Regulation section:

866.1640 Short Term Antimicrobial Susceptibility Test System

2. Classification:

II

3. Product code:

JWY – Manual reading of AST testing

LTT – Panels Test, Susceptibility, Antimicrobial

LTW – Susceptibility Test Cards, Antimicrobial

4. Panel:

83 Microbiology

H. Intended Use:

1. Intended use(s):

The Sensititre *Haemophilus influenzae*/*Streptococcus pneumoniae* (HP) MIC Susceptibility plate is an in vitro diagnostic product for clinical susceptibility testing of *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Streptococcus* species.

2. Indication(s) for use:

The Sensititre® *Haemophilus influenzae*/*Streptococcus pneumoniae* (HP) MIC Susceptibility Plates with Dtest (containing erythromycin at 1 µg/ml and clindamycin at 0.5 µg/ml) broth test for *Streptococcus pneumoniae* and *Streptococcus* spp.-β-Hemolytic Group is an in vitro diagnostic product for clinical susceptibility testing.

The Dtest for broth microdilution test is for manual read detection of inducible clindamycin resistance in *Streptococcus pyogenes* and *Streptococcus agalactiae* resistant to erythromycin (MICs ≥ 1 µg/mL) and susceptible or intermediate to clindamycin (MICs ≤ 0.25 µg/mL or 0.5 µg/mL), and to determine absence of inducible clindamycin resistance in *Streptococcus pneumoniae*. The performance of this test for the detection of inducible clindamycin resistance in isolates of *S. pneumoniae* has not been established.

With *S. pyogenes* and *S. agalactiae*, a Dtest (1/0.5 µg/mL) positive (growth) test, determined by manual read, should be reported as inducible clarithromycin resistance.

3. Special conditions for use statement(s):

Prescription use

4. Special instrument requirements:

AIM (Automated Inoculation Delivery System)

I. Device Description:

The Sensititre *Haemophilus influenzae/Streptococcus pneumoniae* (HP) susceptibility plates are *in vitro* diagnostic devices for clinical susceptibility testing of *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Streptococcus* species. Each plate is dosed with antimicrobial agents at appropriate dilutions. A standardized organism suspension is prepared in cation-adjusted Mueller-Hinton broth with TES buffer and lysed horse blood; 100 µL of the organism suspension is inoculated into the antibiotic-containing well. Plates are sealed and incubated at 34 - 36° C for 20 – 24 hours. Results for the Dtest are read manually by visual observation of growth using either the Vizion Reader or on a manual viewer.

Table 1. Interpretation of Results for Dtest

Organism	Negative for inducible clindamycin resistance	Positive for inducible clindamycin resistance
<i>S. pneumoniae</i>	No growth	N/A*
<i>S. pyogenes</i> and <i>S. agalactiae</i>	No growth	Growth

* N/A, not applicable. Due to an insufficient number of Dtest positive *S. pneumoniae* isolates tested, the ability of the device to detect Dtest positive *S. pneumoniae* has not been determined (See below).

J. Substantial Equivalence Information:

1. Predicate device name(s):

VITEK®2 Gram Positive Inducible Clindamycin Resistance

2. Predicate 510(k) number(s):

K111909

3. Comparison with predicate:

Table 2. Comparison with the Predicate Device

Similarities		
Item	Device Sensititre <i>Haemophilus influenzae/Streptococcus pneumoniae</i> (HP) MIC Susceptibility Plates, Dtest	Predicate VITEK®2 <i>Streptococcus Inducible Clindamycin Resistance</i> K111909
Intended Use	The Sensititre® <i>Haemophilus influenzae/Streptococcus pneumoniae</i> (HP) MIC Susceptibility Plates with	VITEK®2 Streptococcus Inducible Clindamycin Resistance is designed for antimicrobial susceptibility testing of Streptococcus

