# 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 by manual methods, 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 manually 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.
- The 30-test box contains 30 strips individually packed in desiccant envelops.
- The 100-test box contains 100 strips in a canister with a desiccant built into the lid.

This instruction sheet is available from **www.liofilchem.com/MTS/US**

## DIRECTIONS FOR USE

### Storage

Unopened foil packages and canisters: 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 canisters: MTS™ in canister can be used for up to 2 months from first opening (record the date on which the canister was open) and must be stored at the label storage temperature. Before using the remaining strips, check the expiry date indicated on the packaging. Do not store near sources of heat and do not expose to excessive temperature variations.

Protect MTS™ from moisture, heat and direct exposure to strong light at all times.

### 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/freezer, 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. Use forceps or a similar device to pick up a strip.

When using MTS™ from a canister, replace the lid immediately after use and store as outlined under STORAGE.

### Precautions

The MTS™ is not classified as being hazardous according to current regulations. 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.

Per the FDA-Recognized Susceptibility Test Interpretive Criteria website, the safety and efficacy of antimicrobial drugs, for which antimicrobial susceptibility is tested by this AST device, may or may not have been established in adequate and well-controlled clinical trials for treating clinical infections due to microorganisms outside of those found in the indications and usage in the drug label. The clinical significance of susceptibility information in those instances is unknown. The approved labeling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved.

### 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.

McFarland turbidity standards do not guarantee the correct number of viable cells in the suspension. In order to verify that your procedure gives the correct inoculum density in terms of CFU/mL performing regular colony counts is recommended. An acceptable inoculum should give approximately 1-2 x $10^8$ CFU/mL.

**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™.

Use well-defined, high quality media for AST that supports good growth. The brand chosen should have good batch-to-batch reproducibility to ensure that accurate and reliable MIC values are obtained.

The agar medium should have a depth of 4.0 ± 0.5 mm, a pH of 7.3 ± 0.1 and all other quality specifications should be fulfilled. Refer to the media manufacturer's instructions for more information.

**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 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.

**Reading the MIC**
After the required incubation period, and only when an even lawn of growth is distinctly visible, read the MIC value where the relevant inhibition ellipse intersects the strip. Do not read the plate if the culture appears mixed or if the lawn of growth is too light or too heavy.

**NOTES:**

- Antimicrobial drugs can be either "-static" (e.g. bacteriostatic, fungistatic) or "-cidal" in their interactions with target organisms and this needs to be considered for determining correctly the MIC endpoint. For bactericidal drugs, e.g. beta-lactams, read the MIC at the point of complete inhibition of all growth. Haze and macrocolonies or microcolonies within 3 mm from the strip should be read as growth. For bacteriostatic drugs, e.g. trimethoprim-sulfamethoxazole, in case of trailing endpoints, read at 80% inhibition, i.e. the first point of significant inhibition as judged by the naked eye. Consult MTS30 (cidal-static technical sheet) for more information.
- 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. Intersection between two scale segments should be rounded up to the higher value. An MIC of 0.125 µg/mL is considered the same as 0.12 µg/mL for reporting purposes. See the appropriate MTS™ technical sheets for example specific drug-organism photographs. Also consult the MTS™ Photographic Guide.
- Excessively wet plates prior to inoculation, insufficient drying before applying strips and/or unevenly streaked surfaces may give non confluent growth or jagged ellipse edges. Repeat the test if MIC endpoints are difficult to read. In the case of uneven MIC intersections, read the higher value. Repeat the test if the discrepancy is >1 dilution.
- Occasionally, certain antimicrobial agent/microorganism combinations may give unusual results. In these cases, judgment of the MIC endpoint may be difficult for the inexperienced personnel. However, individuals can be trained through regular use of quality control strains , MTS™ reading guides and comparison with experienced personnel to correctly assess MIC endpoints.

**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.

**NOTES**:

- As with all AST data, MTS™ results are *in vitro* values only and may provide an indication of the organism's potential *in vivo* susceptibility. The use of results to guide therapy selection must be the sole decision and responsibility of the attending physician. Their judgement should be based on the medical history and knowledge of the patient, pharmacokinetics/pharmacodynamics of the antimicrobial agent, and clinical experience in treating infections caused by the particular microbial pathogen. The drug, dose and dosing regimen must also be considered.
- For details of specific interpretive limitations and/or limitations on the clinical use of an antimicrobial agent in various therapeutic situations, please refer to the tables and footnotes of MIC interpretive standards in the latest CLSI documents.

