Update on EUCAST methods and breakpoints, 2015

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Departamento de Microbiología II
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www.eucast.org

The European Committee on Antimicrobial Susceptibility Testing - EUCAST


EUCAST deals with breakpoints and technical aspects of phenotypic in vitro antimicrobial susceptibility testing and functions as the breakpoint committee of EMA and ECDC. EUCAST does not deal with antibiotic policies, surveillance or containment of resistance or infection control. The Steering Committee is the decision making body. It is supported by a General Committee with representatives from European and other national committees and infectious disease testing device manufacturers.

EUCAST has a General Committee:

Most antimicrobial agents:
- Breakpoints for these agents are developed through EMA. EUCAST has accepted and approved the EMA breakpoints. EUCAST also has devices for automated susceptibility testing which are calibrated to EUCAST MIC breakpoints.

EUCAST invites anyone with an interest in antimicrobial agents in general and antimicrobial breakpoints in particular to contact EUCAST, ESCMID or one of the EUCAST Steering Committee members.

Continuously updated and freely available
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<th>Top countries</th>
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**Visits:**

- 50,000-60,000 visitors/month (60% from EU)

**Pages more visited** (each visitor may see each page more than once)

- **home** 45.9%
- **clinical breakpoints** 69.2%
- MIC/zone distributions 5.5%
- expert rules 3.3%
- resistance mechanisms 3.2%
Number of visitors per month

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EUCAST-related publications

- Yearly evolution of publications in PubMed including “EUCAST” in the title and/or abstract

*January-March, 2015*
2015

EUCAST General Committee (GC)
All European Countries + Countries from outside

EUCAST Steering Committee
BSAC, CA-SFM, CRG, NWGA, SRGA, NAK
+ 2 reps from the GC ± 1-2 “visiting” members from the GC

Subcommittees
Antifungals (AFST)
VetCAST
Whole genome sequencing and AST

National Breakpoint Committees
F, N, NL, S, UK, DE

NACs = National Antimicrobial Susceptibility Testing Committees

Experts (ECDC Networks, ESCMID Study Groups)
Industry

Contract 2011-14

www.eucast.org

ESCMID Online Lecture Library

@ by author
EUCAST translations
Implementation of EUCAST breakpoints, April 2015

% Laboratories
- >50%
- 10-50%
- <10%
- No information

Countries not on this map: Australia, Brazil, Iceland, Israel, Morocco, New Zealand, South Africa, USA
National Antimicrobial Committees (NACs) outside Europe

Countries with a NAC operating under EUCAST standards

Countries with interest to establish a NAC under EUCAST standards
EUCAST General Committee (GC)
All European Countries + Countries from outside

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www.eucast.org
Subcommittees

Subcommittee on Antifungal Susceptibility Testing (EUCAST AFST) *Standing subcommittee established in 2002*

Veterinary Subcommittee on Antimicrobial Susceptibility Testing (VetCAST). *Standing Subcommittee established in 2015*

Subcommittee on the role of whole genome sequencing in antimicrobial susceptibility testing. *Established in 2015.*

Former subcommittees


Subcommittee on Anaerobe Susceptibility Testing *Established in 2007, disbanded 2011.*

Subcommittee on the detection of resistance mechanisms of clinical and/or public health importance. *Established in 2011, disbanded 2014.*
Veterinary committee on AST (VetCAST)

- Formed in 2015, dealing with antimicrobial susceptibility testing (AST) of bacterial pathogens of animal origin and zoonotic bacteria

- Remit...

  - To establish a science-based committee to cooperate with EU professionals in veterinary medicine, EMA, ECDC and EFSA
  - To determine antimicrobial breakpoints specific to the veterinary field
  - To harmonize veterinary AST in the EU
  - To provide AST/antimicrobial therapy education in the veterinary field
  - To initiate and coordinate EU research aimed at filling the current gaps in veterinary AST
    - Missing or insufficient veterinary specific breakpoints
    - Optimized methods for AST of bacterial pathogens of animal origin
  - To ensure that AST protocols and interpretive criteria are freely accessible online through the EUCAST website

- Chairman (Dik Mevious), Secretary (Peter Damborg), …
Subcommittee on the role of whole genome sequencing (WGS) in AST of bacteria

- Formed in 2015 with the following *remit*
  - perform a systematic literature review of the role of WGS in antimicrobial susceptibility testing (AST) of bacteria (excluding mycobacteria)
  - determine the sensitivity and specificity of WGS compared with standard phenotypic AST
  - determine how WGS may be applied in clinical laboratories and the likely implications for phenotypic and other genotypic methods in use
  - determine the epidemiological implications of using WGS
  - determine the clinical implications of WGS for the selection of antimicrobial therapy
  - determine the principles of how the result of WGS for AST would be best presented to clinical users
  - describe the drivers and barriers to routine use of WGS

- Coordinator: ...
EUCAST Development Laboratories (Nov 2014 …)

- Development and maintenance of EUCAST antimicrobial susceptibility testing (AST) methods
  - Bacteria (Växjö, Sweden)
  - Fungi (Statens Serum Institut, Copenhagen, Denmark)
- Coordination of the EUCAST Network Laboratories in the development and validation of EUCAST methods, training, education and technical support to other laboratories.

