Liofilchem® MTS™

Rx only IVD

SUMMARY AND EXPLANATION OF THE TEST

The Liofilchem® MTS™ (MIC Test Strip) are gradient tests used to determine the minimum inhibitory concentration (MIC) of select bacteria to indicate appropriate patient treatment and for identifying resistance patterns. The MIC is the minimum inhibitory concentration of an antibiotic that will inhibit the growth of bacteria under standardized *in vitro* conditions. Broth and agar dilution MIC procedures based on two-fold serial dilutions of antibiotics are the reference methodologies; expected reproducibility of which is within ± 1 two-fold dilution ([1]).

PRINCIPLE OF THE METHOD

MTS™ are made of special high quality paper impregnated with a predefined concentration gradient of antibiotic, across 15 two-fold dilutions like those of a conventional MIC method. When the MTS™ is applied onto an inoculated agar surface, the preformed exponential gradient of antimicrobial agent diffuses into the agar for over an hour. After 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 MTS™.

REAGENTS

MTS™ is supplied in 3 different packaging options (no additional reagents are included):

- The 10-test box contains 10 strips individually packed in desiccant envelops and an instruction sheet.
- The 30-test box contains 30 strips individually packed in desiccant envelops and an instruction sheet.
- The 100-test box contains 10 desiccant envelops, each containing 10 strips, and an instruction sheet. The 100-test pack also contains a storage tube.

DIRECTIONS FOR USE

Storage

Unopened foil packages: On receipt, store MTS™ at –20°C to +8°C until the given expiry date. Some MTS™ (e.g. carbapenems) should be stored frozen at –20°C. Check the drug-specific MTS™ supplement for the specific storage temperature.

Opened foil packages: Leftover MTS™ from an opened foil package (valid for 100 strip pack only, as the 10 and 30 strip packs contain individually packed strips) must be stored at 2-8°C in the airtight tube, containing desiccant, provided in the pack for no more than 7 days. Do not store near sources of heat and do not expose to excessive temperature variations.

Handling

Before using the MTS™ from an unopened package, visually inspect to ensure the package is intact. Do not use the strips if the package has been damaged. When removed from the refrigerator, allow the package or storage container to reach room temperature for about 30 minutes. Moisture condensing on the outer surface must evaporate completely before opening the package.

Precautions

The MTS™ is not classified as being hazardous according to current regulations but fall within the specific field of application where a safety data sheet must be supplied because they can cause phenomena of sensitization in sensitive subjects if they come into contact with the skin. The MTS™ is a disposable product. The MTS™ is only for diagnostic *in vitro* use and is intended for professional use. They must be used in the laboratory by properly trained operators using approved aseptic and safety methods for pathogenic agents.

Materials Required but Not Provided:

- Agar plate medium (validated by the media manufacturer for use with antimicrobial susceptibility testing, 90 or 150 mm plates)
- Suspension medium
- McFarland turbidity standard

  (The medium to be used as well as the inoculum suspension will depend on the organism under investigation, see the MTS™ Supplement for more information)
- Sterile loops, swabs (not too tightly spun), test tubes, pipettes and scissors
- Forceps
- Incubator (35 ± 2°C)
- Quality control organisms
- Additional technical information from **www.liofilchem.com**

Inoculum Preparation

Suspend well-isolated colonies from an overnight agar plate into the suspension medium to achieve the turbidity of the recommended McFarland standard. If the inoculum concentration is correct, a confluent lawn of growth will be obtained after incubation. If insufficient growth occurs, the testing should be repeated. In order to verify that your procedure gives the correct inoculum density in terms of CFU/mL (a 0.5 McFarland approximately corresponds to 1-2 x 10^8 CFU/mL for *E. coli*) performing regular colony counts is recommended.

Inoculation

Dip a sterile swab in the broth culture or in a diluted form thereof and squeeze it on the wall of the test tube to eliminate excess liquid. Streak the swab over the entire sterile agar surface. Repeat this procedure by streaking 2 more times, rotating the plate approximately 60 degrees each time to ensure an even distribution of inoculum. Allow excess moisture to be absorbed so that the surface is completely dry before applying MTS™.

Application

Apply the strip to the agar surface with the scale facing upwards and code of the strip to the outside of the plate, pressing it with a sterile forceps on the surface of the agar and ensure that whole length of the antibiotic gradient is in complete contact with the agar surface. Once applied, do not move the strip.

Incubation

Incubate the agar plates in an inverted position at the appropriate temperature, atmosphere and time. Refer to the drug-specific MTS™ Supplement for specific incubation instructions.