**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.

## 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*. 12th ed. CLSI standard M07. Wayne, PA: Clinical and Laboratory Standards Institute; 2024.

## GLOSSARY OF TERMS

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
|  | Do not reuse | LOT | Batch code |  | Manufacturer | IVD | *In vitro* diagnostic medical device |  | Upper limit of temperature |
|  | Use by | REF | Catalog number |  | Contains sufficient for <n> tests |  | Temperature limitation |  | Consult instructions for use |

# Drug Specific Supplement for MTS™ Ceftobiprole

Rx only IVD

## Indications for Use/Intended Use

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

MTS™ BPR can be used to determine the MIC of ceftobiprole against the following microorganisms for which ceftobiprole has been shown to be active both clinically and/or *in vitro* according to the FDA drug approved label:

*Escherichia coli*
*Klebsiella pneumoniae*
*Staphylococcus aureus* (includes methicillin resistant isolates)

## Specifications

Antibiotic code: BPR
MIC range: 0.002-32 µg/mL
Antibiotic group: Cephem

## Directions for Use

Follow the MTS™ package insert instructions.

Procedures specific to MTS™ Ceftobiprole:

| | |
|---|---|
| **Storage** | Temperature between –20°C and +8°C |
| **Organism** | *Enterobacterlaes, S. aureus* |
| **Medium** | Mueller Hinton Agar |
| **Inoculum** | Suspension in saline (0.85% NaCl) to 0.5 McFarland standard (1 if mucoid) |
| **Incubation** | Agar plates in inverted position at 35 ± 2°C for 16-20 hours in ambient atmosphere |
| **Reading** | Interpret the MIC as 100% inhibition |

## FDA ceftobiprole 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* ceftobiprole MIC of 0.047 µg/mL is reported as 0.06 µg/mL (see reading guide section for example pictures).

| Bacterial Species | Susceptible | Intermediate | Resistant |
|---|---|---|---|
| *Enterobacterales* | ≤0.25 | 0.5 | ≥1 |
| *Staphylococcus aureus* (includes methicillin resistant isolates) | ≤2 | 4 | ≥8 |

**US FDA Susceptibility Interpretive Criteria (STIC) Ref:**
**https://www.fda.gov/STIC**

## Quality Control range (µg/mL) (CLSI M100S Performance Standards for Antimicrobial Susceptibility Testing, 35ed Edition)

To check the performance of the MTS™ ceftobiprole, media and procedure, test ***E. coli* ATCC 25922 or S. *aureus* ATCC 29213** 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 [a] | Acceptable MIC Range (µg/mL) |
|---|---|
| *Escherichia coli,* ATCC® 25922 | 0.03 – 0.12 |
| *Staphylococcus aureus,* ATCC® 29213 | 0.12 – 1 |

[a] Strains recommended for routine QC with ceftobiprole by CLSI M100Ed35.

## Performance Characteristics

Correlation to Reference Method

| | N | % Essential Agreement | % Category Agreement |
|---|---|---|---|
| *Enterobacterales* | 364 | 98.6 | 98.9 |
| *Stapylococcus aureus* [1,2] | 431 | 98.8 | 88.9 |

1 MTS™ Ceftobiprole MIC values tended to be in exact agreement or at least one doubling dilution higher when testing *S. aureus* compared to the CLSI reference broth microdilution.

2 The Category Agreement was <90% for *S. aureus*. The performance is acceptable since the Essential Agreement was >90% and all categorical errors were minor errors.

Reproducibility

99.6% of MTS™ Ceftobiprole results for non-fastidious Gram-negative bacteria (5 *E. coli*, 5 *K. pneumoniae* tested in triplicate at 3 sites on 3 days) were within a doubling dilution of reference broth microdilution results. 100% of MTS™ Ceftobiprole results for Staphylococcus aureus (5 methicillin susceptible, 5 methicillin resistant tested in triplicate at 3 sites on 3 days) were within a doubling dilution of reference broth microdilution results.

