510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K172109

B. Purpose for Submission:

To obtain a substantial equivalence determination for the Liofilchem MIC Test Strip (MTS) containing Erythromycin at concentrations of 0.016 -256 µg/mL for susceptibility testing of *Staphylococcus aureus*

C. Measurand:

Erythromycin 0.016-256 µg/mL

D. Type of Test:

Quantitative AST growth based detection

E. Applicant:

Liofilchem s.r.l.

F. Proprietary and Established Names:

Liofilchem MIC Test Strip (MTS), Erythromycin 0.016-256 µg/mL

G. Regulatory Information:

1. Regulation section:

   866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

   II

3. Product code:

   JWY - Manual Antimicrobial Test Systems

4. Panel:

   83 – Microbiology

H. Intended Use:

1. Intended use(s):

   The Liofilchem MIC Test Strip (MTS) is a quantitative method intended for the *in vitro* determination of antimicrobial susceptibility of bacteria. MTS consists of specialized paper impregnated with a pre-defined concentration gradient of an antimicrobial agent, which is used to determine the minimum inhibitory concentration (MIC) in µg/mL of antimicrobial agents against bacteria as tested on agar media using overnight incubation and manual reading procedures.

   The Erythromycin MTS at concentrations of 0.016-256 µg/mL should be interpreted at 16-20 hours of incubation

   Erythromycin has been shown to be active both clinically and *in vitro* against the non-fastidious bacteria listed below according to the FDA label:
   Staphylococcus aureus

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   For prescription use

4. Special instrument requirements:

   Manual reading only

I. Device Description:

The Erythromycin MIC Test Strip (MTS) consists of specialized paper impregnated with a predefined concentration gradient of Erythromycin across 15 two-fold dilutions like those of a conventional MIC method. One side of the strip is labelled with the Erythromycin code (E) and the MIC reading scale in µg/mL. When the MIC Test Strip is applied onto an inoculated agar surface, the preformed exponential gradient of antimicrobial agent is immediately transferred to the agar matrix. After 16- 20 hours incubation, a symmetrical inhibition ellipse centered along the strip is formed. The MIC is read directly from the scale in terms of µg/mL at the point where the edge of the inhibition ellipse intersects the MIC Test Strip. Since MTS strip generates MIC values which fall between two-fold dilutions for interpretation, the MIC value read is recorded to the next two-fold dilution value.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Liofilchem MTS, vancomycin

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

   K153687

3. Comparison with predicate:

Table 1: Comparison with the Predicate Device

Similarities		
Item	Device (K172109)	Predicate Liofilchem MTS, vancomycin (K153687)
Intended Use	Quantitative susceptibility to antimicrobial agents	Same
Media	Mueller Hinton agar	Same
Inoculation	Isolated colonies from culture in suspension equivalent to 0.5 McFarland. Inoculum is applied manually using the manual plate inoculation method or plate rotator for even distribution of inoculum	Same
Reading	Manual; the point where the edge of inhibition ellipse intersects the MIC Test Strip	Same
Result	MIC	Same

Differences		
Item	Device	Predicate
Antibiotic	Erythromycin (E)	Vancomycin (VA)
Incubation	35 ± 2°C for 16 – 20 hours	35 ± 2°C for 24 hours

K. Standard/Guidance Document Referenced:

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

CLSI M07-A10 "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard, Tenth Edition January 2015"

CLSI M100-S26 "Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fifth Informational Supplement, January 2016"

L. Test Principle:

MTS are made of specialized paper impregnated with a predefined concentration gradient of antibiotic, across 15 two-fold dilutions like those of a conventional MIC method. When the MIC Test Strip is applied onto an inoculated agar surface, the preformed exponential gradient of antimicrobial agent is immediately transferred to the agar matrix. After 16-20 hours incubation, a symmetrical inhibition ellipse centered along the strip is formed. The MIC is read directly from the scale in terms of μg/mL at the point where the edge of the inhibition ellipse intersects the strip MIC Test Strip.

Growth along the entire gradient (i.e., no inhibition ellipse) indicates that the MIC value is greater than or equal to (≥) the highest value on the scale. An inhibition ellipse that intersects below the lower end of the scale is read as less than (<) the lowest value. An MIC of 0.125 μg/mL is considered to be the same as 0.12 μg/mL for reporting purposes.

