Coagulase-negative staphylococci

Calibration of zone diameter breakpoints to MIC values and/or resistance mechanisms

Version 3.0
January 2020
Coagulase-negative staphylococci MIC and zone diameter correlates

- The following histograms present inhibition zone diameter distributions from EUCAST antimicrobial susceptibility testing. In most, the different colours of the bars indicate different MIC values. In some, the colours of the bars indicate a resistance gene or a resistance mechanism.

- The distributions include data for wild-type isolates and for isolates with acquired resistance mechanisms. A large number of isolates with MIC values close to the edge of the wild-type distribution and/or close to EUCAST clinical breakpoints were intentionally included. These distributions can not be used to infer resistance rates or the performance of the tests with routine isolates.

- For some agents, isolates were tested on more than one occasion, including parallel tests with disks and media from several manufacturers. When this is the case, data are presented as both the “number of isolates tested” and the “total number of MIC-zone diameter correlates”, including replicate tests and parallel tests with disks and media from different sources.
Coagulase-negative staphylococci
Materials and methods

• Antimicrobial susceptibility testing was performed on clinical isolates of coagulase-negative staphylococci (CoNS), including isolates with known resistance mechanisms. The collection comprised *S. capitis*, *S. cohnii*, *S. epidermidis*, *S. haemolyticus*, *S. hominis*, *S. lugdunensis* and *S. warneri*. Disk diffusion was performed according to EUCAST methodology and MICs were determined with the ISO broth microdilution method. Species identification was performed with MALDI-TOF MS.

• The distributions of MIC vs. zone diameter in this presentation are the result of a collaboration between EUCAST and several other laboratories (JMI Laboratories, Iowa, US; Statens Serum Institut, Copenhagen, Denmark; K-res, Tromsø, Norway; Clinical Microbiology, Lund, Sweden; St. Olav Hospital, Trondheim, Norway; Slagelse-Næstved Hospital, Denmark; Centre National de Référence des Staphylocoques, Lyon, France and Laboratory Specialists Inc., USA).

• Data on cefoxitin screen for methicillin resistance are presented at the end of this presentation.

• This presentation is based on EUCAST Clinical Breakpoint Tables v. 10.0.
Changes from previous version (2.2)

<table>
<thead>
<tr>
<th>Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• MIC and zone diameter breakpoints changed for ciprofloxacin, levofloxacin, ofloxacin, amikacin, minocycline and trimethoprim.</td>
</tr>
<tr>
<td>• Zone diameter breakpoints changed for tigecycline.</td>
</tr>
<tr>
<td>• Data added for linezolid.</td>
</tr>
<tr>
<td>• New distribution for tedizolid.</td>
</tr>
</tbody>
</table>
Explanation of graphs:

These graphs show zone diameter distributions with MIC values or resistance mechanisms as coloured bars. Colours are related to current EUCAST MIC breakpoints.

**Agent X**

- MIC (mg/L):
  - ≥8
  - 4
  - 2
  - 1
  - 0.5
  - ≤0.25

- Breakpoint:
  - Resistant
  - Susceptible, increased exposure
  - Susceptible, standard dosing regimen

**Agent Y**

- MIC (mg/L):
  - ≥64
  - 32
  - 16
  - 8
  - 4
  - 2
  - 1
  - 0.5
  - ≤0.25

- Breakpoint:
  - Resistant
  - Susceptible, increased exposure
Ciprofloxacin 5 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

Breakpoints
- MIC: S≤0.001, R>1 mg/L
- Zone diameter: S≥50, R<24 mm
Levofloxacin 5 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

No of observations

Inhibition zone diameter (mm)

Breakpoints

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Breakpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥16</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>≤0.125</td>
<td></td>
</tr>
</tbody>
</table>

Zone diameter: S≥50, R<24 mm
MIC: S≤0.001, R>1 mg/L
Moxifloxacin 5 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>No of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>0.25</td>
<td>2</td>
</tr>
<tr>
<td>0.125</td>
<td>2</td>
</tr>
<tr>
<td>≤0.06</td>
<td>2</td>
</tr>
</tbody>
</table>

Breakpoints
MIC S≤0.25, R>0.25 mg/L
Zone diameter S≥28, R<28 mm
Ofloxacin 5 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

No of observations

Inhibition zone diameter (mm)

No of observations

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Breakpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8</td>
<td>S≥50, R&lt;24 mm</td>
</tr>
<tr>
<td>4</td>
<td>S≥50, R&lt;24 mm</td>
</tr>
<tr>
<td>2</td>
<td>S≥50, R&lt;24 mm</td>
</tr>
<tr>
<td>1</td>
<td>S≥50, R&lt;24 mm</td>
</tr>
<tr>
<td>0.5</td>
<td>S≥50, R&lt;24 mm</td>
</tr>
<tr>
<td>≤0.25</td>
<td>S≥50, R&lt;24 mm</td>
</tr>
</tbody>
</table>
The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance. Isolates categorised as susceptible to norfloxacin can be reported susceptible to moxifloxacin and “susceptible increased exposure” (I) to ciprofloxacin, levofloxacin and ofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.