Limitations

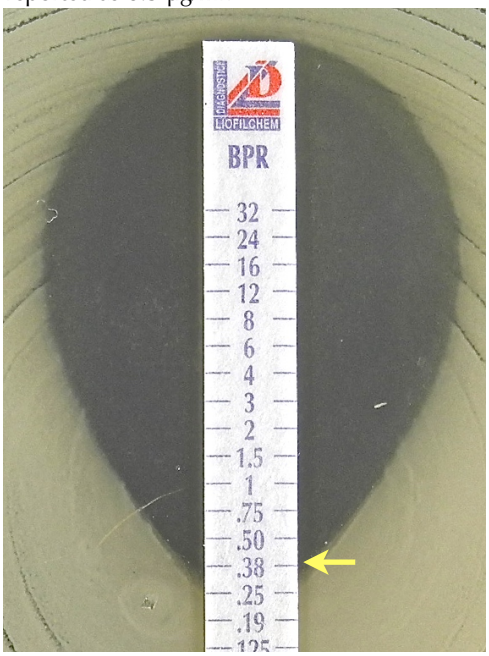
The ability of the MTS™ to detect resistance or non-susceptibility to antimicrobics as shown below is unknown because resistant strains were not available at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory.

Ceftobiprole: *Staphylococcus aureus*

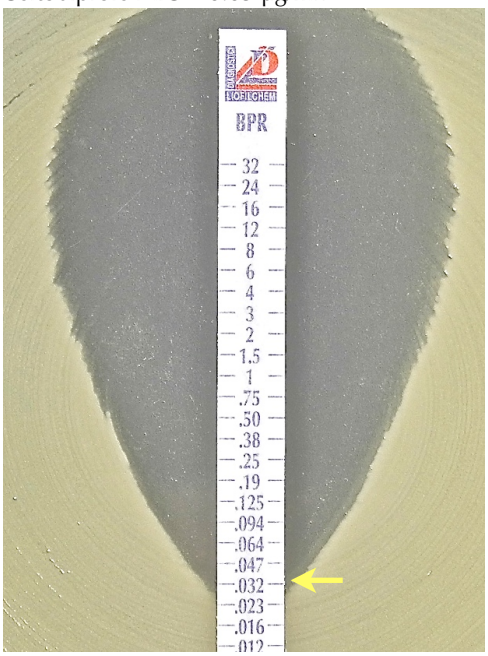
# MTS™ Ceftobiprole Reading Guide

**Note**: Interpret the MIC as 100% inhibition

Example 1:
Ceftobiprole MIC = 0.38 µg/mL,
reported as 0.5 µg/mL

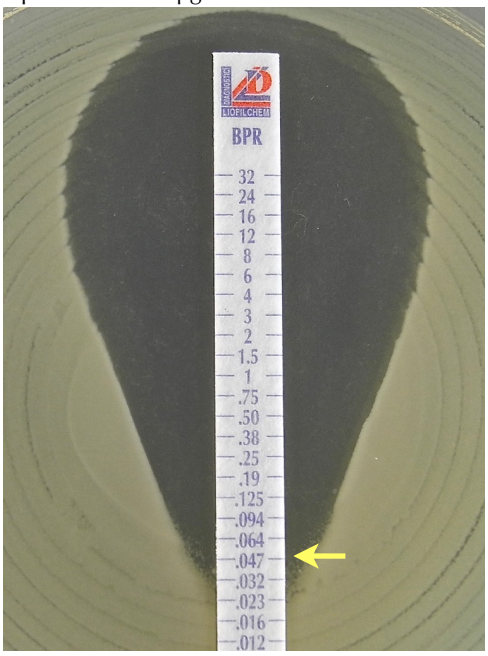



Example 2:
Ceftobiprole MIC = 0.03 µg/mL




Example 3:
Ceftobiprole MIC = 0.094 µg/mL,
reported as 0.125 µg/mL


Example 4:
Ceftobiprole MIC = 0.047 µg/mL,
reported as 0.06 µg/mL



| PRESENTATION | µg/mL | Code | Packaging | Ref. |
|---|---|---|---|---|
| MTS™ Ceftobiprole | 0.002 - 32 | BPR | 10<br>30<br>100 | 921401<br>92140<br>921400 |

**REVISION HISTORY**

| Document | Release Date | Change Summary |
|---|---|---|
| eIFU<br>92140 IFU-0 MTS BPR US | 2025-01-30 | Not applicable (Initial release) |

**Note:** Minor typographical, grammar, and formatting changes are not included in the revision history.

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



**Liofilchem Inc., US Distributor and Customer Service**
465 Waverley Oaks Rd, Waltham, MA
Phone: 781-902-0312