An MTS MIC value which falls between standard two-fold dilutions must be rounded up to the next standard upper two-fold value before categorization.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility testing was performed using ten *Staphylococcus aureus* isolates. These ten isolates (5 MSSA and 5 MRSA) were tested at three sites in triplicates on three days. The mode of MIC value was determined and the reproducibility was calculated based on the number of MIC values that fell within ±1 doubling dilution of the mode. The testing resulted in overall reproducibility of greater than 95%. The results were acceptable.

b. Linearity/assay reportable range:

Not applicable

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

The recommended QC isolates were tested a sufficient number of times (i.e., at least 20/site) at all three sites with acceptable results in comparison to the reference method. All results were within the expected range greater than 95% of the time. The results are summarized in Table 2.

Table 2: Erythromycin MTS QC results

Organism	Concentration (µg/mL)	Reference	MTS
S. aureus ATCC 29213 Expected Result 0.25- 1µg/mL	0.12	1	
	0.25	17	39
	0.5	43	22
	1		
	2		
E. faecalis ATCC 29212 Expected Result 1- 4µg/mL	0.5		
	1	27	2
	2	30	27
	4	4	30
	8		2

The inoculum was prepared to achieve a 0.5 McFarland standard turbidity. Colony counts were performed periodically at each site. Inoculum density checks were performed and the average colony counts of each QC strain were within the recommended range of approximately 1x 10^8 CFU/mL.

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:

Clinical testing was conducted at three sites (two U.S. sites and one site outside the U.S). A total of 353 *Staphylococcus aureus* isolates were tested. There were 252 (71.4%) isolates that were tested within seven days of collection and 101 (28.6%) isolates that were tested after 7 days but within one year of collection. The 353 clinical isolates included 201 MSSA and 152 MRSA. An additional 75 challenge *Staphylococcus aureus* (11 MSSA and 64 MRSA) were tested, resulting in a total of 428 clinical and challenge isolates.

Results obtained with Liofilchem MIC Test Strip (MTS) with Erythromycin were compared to results obtained from frozen reference MIC panels. Reference panels were prepared and interpreted as outlined in CLSI recommendations in M7-A10.

Isolated colonies from an overnight blood agar plate were suspended in saline to achieve a 0.5 McFarland standard turbidity (approximately 10^8 CFU/mL). Testing conditions consisted of incubation of the inoculated Mueller Hinton agar plates in and inverted position at 35°C ±2 for 16-20 hours. At the end of incubation, the MIC value where the edge of the inhibition ellipse intersects the strip was compared to the reference method. Erythromycin is bacteriostatic; MIC is read at 80% inhibition when trailing is seen. The performance is listed in Table 3 below.

Table 3: Performance of *Staphylococcus aureus* isolates*

Erythromycin	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#R	min	maj	vmj
	***Staphylococcus* spp. ≤0.5 (Susceptible), 1-4 (Intermediate), ≥8 (Resistant)**											
Clinical	353	332	94.1	234	219	93.6	342	96.7	196	11	0	0
Challenge	75	74	98.7	33	32	97.0	74	98.7	61	1	0	0
Total	**428**	**406**	**94.9**	**267**	**251**	**94.0**	**416**	**97.2**	**257**	**12**	**0**	**0**

***EA -** Essential Agreement
CA - Category Agreement
R- resistant isolates
maj – major discrepancies
vmj- very major discrepancies
min- minor discrepancies

Essential Agreement (EA) is when the Liofilchem MIC Test Strip (MTS) results agree exactly or within one doubling dilution of the reference broth microdilution results. Category Agreement (CA) is when the Liofilchem MIC Test Strip (MTS) result interpretation agrees exactly with the reference broth microdilution result interpretation.

The overall performance of *Staphylococcus aureus* was acceptable with 94.9% EA and 97.2% CA. There were twelve minor discrepancies but no major or very major discrepancies.

Growth Rate:
The growth rate for the Liofilchem MIC Test Strip (MTS) with Erythromycin was 100%.

Trending

The analysis showed that there was no trending observed in the overall performance of *Staphylococcus aureus.*

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:

Table 5: FDA Interpretive Criteria for Erythromycin (µg/mL)

Organisms	S	I	R
Staphylococcus aureus	≤0.5	1-4	≥8

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.