Coagulase-negative staphylococci

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

Version 2.0
March 2017
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 and Centre National de Référence des Staphylocoques, Lyon, France).

- 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. 7.1.
# Changes from previous version (1.3)

<table>
<thead>
<tr>
<th>Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• MIC data added for several antimicrobial agents.</td>
</tr>
<tr>
<td>• Zone diameter breakpoints changed for ciprofloxacin, ofloxacin and linezolid.</td>
</tr>
<tr>
<td>• Zone diameter and MIC breakpoints changed for levofloxacin and moxifloxacin.</td>
</tr>
<tr>
<td>• New distributions for erythromycin, erythromycin vs. azithromycin, erythromycin vs. clarithromycin and erythromycin vs. roxithromycin.</td>
</tr>
<tr>
<td>• Zone diameter breakpoints for cefoxitin screen for methicillin resistance changed and separate distributions shown for each species.</td>
</tr>
</tbody>
</table>
Explanation of graphs:

Zone diameter distribution with MIC values or resistance mechanisms as coloured bars.

Gentamicin 10 µg vs. MIC
CoNS, 93 isolates

Zone diameter breakpoint

MIC (mg/L)
- ≥8
- 4
- 2
- 1
- 0.5
- 0.25
- ≤0.125

No of observations

Inhibition zone diameter (mm)

Resistant by EUCAST MIC breakpoints

Susceptible by EUCAST MIC breakpoints
Ciprofloxacin 5 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

Breakpoints

MIC
S ≤ 1, R > 1 mg/L

Zone diameter
S ≥ 24, 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>S≤1, R&gt;1 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone diameter</td>
<td>S≥24, R&lt;24 mm</td>
</tr>
</tbody>
</table>
Moxifloxacin 5 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

Breakpoints

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Breakpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8</td>
<td>S≤0.25, R&gt;0.25 mg/L</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>
<tr>
<td>≤0.06</td>
<td></td>
</tr>
</tbody>
</table>

No of observations

Inhibition zone diameter (mm)
Ofloxacin 5 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>≥8</td>
<td>S≥24, R&lt;24 mm</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>
</tbody>
</table>

**No of observations**

**Inhibition zone diameter (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 ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.
The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance. Isolates categorised as susceptible to norfloxacin can be reported susceptible to ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.
The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance. Isolates categorised as susceptible to norfloxacin can be reported susceptible to ciprofloxacin, levofloxacin, moxifloxacin 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 ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin. Isolates categorised as non-susceptible should be tested for susceptibility to individual agents.
Amikacin 30 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

No of observations

Inhibition zone diameter (mm)

Breakpoints
MIC  
S≤8, R>16 mg/L

Zone diameter  
S≥22, R<19 mm
Gentamicin 10 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≤1, R&gt;1</td>
<td>S≥22, R&lt;22 mm</td>
</tr>
</tbody>
</table>

No of observations

Inhibition zone diameter (mm)

- MIC ≥8
- MIC 4
- MIC 2
- MIC 1
- MIC 0.5
- MIC 0.25
- MIC ≤0.125
Tobramycin 10 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

**Breakpoints**
- MIC: $S \leq 1, R > 1$ mg/L
- Zone diameter: $S \geq 22, R < 22$ mm
Erythromycin 15 µg vs. MIC
CoNS, 92 isolates

(2 data sources)

Breakpoints

MIC: $S \leq 1$, $R > 2$ mg/L
Zone diameter: $S \geq 21$, $R < 18$ 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.

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>No of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥16</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>≤0.5</td>
</tr>
</tbody>
</table>

**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

**MIC (mg/L)**

- >=8
- 4
- 2
- 1
- ≤0.5
Clindamycin 2 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

Breakpoints

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>S ≤ 0.25, R &gt; 0.5 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone diameter</td>
<td>S ≥ 22, R &lt; 19 mm</td>
</tr>
</tbody>
</table>
Quinupristin-dalfopristin 15 µg vs. MIC
CoNS, 93 isolates
(2 data sources)

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)

No of observations

MIC (mg/L)
- no MIC
- 16
- 8
- 4
- 2
- 1
- 0.5
- 0.25
- 0.125

Breakpoints
MIC S≤0.5, R>1 mg/L
Zone diameter S≥23, R<20 mm
Tetracycline 30 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>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>
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<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>
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</tbody>
</table>

MIC

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

(2 data sources)

<table>
<thead>
<tr>
<th>No of observations</th>
<th>Inhibition zone diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----</td>
</tr>
</tbody>
</table>
|                     | 0.25| ≤0.125| S≤0.5, R>0.5 mg/L | S≥18, R<18 mm | MIC (mg/L)

Breakpoints

- MIC: S≤0.5, R>0.5 mg/L
- Zone diameter: S≥18, R<18 mm
Linezolid 10 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

No of observations

Inhibition zone diameter (mm)

Breakpoints
MIC $\leq 4$, $R > 4$ mg/L
Zone diameter $S \geq 21$, $R < 21$ mm
Chloramphenicol 30 µg vs. MIC
CoNS, 93 isolates

(2 data sources)

No of observations

Inhibition zone diameter (mm)

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

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Zone diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥16</td>
<td>S≥24, R&lt;24 mm</td>
</tr>
<tr>
<td>8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
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<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>

No of observations

Inhibition zone diameter (mm)
Rifampicin 5 µg vs. MIC
CoNS, 93 isolates

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≤2, R>4 mg/L
Zone diameter  S≥17, R<14 mm
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)

**No of observations**

**Inhibition zone diameter (mm)**

2 *S. hominis* isolates with confirmed silent *mecA* gene

**Breakpoints**

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

(2 data sources)

**mecA status**
- Positive
- Negative

**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)

**mecA status**
- Positive
- Negative

2 isolates with confirmed silent mecA gene

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

(2 data sources)

**Breakpoints**

Zone diameter (screen)  \( S \geq 22, R < 22 \text{ mm} \)