Similarities		
Item	Device Sensititre <i>Haemophilus influenzae</i>/Streptococcus pneumoniae (HP) MIC Susceptibility Plates, Dtest	Predicate VITEK®2 <i>Streptococcus Inducible Clindamycin Resistance</i> K111909
	<p>Dtest (containing erythromycin at 1 µg/ml and clindamycin at 0.5 µg/ml) broth test for <i>Streptococcus pneumoniae</i> and <i>Streptococcus</i> spp.-β-Hemolytic Group in an in vitro diagnostic product for clinical susceptibility testing.</p> <p>The Dtest for broth microdilution test is for manual read detection of inducible clindamycin resistance in <i>Streptococcus pyogenes</i> and <i>Streptococcus agalactiae</i> resistant to erythromycin (MICs ≥ 1 µg/mL) and susceptible or intermediate to clindamycin (MICs ≤ 0.25 µg/mL or 0.5 µg/mL), and to determine absence of inducible clindamycin resistance in <i>Streptococcus pneumoniae</i>. The performance of this test for the detection of inducible clindamycin resistance in isolates of <i>S. pneumoniae</i> has not been established.</p> <p>With <i>S. pyogenes</i> and <i>S. agalactiae</i>, a Dtest (1/0.5 µg/mL) positive (growth) test, determined by manual read, should be reported as inducible clarithromycin resistance.</p>	<p>agalactiae and <i>Streptococcus pyogenes</i>. VITEK®2 <i>Streptococcus Inducible Clindamycin Resistance</i> 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.</p>

Similarities		
Item	Device	Predicate
	Sensititre <i>Haemophilus influenzae</i>/Streptococcus pneumoniae (HP) MIC Susceptibility Plates, Dtest	VITEK®2 <i>Streptococcus Inducible Clindamycin Resistance</i> K111909
Antibiotics	Clindamycin 0.5 µg/mL and erythromycin 1.0 µg/mL	Clindamycin 0.5 µg/mL and Clindamycin/Erythromycin 0.25/0.5 µg/mL.
Technology	Broth microdilution (MIC) susceptibility test	Same
Specimen	Isolated colonies from pure culture	Same
Inoculum	Automated after preparation of standardized suspension	Same
Incubation Temperature	34-36° C	Same
Incubation Atmosphere	Ambient air	Same

Differences		
Item	Device	Predicate
Instrument	None	VITEK®2 and VITEK®2 Compact Systems
Test organisms	<i>Streptococcus agalactiae</i> <i>Streptococcus pyogenes</i> <i>Streptococcus pneumoniae</i>	<i>Streptococcus agalactiae</i> <i>Streptococcus pyogenes</i>
Incubation Time	20-24 hours	Up to 18 hours
Reading Method	Manual only	Autoread only

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

CLSI M07-A9, *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard*. 2012.

CLSI M100-S23, *Performance Standards for Antimicrobial Susceptibility Testing; Twenty Third Informational Supplement*. 2013.

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA, 2009.

L. Test Principle:

The Dtest is performed on isolates that are resistant to erythromycin (MICs $\geq 1\mu\text{g/mL}$) and susceptible (MICs $\leq 0.25\mu\text{g/mL}$) or intermediate (MIC of $0.5\mu\text{g/mL}$) to clindamycin. The

Dtest is performed in a single well containing 1.0 µg/mL of erythromycin and 0.5 µg/ml of clindamycin. After incubation results are interpreted by manual read. Growth appears as turbidity or as a deposit of cells at the bottom of the well. Growth in the well indicates the presence of inducible clindamycin resistance. No growth in the well indicates the absence of inducible clindamycin resistance.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Streptococcus species representing Dtest negative isolates of *S. pneumoniae*, and D test positive and negative isolates of *S. pyogenes* and *S. agalactiae* were tested once at each of three sites. Growth or no growth in the Dtest well was recorded, indicating inducible clindamycin resistance, or no inducible clindamycin resistance, respectively.

Reproducibility was 100% for all isolates at all test sites.

b. *Linearity/assay reportable range:*

N/A

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

The CLSI recommended quality control isolates *S. pneumoniae* ATCC 49619 (negative control) and *Staphylococcus aureus* BAA-977 (positive control) were tested a sufficient number of times using manual read; acceptable results were obtained for all tests. The Dtest quality control test results demonstrate that the device can provide the expected QC results when read manually.

Table 3. Results of Manual Reading of the QC isolates

QC Organism	Expected Result	Manual Read	
		No. Positive	No. Negative
<i>S. pneumoniae</i> ATCC 49619	negative	0	60
<i>S. aureus</i> ATCC BAA-977	positive	60	0

Due to a lack of positive quality control strain for the automated procedural option, the following limitation was included in the device labeling: “*Dtest results should be interpreted using manual read only. The ability of the Sensititre system to detect a positive Dtest by autoread cannot be confirmed due to the lack of Dtest positive quality control isolate for Autoread.*”

Growth Failure Rate: All isolates tested during the clinical testing grew in both the frozen reference panel and the dried Sensititre panels.