Eliminating Used Material

After use, MTS™ and the material that comes into contact with the sample must be decontaminated and disposed of in accordance with current laboratory techniques for the decontamination and disposal of potentially infected material.

Reading the MIC
Observe where the relevant inhibition ellipse intersects the strip and read the MIC at complete inhibition (unless otherwise instructed in the drug-specific MTS™ Supplement). Growth along the entire gradient i.e. no inhibition ellipse indicates that the 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 the same as 0.12 µg/mL for reporting purposes. See the appropriate MTS™ product supplements for example specific drug/organism photographs. Also consult the MTS™ Photographic Guide.

Result Interpretation
To categorize the result according to the interpretive criteria, refer to the appropriate MTS™ product supplement for the specific antimicrobial agent interpretive criteria. Since MTS™ generates MIC values which fall between two-fold dilutions for interpretation, 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. For example a *S. aureus* vancomycin MIC of 1.5 µg/mL is reported as 2 µg/mL.

QUALITY CONTROL
To check the performance of the MTS™ result, test the quality control strain(s) as shown in the appropriate MTS™ product supplement. Patient isolate results are considered satisfactory if the quality control result(s) fall within the expected range(s). Patient isolate results should not be reported if the quality control results are outside of this stated QC range. MIC results for a QC strain that fall a half dilution below the lower QC limit should be rounded up to the next upper two-fold value which would establish QC compliance. MIC results that are a half dilution above the upper limit would be rounded up to the next upper two fold value which would result in non-QC compliance.

LIMITATIONS
Refer to the drug-specific MTS™ Supplement.

EXPECTED VALUES
Expected results for susceptibility tests will vary based on location and institution. Organism resistance patterns will be directly related to the population of organisms at each site.

PERFORMANCE CHARACTERISTICS
Refer to the drug specific MTS™ Supplement.

REFERENCES
1. CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.

GLOSSARY OF TERMS

	Do not reuse		Batch code		Manufacturer		*In vitro* diagnostic medical device
	Use by		Catalog number		Contains sufficient for <n> tests		Temperature limitation

	Upper limit of temperature
	Consult instructions for use

MTS™ (MIC Test Strip), International Patent

For all inquiries please fill out the form at https://www.liofilchem.com/en-us/contacts.html

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Drug Specific Supplement for MTS™ Eravacycline

Rx only IVD

Indications for Use/Intended Use

The Liofilchem® MTS™(MIC Test Strip) Eravacycline 0.002-32 µg/mL 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 MTS™ Eravacycline at concentrations of 0.002 – 32 µg/mL should be interpreted at 16-20 hours of incubation.

MTS™ ERV can be used to determine the MIC of eravacycline against the microorganisms listed in the table below:

Eravacycline Activity According to the FDA Drug Approve Label		
Clinical and *in vitro*		***in vitro* only**
Gram-positive bacteria	**Gram-negative bacteria**	**Non-fastidious bacteria**
Enterococcus faecalis *Enterococcus faecium* *Staphylococcus aureus*	*Citrobacter freundii* *Enterobacter cloacae* *Escherichia coli* *Klebsiella oxytoca* *Klebsiella pneumoniae*	*Citrobacter koseri* *Klebsiella (Enterobacter) aerogenes*

Specifications

Antibiotic code: ERV
MIC range: 0.002-32 µg/mL
Antibiotic group: Fluorocycline

Directions for Use

Follow the MTS™ package insert instructions.

Procedures specific to MTS™ Eravacycline:

Storage	Temperature between –20°C and +8°C
Organism	*Enterobacteriaceae, E. faecalis, E. faecium, S. aureus*
Medium	Mueller Hinton Agar
Inoculum	Suspension in saline (0.85% NaCl) to 0.5 McFarland standard
Incubation	Agar plates in inverted position at 35 ± 2°C for 16-20 hours in ambient atmosphere
Reading	Interpret the MIC as 80% inhibition when trailing is seen

FDA eravacycline interpretive criteria (µg/mL)

Use the following breakpoints to categorize the result according to the interpretive criteria (i.e. susceptible or resistant). 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. For example a *K. pneumoniae* eravacycline MIC of 0.19 µg/mL is reported as 0.25 µg/mL (see reading guide for example pictures).