EUCAST network laboratories (Nov 2014 …)

- Microbiology laboratories with particular expertise and training in EUCAST AST for bacteria and/or fungal isolates
- Develop, validate and troubleshoot EUCAST methods and/or train and educate other laboratories
- Assist clinical breakpoint development by providing species-specific MIC datasets
**EUCAST Development & Network Laboratories**

### Bacteria

**EUCAST Development Laboratory for bacteria, Växjö, Sweden**

**Network Laboratories (n=11)**
- Acibadem Labmed Clinical Laboratories, Istanbul, Turkey
- Analyse BioLab, Linz, Austria
- Clinical Microbiology, Aarhus, Denmark
- Clinical Microbiology, Bergen, Norway
- Clinical Microbiology, Kalmar, Sweden
- Hospital Universitario Ramon y Cajal, Madrid, Spain
- Karolinska University Hospital, Solna, Sweden
- Medical Microbiology, Stavanger, Norway
- Norwegian National Advisory Unit on Detection of AR, Tromsø, Norway
- Southmead Hospital, Bristol, UK
- University of Verona, Italy

### Fungi

**EUCAST Development Laboratory for fungi, SSI, Copenhagen, Denmark**

**Network Laboratories (n=8)**
- Clinical Microbiology Laboratory, Athens, Greece
- Department of Medical Microbiology and Infectious Diseases, NL
- Gregorio Marañón Hospital. Madrid, Spain
- Hospital Européen Georges Pompidou, Paris, France
- Mycology Reference Centre, Manchester
- National and Kapodistrian University of Athens, Greece
- National Reference Centre for Invasive Mycoses, Jena, Germany
- Spanish Mycology Reference Laboratory
Template for RDs, 40 documents
(New: ceftaroline; Drafted: ceftobiprol, macrolides, penicillins, cephalosporins, SXT, aztreonam, chloramphenicol)

SOP 8.0. Format and updating of EUCAST documents

SOP 9.0. Procedure for establishing zone diameter breakpoints and QC criteria for new antibiotics

- Implementation of EUCAST breakpoints for AST (Euro surveillance)
Widespread implementation of EUCAST breakpoints for antibacterial susceptibility testing in Europe

Uptake of EUCAST guidelines by participants in UKNEQAS *(updated)*
(630-750 participants per year from a total of 40 countries)

**Courtesy of Derek Brown and Christine Walton**
- MIC vs zone diameters files
- Disk diffusion manual and slide show
- Breakpoint and QC tables v5.0
- Compliance of manufacturers

- Frequently Asked Questions
  March 23rd, 2015
European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs and zone diameters

Version 5.0, valid from 2015-01-01

This document should be cited as

### EUCAST breakpoints, 2015 (version 5.0)

- Links to different pages (microorganisms) and EUCAST documents:
  - guidance documents, expert rules
  - detection of resistance mechanisms
  - breakpoints for topical use of antimicrobial agents

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<table>
<thead>
<tr>
<th>Content</th>
<th>Page</th>
<th>Additional information</th>
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</thead>
<tbody>
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<td>Notes</td>
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<td>Stenotrophomonas maltophilia</td>
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<td>Link to Guidance Document on Stenotrophomonas maltophilia</td>
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<td>Burkholderia cepacia</td>
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<td>Link to Guidance Document on Burkholderia cepacia group</td>
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<td>Streptococcus groups A, B, C and G</td>
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<td>Streptococcus pneumoniae</td>
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<td>Viridans group streptococci</td>
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<td>Haemophilus influenzae</td>
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<td>Moraxella catarrhalis</td>
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<td>Neisseria gonorrhoeae</td>
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<td>Neisseria meningitidis</td>
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<td>Gram-positive anaerobes</td>
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<td>Clostridium difficile</td>
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<td>Gram-negative anaerobes</td>
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<td>Campylobacter jejuni and coli</td>
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<td>Corynebacterium spp.</td>
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<td>Mycobacterium tuberculosis</td>
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<td>PK/PD (Non-species related) breakpoints</td>
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<td>Link to EUCAST Expert Rules</td>
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<td>Link to EUCAST Guidelines on Detection of Resistance Mechanisms</td>
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<td>Link to Guidance Document on topical agents</td>
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EUCAST breakpoints, 2015 (version 5.0)

Guidance on reading EUCAST breakpoint tables

The intermediate category is not listed but is interpreted as the values between the S and the R breakpoints. If the S and R breakpoints are the same value there is no intermediate category.