**Breakpoints**

- **Ciprofloxacin MIC**
  - S \leq 0.001, R > 1 mg/L

- **Norfloxacin zone diameter (screen)**
  - S \geq 17 mm
The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance. Isolates categorised as susceptible to norfloxacin can be reported susceptible to moxifloxacin and “susceptible increased exposure” (I) to ciprofloxacin, levofloxacin and ofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.
Norfloxacin 10 µg vs. Moxifloxacin MIC
CoNS, 93 isolates

(2 data sources)

The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance. Isolates categorised as susceptible to norfloxacin can be reported susceptible to moxifloxacin and “susceptible increased exposure” (I) to ciprofloxacin, levofloxacin and ofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.

Breakpoints
Moxifloxacin MIC  S≤0.25, R>0.25 mg/L
Norfloxacin zone diameter (screen)  S≥17 mm
The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance. Isolates categorised as susceptible to norfloxacin can be reported susceptible to moxifloxacin and “susceptible increased exposure” (I) to ciprofloxacin, levofloxacin and ofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.

**Breakpoints**

- **Ofloxacin MIC**  
  \( S \leq 0.001, R > 1 \text{ mg/L} \)

- **Norfloxacin zone diameter (screen)**  
  \( S \geq 17 \text{ mm} \)
Amikacin 30 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

No of observations

Inhibition zone diameter (mm)

MIC (mg/L)
- 64
- 32
- 16
- 8
- 4
- ≤2

Breakpoints
- MIC: S≤8, R>8 mg/L
- Zone diameter: S≥22, R<22 mm
Gentamicin 10 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

No of observations

Inhibition zone diameter (mm)

Breakpoints

**MIC**
S≤1, R>1 mg/L

**Zone diameter**
S≥22, R<22 mm
Tobramycin 10 µg vs. MIC
CoNS, 93 isolates

Breakpoints

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Zone diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.125</td>
<td>≥22, R&lt;22 mm</td>
</tr>
<tr>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
<tr>
<td>≥8</td>
<td></td>
</tr>
</tbody>
</table>

No of observations

Inhibition zone diameter (mm)
Erythromycin 15 µg vs. MIC
CoNS, 92 isolates

(2 data sources)

Breakpoints

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>No of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8</td>
<td>33</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>≤0.25</td>
<td>1</td>
</tr>
</tbody>
</table>

No of observations

Inhibition zone diameter (mm)

Breakpoints

MIC        S≤1, R>2 mg/L
Zone diameter S≥21, R<18 mm
Erythromycin 15 µg vs. Azithromycin MIC
CoNS, 92 isolates

(2 data sources)

Erythromycin can be used to determine susceptibility to azithromycin, clarithromycin and roxithromycin.

Breakpoints
Azithromycin MIC
S≤1, R>2 mg/L

Erythromycin zone diameter
S≥21, R<18 mm
Erythromycin can be used to determine susceptibility to azithromycin, clarithromycin and roxithromycin.
Erythromycin 15 µg vs. Roxithromycin MIC
CoNS, 92 isolates

(2 data sources)

Erythromycin can be used to determine susceptibility to azithromycin, clarithromycin and roxithromycin.

**Breakpoints**
- Roxithromycin MIC: S≤1, R>2 mg/L
- Erythromycin zone diameter: S≥21, R<18 mm
Clindamycin 2 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

**Breakpoints**

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Zone diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>S≤0.25, R&gt;0.5</td>
<td>S≥22, R&lt;19 mm</td>
</tr>
</tbody>
</table>

**MIC**
- ≥8
- 4
- 2
- 1
- 0.5
- 0.25
- ≤0.125
Quinupristin-dalfopristin 15 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

No of observations

Inhibition zone diameter (mm)

Breakpoints

MIC  S≤1, R>2 mg/L
Zone diameter  S≥21, R<18 mm
Minocycline 30 µg vs. MIC
CoNS, 156 isolates

(1 data source)

No of observations

Inhibition zone diameter (mm)

Breakpoints
MIC    S≤0.5, R>0.5 mg/L
Zone diameter  S≥23, R<23 mm

MIC (mg/L)
no MIC
16
8
4
2
1
0.5
0.25
0.125
Tetracycline 30 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

**Breakpoints**

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Zone diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥16</td>
<td>S≥22, R&lt;19 mm</td>
</tr>
<tr>
<td>8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>≤0.125</td>
<td></td>
</tr>
</tbody>
</table>