Bacterial Species	Susceptible	Non-susceptible
Enterobacteriaceae	≤0.5	≥1
Enterococcus faecalis	≤0.06	≥0.12
Enterococcus faecium	≤0.06	≥0.12
Staphylococcus aureus	≤0.06	≥0.12

US FDA Ref: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211109lbl.pdf

Quality Control range (µg/mL) (CLSI M100S Performance Standards for Antimicrobial Susceptibility Testing, 28th Edition)

To check the performance of the MTS™ Eravacycline, media and procedure, test ***E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 for Gram-negative bacteria** and test ***E. faecalis* ATCC 29212 and *S. aureus* ATCC 29213 for Gram-positive bacteria** according to the method as outlined in the MTS™ package insert. Results are considered satisfactory if they fall within the following ranges:

Quality Control Strain	Acceptable MIC Range (µg/mL)
Escherichia coli, ATCC® 25922	0.03 – 0.12
Pseudomonas aeruginosa, ATCC® 27853	2 – 16
Enterococcus faecalis, ATCC® 29212	0.016 – 0.06
Staphylococcus aureus, ATCC® 29213	0.016 – 0.12

Performance Characteristics

Correlation to Reference Method[1]

	N	% Essential Agreement	% Category Agreement
Enterobacteriaceae	426	99.5	97.4
Enterococcus faecalis	134	94.0	99.3
Enterococcus faecium [2]	154	90.3	99.4
Staphylococcus aureus [2]	240	93.8	100

[1] For the plate inoculation procedure, one testing site utilized a plate rotator (Retro C80) to assist even distribution of inoculum. There was no difference in performance for the site using the plate rotator as compared to sites using the manual plate inoculation method.

[2] MTS™ Eravacycline MIC values tend to be in exact agreement or at least one double dilution lower when testing *S. aureus* (MRSA and MSSA) and *E. faecium* (VRE and VSE) compared to the CLSI reference broth microdilution.

Reproducibility

100% of MTS™ Eravacycline results for non-fastidious Gram-negative bacteria (3 *E. coli*, 3 *K. pneumoniae*, 2 *E. cloacae*, 1 *K. oxytoca* and 1 *C. freundii* tested in triplicate at 3 sites on 3 days) were within a doubling dilution of reference broth microdilution results. 98.9% of MTS™ Eravacycline results for non-fastidious Gram-positive bacteria (4 *S. aureus*, 3 *E. faecalis* and 3 *E. faecium* tested in triplicate at 3 sites on 3 days) were within a doubling dilution of reference broth microdilution results.

Limitations

The ability of MTS™ to detect non-susceptible isolates with the following drug/bacterial species combinations is unknown because resistant isolates were either not available or an insufficient number was encountered at the time of comparative testing:

Eravacycline: *Citrobacter koseri*.

Resistance mechanism characterization was not available for all organisms at the time of comparative testing, and therefore the performance of the MTS™ Eravacycline for non-fastidious Gram-negative bacilli and Gram-positive cocci is unknown for the following: *Enterobacteriaceae* [tet(B)]; *Enterococcus* species [tet(K)].

Due to the lack of an intermediate category for eravacycline, testing of *K. pneumoniae* and *E. cloacae* has resulted in 6 very major errors that are otherwise within essential agreement of the reference method. Given this, the very major error rate of 9.3% (7/75) is adjusted to 1.3% (1/75) if calculated to exclude the errors that are within essential agreement. If critical to patient care, testing should be repeated using an alternative testing/reference method prior to reporting results when the MTS™ Eravacycline is 0.5 µg/mL for *K. pneumoniae* and *E. cloacae*.

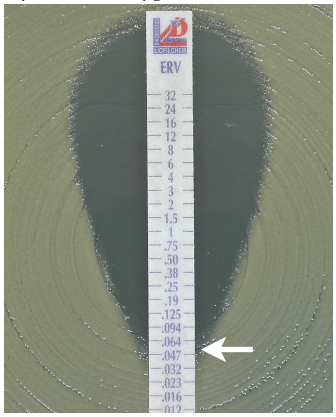
A trend towards lower MIC readings was observed in the overall performance of *S. aureus* and *E. faecium*, although no very major errors were reported. However, due to the lack of an intermediate category for eravacycline and the observed trending, there is a concern for the potential of very major errors. If critical to patient care, testing should be repeated using an alternative testing/reference method prior to reporting results for *S. aureus* and *E. faecium*, when the MTS™ Eravacycline is 0.06 µg/mL.

The safety and efficacy of eravacycline in treating clinical infections due to Gram-negative organisms other than *C. freundii, E. cloacae, E. coli, K. oxytoca* and *K. pneumoniae* and Gram-positive organisms other than *S. aureus, E. faecalis* and *E. faecium*, may not have been established in adequate and well-controlled clinical trials. The clinical significance of susceptibility information in such instances is unknown.