Agent A: No intermediate category
Agent B: Intermediate category: 4 mg/L, 23-25 mm
Agent G: Intermediate category: 1-2 mg/L, 24-29 mm

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC breakpoint (mg/L)</th>
<th>Disk content (µg)</th>
<th>Zone diameter breakpoint (mm)</th>
<th>Notes</th>
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<tr>
<td></td>
<td>S ≤ R &gt;</td>
<td>S ≤ R ≤</td>
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<td></td>
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<tr>
<td>Antimicrobial agent A</td>
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<td>X</td>
<td>20*</td>
<td>1. Comment on MIC breakpoints</td>
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<td>20*</td>
<td>1. Comment on MIC breakpoints</td>
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<tr>
<td>Antimicrobial agent C</td>
<td>IE</td>
<td>IE</td>
<td>IE</td>
<td>2. New comment</td>
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<tr>
<td>Antimicrobial agent D</td>
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<td>Y</td>
<td>20*</td>
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<td>Y</td>
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<td>Antimicrobial agent G</td>
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<td>2</td>
<td>30*</td>
<td>New format for comments</td>
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Screening breakpoint to differentiate between isolates without and with resistance mechanisms

MIC breakpoints in blue are linked to MIC distributions

Antimicrobial names in blue are linked to EUCAST rational documents

Not Applicable

Insufficient evidence that the organism or group is a good target for therapy with the agent

Zone diameter breakpoints in blue are linked to zone diameter distributions

In Preparation

No breakpoints. Susceptibility testing is not recommended

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### EUCAST breakpoints, 2015 (version 5.0)

#### New and revised breakpoints

- **Enterobacteriaceae**
  - Amikacin (*zone diameters*)

- **Staphylococcus spp.**
  - Telavancin (*new* - related to zone diameters)

- **Moraxella catarrhalis**
  - Ceftaroline (*change from dash to IE* - related to zone diameters)

- **Neisseria menigitidis**
  - Ciprofloxacin (*remove intermediate category* - related to zone diameters)

- **Neisseria gonorrhoeae**
  - Cefpodoxime, ceftibuten (*change from IE to dash* - related to zone diameters)

- **Clostridium difficile**
  - Fidaxomicin (*new* - related to zone diameters)

- **M. tuberculosis**
  - Delamanid and bedaquiline (*new* - related to zone diameters)

#### New EUCAST breakpoints, April 2015

- **Staphylococcus spp.**
  - Dalbavancin, Oritavancin, Tedizolid (*new* - related to zone diameters)

- **Strep. group A, B, C, G**
  - Dalbavancin, Oritavancin, Tedizolid (*new* - related to zone diameters)

- **Strep. anginosus group**
  - Dalbavancin, Oritavancin, Tedizolid (*new* - related to zone diameters)
**Rewording of notes, new notes**

- **Telavancin, tigecycline, daptomycin, fosfomycin**
  - Information on testing conditions
- **Aztreonam**
- **Trimethoprim-sulfameth.**
  - *Stenotrophomonas maltophilia*
  - *Enterococcus* spp.
- **Cephalosporins**
  - *Staphylococcus* spp.
- **Clindamycin**
  - *Strept.* groups A, B, C and D
  - *Streptococcus pneumoniae*
  - Viridans group streptococci

**New data of Quality Control**

- **Haemophilus influenzae**
- **Moraxella catharralis**
- **Pasterurella multocida**
### EUCAST breakpoints, 2015 (version 5.0)

**Clindamycin inducible phenotype (MLS<sub>B</sub>)**

- Inducible clindamycin resistance can be detected by antagonism of clindamycin activity by a macrolide agent.
- Place the erythromycin and clindamycin disks 12-20 mm apart (edge to edge) and look for antagonism (the D phenomenon).

