**Indications for Use/Intended Use**

The MTS™ (MIC Test Strip) Imipenem-relebactam 0.002/4-32/4 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™ Imipenem-relebactam at concentrations of 0.002/4 – 32/4 µg/mL should be interpreted at 16-20 hours of incubation.

Imipenem-relebactam has been shown to be active both clinically and *in vitro* against these bacterial species according to the FDA drug approved label:

**Gram-negative bacteria**
- *Citrobacter freundii*
- *Enterobacter cloacae*
- *Escherichia coli*
- *Klebsiella aerogenes*
- *Klebsiella oxytoca*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*

Imipenem-relebactam has been shown to be active *in vitro* only against the non-fastidious bacteria listed below according to the FDA drug approved label:

**Gram-negative bacteria**
- *Citrobacter koseri*

**Specifications**

- **Antibiotic code:** I/R
- **MIC range:** 0.002/4-32/4 µg/mL
- **Antibiotic group:** Carbapenem and bicyclic diazabicyclooctane

**Directions for Use**

Follow the MTS™ package insert instructions.

**Procedures specific to MTS™ Imipenem-relebactam:**

<table>
<thead>
<tr>
<th>Storage</th>
<th>Temperature at −20°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organism</td>
<td>Enterobacteriaceae, <em>Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td>Medium</td>
<td>Mueller Hinton Agar</td>
</tr>
<tr>
<td>Inoculum</td>
<td>Suspension in saline (0.85% NaCl) to 0.5 McFarland standard (1 if mucoid)</td>
</tr>
<tr>
<td>Incubation</td>
<td>Agar plates in inverted position at 35 ± 2°C for 16-20 hours in ambient atmosphere</td>
</tr>
<tr>
<td>Reading</td>
<td>Interpret the MIC as 100% inhibition</td>
</tr>
</tbody>
</table>

**FDA imipenem-relebactam 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* imipenem-relebactam MIC of 0.19 µg/mL is reported as 0.25 µg/mL (see reading guide section for example pictures).

<table>
<thead>
<tr>
<th>Bacterial Species</th>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae</td>
<td>≤1/4</td>
<td>2/4</td>
<td>≥4/4</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>≤2/4</td>
<td>4/4</td>
<td>≥8/4</td>
</tr>
</tbody>
</table>

**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, 30th Edition)**

To check the performance of the MTS™ Imipenem-relebactam, media and procedure, test *K. pneumoniae ATCC BAA-1705* and *K. pneumoniae ATCC BAA-2814* according to the method as outlined in the MTS™ package insert. Also test the respective QC organism with imipenem to confirm the presence of the resistance mechanism (*K. pneumoniae ATCC BAA-1705* MIC range = 4-16 µg/mL, *K. pneumoniae ATCC BAA-2814* MIC range = 16-64 µg/mL). Results are considered satisfactory if they fall within the following ranges:

<table>
<thead>
<tr>
<th>Quality Control Strain</th>
<th>Acceptable MIC Range (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Klebsiella pneumoniae, ATCC® BAA-1705</em></td>
<td>0.03/4 – 0.25/4</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae, ATCC® BAA-2814</em></td>
<td>0.06/4 – 0.5/4</td>
</tr>
</tbody>
</table>

Additional quality control for MTS™ imipenem-relebactam, which will verify imipenem activity only:

<table>
<thead>
<tr>
<th>Quality Control Strain</th>
<th>Acceptable MIC Range (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli, ATCC® 25922</em></td>
<td>0.06/4 – 0.25/4</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa, ATCC® 27853</em></td>
<td>0.25/4 – 1/4</td>
</tr>
</tbody>
</table>

**Performance Characteristics**

**Correlation to Reference Method**

<table>
<thead>
<tr>
<th>Bacterial Species</th>
<th>N</th>
<th>% Essential Agreement</th>
<th>% Category Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae</td>
<td>319</td>
<td>97.5</td>
<td>97.8</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>74</td>
<td>100</td>
<td>91.9</td>
</tr>
</tbody>
</table>

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™ Imipenem-relebactam MIC values tended to be in exact agreement or at least one doubling dilution higher when testing C. freundii, E. cloacae and E. coli compared to the CLSI reference broth microdilution.

Reproducibility
100% of MTS™ Imipenem-relebactam results for non-fastidious Gram-negative bacteria (1 E. cloacae, 2 E. coli, 1 K. aerogenes, 1 K. oxytoca, 2 K. pneumoniae, and 2 P. aeruginosa tested in triplicate at 3 sites on 3 days) were within a doubling dilution of reference broth microdilution results. 100% of MTS™ Imipenem-relebactam results for non-fastidious Gram-negative bacteria (1 C. freundii tested in triplicate at 1 site on 3 days with 3 readers) were within a doubling dilution of reference broth microdilution results.

Limitations
The ability of the MTS™ to detect resistant 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.

Imipenem-relebactam: C. koseri
Due to a limited number of isolates for testing, performance for E. asburiae could not be adequately evaluated. Therefore, an alternative test should be performed for MTS™ imipenem-relebactam when E. asburiae is isolated.

Due to low essential agreement (13/17 = 76.5%) and categorical agreement (12/17 = 70.6%) for P. mirabilis, an alternative test should be performed for MTS™ Imipenem-relebactam when P. mirabilis is isolated.

MTS™ Imipenem-relebactam Reading Guide

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

Example 1:
E. coli, I/R MIC = 0.25 µg/mL

Example 2:
K. pneumoniae, I/R MIC = 0.125 µg/mL, reported as 0.12 µg/mL

Example 3:
C. freundii, I/R MIC = 0.25 µg/mL

Example 4:
P. aeruginosa, I/R MIC = 0.38 µg/mL, reported as 0.5 µg/mL

<table>
<thead>
<tr>
<th>PRESENTATION</th>
<th>µg/mL</th>
<th>Code</th>
<th>Packaging</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTS™ Imipenem-relebactam</td>
<td>0.002/4 - 32/4</td>
<td>I/R</td>
<td>10</td>
<td>920761</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td>920756</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td>920760</td>
</tr>
</tbody>
</table>

MTS™ (MIC Test Strip)
International Patent

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

Liofilchem®, the Liofilchem company logo and the MTS logo are registered trademarks of LIOFILCHEM s.r.l.
**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. 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:**
- 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](http://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, 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 onto the entire 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 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. Intersection between two scale segments should be rounded up to the higher value. In the case of uneven MIC intersections, read the higher value. Repeat the test if the discrepancy is >1 dilution. 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**


**GLOSSARY OF TERMS**

- LOT: Batch code
- REF: Catalog number
- Manufacturer: Contains sufficient for <n> tests
- Upper limit of temperature
- Consult instructions for use
- IVD: In vitro diagnostic medical device
- Temperature limitation