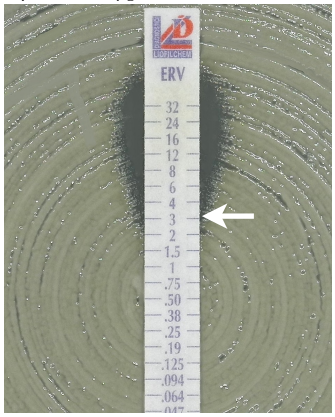
MTS™ Eravacycline Reading Guide

Note: Interpret the MIC as 80% inhibition

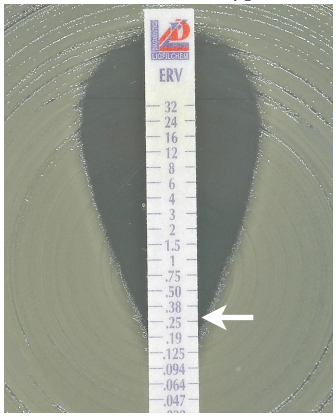
Example 1:
E. coli, ERV MIC = 0.047 µg/mL,
reported as 0.06 µg/mL



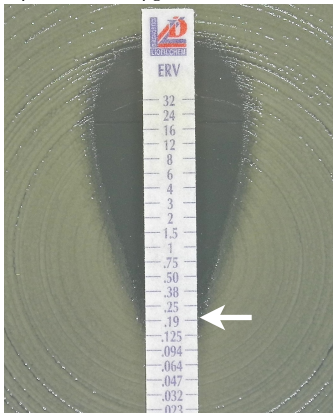
Example 2:
K. pneumoniae, ERV MIC = 3 µg/mL,
reported as 4 µg/mL



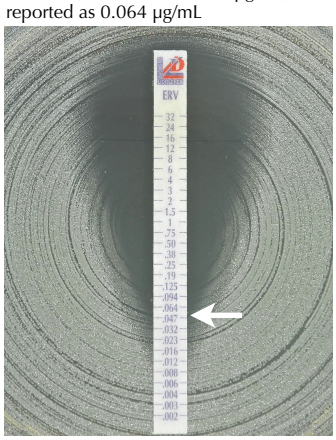
Example 3:
E. cloacae, ERV MIC = 0.25 µg/mL



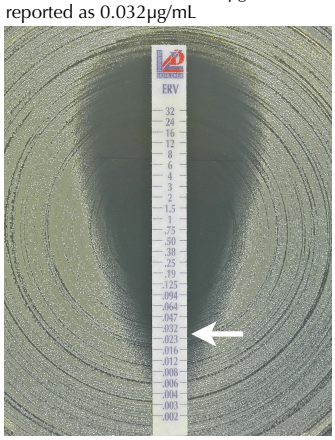
Example 4:
C. freundii, ERV MIC = 0.19 µg/mL,
reported as 0.25 µg/mL



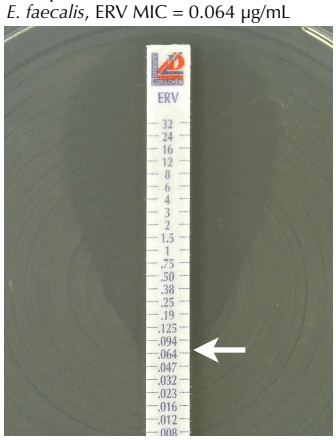
Example 5:
S. aureus, ERV MIC = 0.047 µg/mL,
reported as 0.064 µg/mL



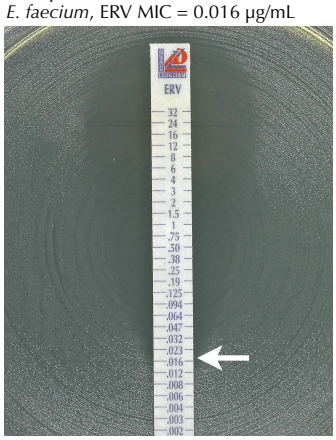
Example 6:
S. *aureus*, ERV MIC = 0.023 µg/mL,
reported as 0.032µg/mL



Example 7:
E. faecalis, ERV MIC = 0.064 µg/mL



Example 8:
E. faecium, ERV MIC = 0.016 µg/mL



PRESENTATION		µg/mL	Code	Packaging	Ref.
MTS™	Eravacycline	0.002 - 32	ERV	10 30 100	921041 92104 921040

MTS™ (MIC Test Strip), International Patent

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