<table>
<thead>
<tr>
<th>Antagonisms</th>
<th>Report clindamycin</th>
<th>Organisms</th>
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<td>Detected</td>
<td>R</td>
<td>Staphylococcus spp. Strept. group A,B,C,G</td>
<td>Clindamycin may still be used for short-term therapy of less serious skin and soft tissue infections as constitutive resistance is unlikely to develop during such therapy</td>
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<tr>
<td></td>
<td>R</td>
<td>S. pneumoniae Viridans g. streptococci</td>
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More information: Tuesday 07.45 – 08.45, Hall I  
Meet the Experts. EUCAST: frequently asked questions
EUCAST breakpoints: Delamanid and Bedaquiline

- EUCAST Clinical Breakpoint Table v. 5.0, valid from 2015-01-01

**Mycobacterium tuberculosis**

EUCAST was tasked with suggesting to EMA breakpoints for new agents but has so far not addressed breakpoints for existing agents.

<table>
<thead>
<tr>
<th>MIC breakpoint (mg/L)</th>
<th>Notes</th>
<th>Numbers for comments on MIC breakpoints</th>
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<tr>
<td></td>
<td>R &gt; Bedaquiline 0.25</td>
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</table>

Recommended methods for antimicrobial susceptibility testing of mycobacteria are currently under discussion.
## EUCAST breakpoints

- Reviewed breakpoints with no changes:
  - linezolid and staphylococci and enterococci
  - teicoplanin and coagulase negative staphylococci
  - fluoroquinolones and *Corynebacterium* spp.
  - metronidazole and anaerobes
  - daptomycin and enterococci
Guidance note on breakpoints for topical agents

- ECOFFs and systemic clinical breakpoints for antimicrobial agents that are used topically

<table>
<thead>
<tr>
<th>Organisms</th>
<th>ECOFF (mg/L)</th>
<th>Gentamicin&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Ciprofloxacin&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Levofloxacin&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Ofoxacin&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Chloramphenicol&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Colistin&lt;sup&gt;1&lt;/sup&gt; (for Polymyxin B)</th>
<th>Fusidic acid&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Neomycin (francymycin)</th>
<th>Bacitracin</th>
<th>Mupirocin</th>
<th>Retapamulin</th>
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<td>1/2</td>
<td>-</td>
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<td>1</td>
<td>0.5</td>
<td>1</td>
<td>-</td>
<td>2</td>
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<td>1/2</td>
<td>1/2</td>
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<td>IE</td>
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<td>1/1</td>
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</table>

- = inappropriate combination; IE = insufficient evidence to set a clinical breakpoint; ND = No ECOFF defined on EUCAST MIC distribution website. <sup>1</sup>Agents also available for systemic use. <sup>2</sup>Breakpoints for nasal decontamination S≤1, R>256 mg/l.
New and ongoing breakpoints (BP) and methodology

- EMA β-lactam-β-lactamase inhibitor combinations, cephalosporins aminoglycosides, and oxazolidinones, pleuromutilin guidelines for companies submitting anti-mycobacterial agents

- CLSI colistin and methodology

- NACs temocillin, nitroxoline, spiramycin, tigecycline, sulbactam

- Antimicrobial groups: **fluoroquinolones and carbapenems**

- *Neisseria gonorrhoeae* and different antimicrobials

- Disk diffusion breakpoints for
  - *Kingella kingae*
  - *Actinomyces* spp.
  - *Aerococcus* spp.
  - *Eikenella corrodens*
  - … … … … … … … … …
EUCAST: What is coming for 2015-16?

- Zone diameter breakpoints for fosfomycin disk
- New RD documents
  - new agents and new RD due to revised BP
- New documents, technical notes / guidance documents
  - new version of expert rules (v3), SOPs (revision of breakpoints)
- New EUCAST definition of the intermediate category and ECOFF
- New ESCMID Postgraduate Technical Workshop
www.eucast.org

EUCAST Online Lecture Library

NEWS

EUCAST News

Frequently Asked Questions - updated version 2015-03-23

Sad news! Dr William A. Craig died on the 11th of March.

EUCAST Workshops in Australia

General committee 2015 Agenda now available

MIC vs zone diameters - files updated 2015-02-20

About Newsfeed

EUCAST invites anyone with an interest in antimicrobial agents in general and antimicrobial breakpoints in particular to contact EUCAST, ESCMID or one of the

ESCMID by author
More information:

- Saturday 16:30 – 18:30, Hall B
  Resurrecting old antimicrobial agents

- Sunday 09.00 – 10.30, Meeting Room 19
  EUCAST Subcommittee on Antifungal Susceptibility Testing (AFST) General Committee Meeting
  11.30 – 12.30, Hall B
  Benefits and challenges of site-specific breakpoints

- Monday 13.00 – 14.30, Hall N
  EUCAST General Committee meeting
  17.30 – 18.30, Meeting Room 6
  EUCAST Veterinary Subcommittee on Antimicrobial Susceptibility Testing (VetCAST)

- Tuesday 07.45 – 08.45, Hall I
  Meet the Experts. EUCAST: frequently asked questions