**MIC**

S≤1, R>2 mg/L
Tigecycline 15 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>No of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>S≥19, R&lt;19 mm</td>
</tr>
<tr>
<td>≤0.125</td>
<td>S≤0.5, R&gt;0.5 mg/L</td>
</tr>
</tbody>
</table>

Breakpoints
- MIC: S≤0.5, R>0.5 mg/L
- Zone diameter: S≥19, R<19 mm
Linezolid 10 µg vs. MIC
CoNS, 131 isolates (345 correlates)

(3 data sources)

No of observations

Inhibition zone diameter (mm)

MIC (mg/L)
- ≥128
- 64
- 32
- 16
- 8
- 4
- 2
- ≤1

Breakpoints
- MIC: S≤4, R>4 mg/L
- Zone diameter: S≥21, R<21 mm
Tedizolid 2 µg vs. MIC
CoNS, 63 isolates (504 correlates)

(1 data source)

**Breakpoints**
- **MIC**
  - S≤0.5, R>0.5 mg/L
- **Zone diameter**
  - S≥21, R<21 mm
Chloramphenicol 30 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

Breakpoints
MIC
S≤8, R>8 mg/L
Zone diameter
S≥18, R<18 mm
Fusidic acid 10 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

Breakpoints
MIC
S≤1, R>1 mg/L
Zone diameter
S≥24, R<24 mm
Rifampicin 5 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

No of observations

Inhibition zone diameter (mm)

Breakpoints
MIC
S ≤ 0.06, R > 0.5 mg/L

Zone diameter
S ≥ 26, R < 23 mm
Trimethoprim 5 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

Breakpoints
MIC S≤4, R>4 mg/L
Zone diameter S≥14, R<14 mm

No of observations

Inhibition zone diameter (mm)

MIC (mg/L)
- ≥32
- 16
- 8
- 4
- 2
- 1
- 0.5
- 0.25
Trimethoprim-sulfamethoxazole 1.25-23.75 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

Breakpoints
MIC S≤2, R>4 mg/L
Zone diameter S≥17, R<14 mm
Coagulase-negative staphylococci

Cefoxitin 30 µg as screen for methicillin resistance
Coagulase-negative staphylococci

• Cefoxitin 30 µg can be used to screen for methicillin resistance in coagulase-negative staphylococci (CoNS).

• For CoNS other than *S. epidermidis*, the cefoxitin screening breakpoint is $S \geq 22$ and $R < 22$ mm (same as for *S. aureus*). *S. epidermidis* have a separate screening breakpoint at $S \geq 25$ and $R < 25$ mm.

• If CoNS are not identified to species level, a screening breakpoint of $S \geq 25$ and $R < 25$ mm must be used.
Cefoxitin 30 µg vs. *mecA* status
CoNS (not *S. epidermidis*), 276 isolates (873 correlates)

(2 data sources)

**Breakpoints**
Zone diameter (screen)  $S \geq 22$, $R < 22$ mm

2 *S. hominis* isolates with confirmed silent *mecA* gene
Cefoxitin 30 µg vs. *mecA* status
*S. epidermidis*, 100 isolates (193 correlates)

(2 data sources)

Breakpoints
Zone diameter (screen)  $S \geq 25$, $R < 25$ mm
Cefoxitin 30 µg vs. *mecA* status
CoNS (non-speciated), 376 isolates (1066 correlates)

(2 data sources)

If coagulase-negative staphylococci are not identified to species level, use zone diameter breakpoints S≥25, R<25 mm.

**Breakpoints**
Zone diameter (screen)  S≥25, R<25 mm
Cefoxitin 30 µg vs. *meca* status
*S. capitis*, 57 isolates (138 correlates)

Breakpoints
Zone diameter (screen)  S≥22, R<22 mm
Cefoxitin 30 µg vs. mecA status
*S. cohnii*, 45 isolates (162 correlates)

(2 data sources)

**Breakpoints**
Zone diameter (screen)  S≥22, R<22 mm
Cefoxitin 30 µg vs. *mecA* status
*S. haemolyticus*, 64 isolates (208 correlates)

(2 data sources)

**Breakpoints**
Zone diameter (screen)  S≥22, R<22 mm
Cefoxitin 30 µg vs. mecA status
*S. hominis*, 54 isolates (153 correlates)

(2 data sources)

<table>
<thead>
<tr>
<th>mecA status</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. hominis</td>
<td>54 isolates (153 correlates)</td>
<td></td>
</tr>
</tbody>
</table>

**Breakpoints**

Zone diameter (screen)   $S \geq 22, R < 22$ mm
Cefoxitin 30 µg vs. mecA status
*S. warneri*, 56 isolates (212 correlates)

(2 data sources)

**Breakpoints**
Zone diameter (screen)  S≥22, R<22 mm