Inoculum density check: Inocula were prepared using comparison to a McFarland 0.5 turbidity standard. The inoculum density of the quality control organisms was determined each day of testing. A total of 90 inoculum density checks were performed; the average colony counts for each QC strain at each site were within the recommended range.

d. *Detection limit:*

N/A

e. *Analytical specificity:*

N/A

f. *Assay cut-off:*

N/A

2. Comparison studies:

a. *Method comparison with predicate device:*

The Sensititre Dtest results on the *Haemophilus influenzae*/*Streptococcus pneumoniae* (HP) susceptibility panels were compared to results obtained using a frozen broth microdilution test which was prepared according to CLSI M07-A9 guidelines. Testing was performed at three sites within the U.S. All isolates had recorded MIC results for erythromycin and clindamycin. Each isolate was tested using the Dtest wells on the Sensititre plate and the reference method. Reference panels were inoculated manually. Sensititre panels were inoculated using only the AIM autoinoculator. The following limitation was included in the device labeling, “*Studies were performed using the AIM. Performance with other inoculation methods was not determined.*”

A total of 270 clinical isolates were tested. The organisms consisted of 90 clinical isolates each of *S. pneumoniae*, *S. agalactiae* and *S. pyogenes* (Table 4).

A total of 88 challenge isolates were tested at two sites. The challenge strains included 12 isolates of *S. pneumoniae*, 39 isolates of *S. agalactiae* and 37 isolates of *S. pyogenes* (Table 4).

A total of 102 *S. pneumoniae* isolates were evaluated in this study. Of those, 99 were negative for inducible clindamycin resistance and agreement with the reference method was 100%. However of all *S. pneumoniae* isolates tested, only three were

positive for inducible clindamycin resistance (Tables 4 and 5). This was insufficient for determining the performance of this device to detect inducible clindamycin resistance with this species. The sponsor included the following limitation in the device labeling: “*The ability of the Sensititre system to detect Dtest positive S. pneumoniae isolates is unknown because Dtest positive strains were not tested at the time of comparative testing. Any S. pneumoniae isolate determined to be Dtest positive with the Sensititre system should be subjected to additional testing or submitted to a reference laboratory, if necessary.*”

For *S. agalactiae*, a total of 129 isolates were evaluated for inducible clindamycin resistance; of these, 29 showed inducible resistance. Agreement with the reference method was 100% for both the inducibly resistant and non-inducible strains (Table 5).

For *S. pyogenes*, a total of 127 isolates were evaluated for inducible clindamycin resistance; of these, 25 showed inducible resistance. Agreement with the reference method was 100% for both the inducibly resistant and non-inducible strains (Table 5).

Table 4. Isolates Tested

Organisms	Phenotype	No. Clinical	No. Challenge	Total
<i>S. pneumoniae</i>	Inducible	1	2	3
	Non-inducible	89	10	99
<i>S. agalactiae</i>	Inducible	8	21	29
	Non-inducible	82	18	100
<i>S. pyogenes</i>	Inducible	7	18	25
	Non-inducible	83	19	102

Table 5. Performance of Dtest with Manual Read

Organism	Total	CA	%CA	Neg	Pos	maj	vmj
<i>S. pneumoniae</i>	102	102	100	99	3 ^a	NA ^b	0
<i>S. agalactiae</i>	129	129	100	100	29	0	0
<i>S. pyogenes</i>	127	127	100	102	25	0	0

^a Due to an insufficient number of Dtest positive *S. pneumoniae* isolates tested, the ability of the device to detect Dtest positive *S. pneumoniae* has not been determined (See above).

^b Major discrepancy rate was not determined due to an insufficient number of Dtest positive *S. pneumoniae* isolates tested.

Abbreviations: CA, Category Agreement; Neg, Negative for inducible clindamycin resistance; Pos, Positive for inducible clindamycin resistance; maj, major discrepancies; vmj, very major discrepancies; NA, Not applicable.

b. Matrix comparison:

N/A

3. Clinical studies

a. Clinical Sensitivity:

N/A

b. Clinical specificity:

N/A

c. Other clinical supportive data (when a. and b. are not applicable):

N/A

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

Growth in Dtest well – Positive for inducible clindamycin resistance

No growth in Dtest well – Negative for inducible clindamycin resistance

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.