UPDATE ON EUCAST 2014

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www.eucast.org

Completely updated!
2 new SOPS
3 new versions

Mostly describes EUCAST organization and relationship of EUCAST-SC with NACs

39 documents

10 documents

Standard Operation Procedures

- EUCAST SOP 1.1 Setting breakpoints for new antimicrobial agents (2013-06-09) (previous version)
- EUCAST SOP 2.1 Harmonising breakpoints for existing antimicrobial agents (2013-08-12) (previous version)
- EUCAST SOP 3.0 Review and revisions of breakpoints (2013-01-03)
- EUCAST SOP 4.1 EUCAST Committees and subcommittees (2013-08-19) (previous version)
- EUCAST SOP 5.0 Interactions with NACs (2013-01-03)
- EUCAST SOP 6.0 Organisation and maintenance of EUCAST websites (2013-05-02)
- EUCAST SOP 7.0 Preparation and handling of EUCAST minutes (2014-01-22)
EUCAST General Committee (GC)
All European Countries + Countries from outside

EUCAST Steering Committee
BSAC, CA-SFM, CRG, NWGA, SRGA
+ 3 reps from the GC ± 2 “visiting” members from the GC

Subcommittees
Antifungals
Resistance mechanisms

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

NACs = National Antimicrobial Susceptibility Testing Committees

Experts
(ECDC Networks, ESCMID Study Groups)
Industry

Contract 2011-14
EUCAST general organization

- National breakpoint committees and NACs
  - Nearly all countries in Europe have an active NAC and some non-European countries also have a NAC (Australia, US, Russia)
  - Other countries interested in NACs (South Africa, Brazil, Morocco..)

- EUCAST General Committee
  - representing 36 countries, also including non European countries

- EUCAST Steering committee (11 members)
  - Chairman, scientific secretary, clinical data coordinator
  - National breakpoint committee representatives:
    - BSAC (UK), CA-SFM (France), SRGA (Sweden)
    - CRG (The Netherlands), NWGA (Norway)
  - EUCAST General Committee representatives:
  - Visiting members (≤2) and observers (EMA, ECDC) at each meeting
National AST Committees (NACs), April 2014

- Yes
- In the process of forming a NAC
- No
- No information

Countries not on this map: Australia, Iceland, Israel, USA
EUCAST translations
Implementation of EUCAST breakpoints, April 2014

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

Countries not on the map: 
- Australia
- Iceland
- Israel
- USA
EUCAST-related publications

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

*January-April, 2014*
http://www.eucast.org visits (Q4, 2013)

<table>
<thead>
<tr>
<th>Top Countries</th>
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</table>

01 October 2013 – 31 December 2013

≈ 50,000 visitors/month (60% from Europe)

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

- home 46.5%
- clinical breakpoints 50.9%
- MIC/zone distributions 8.7%
- expert rules 5.8%
- publications 2.9%
- disk diffusion methods 2.2%

ESCMID Online Lecture Library © by author
### New and revised breakpoints

- **Enterobacteriaceae**  
  - Amox/clav (uncomplicated UTI only)  
  - Ciprofloxacin and *Salmonella* spp.  
  - Doripenem

- **P. aeruginosa**  
  - Doripenem

- **S. lugdunensis**  
  - Benzylpenicillin

- **Enterococcus** spp.  
  - Ciprofloxacin, levofloxacin (uncomplicated UTI)

- **H. influenzae**  
  - Cefaclor (removed)

- **M. catarrhalis**  
  - Cefaclor (removed)

- **Corynebacterium** spp.  
  - Different antimicrobials

### New screen tests

Rewording of supplementary tables and notes and new notes
An isolate reported as S in urine might be R in a systemic infection.

The laboratory might not know if the isolates is from uncomplicated or a complicated UTI.

EUCAST recommends reporting isolates using both “uncomplicated UTI only” and systemic breakpoints:

<table>
<thead>
<tr>
<th>MIC (mg/L)</th>
<th>Uncomplicated ITU</th>
<th>Systemic use</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤8</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>16-32</td>
<td>S</td>
<td>R</td>
</tr>
<tr>
<td>&gt;32</td>
<td>R</td>
<td>R</td>
</tr>
</tbody>
</table>
Rationale for amox-clav and UTI new breakpoint

- High concentration of amoxicillin-clavulanic acid in urine
- 2:1 fixed ratio produce lower MICs than a 2 mg/L fixed concentration

- No intermediate category in systemic breakpoint to allocate urine isolates
- Clinical results support higher breakpoints in UTI
  - an MIC of ≤32 mg/L predicts clinical cure

Oliver et al. AAC 1999; 43:862-7
Todd and Benfield Drugs 1990; 39:264-307; Ball IJAA 2007; 305:5113-7
EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance

Version 1.0
December 2013

EUCAST subcommittee for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance:
Christian G. Giske (Sweden, EUCAST Steering Committee and EARS-Net Coordination Group; chairman), Luis Martinez-Martinez (Spain, EUCAST Steering Committee), Rafael Cantón (Spain, chairman of EUCAST), Stefania Stefani (Italy), Robert Skov (Denmark, EUCAST Steering Committee), Youri Glupczynski (Belgium), Patrice Nordmann (France), Mandy Wootton (UK), Vivi Miriagou (Greece), Gunnar Skov Simonsen (Norway, EARS-Net Coordination Group), Helena Zemlickova (Czech republic, EARS-Net Coordination Group), James Cohen-Stuart (The Netherlands) and Marek Gniadkowski (Poland).
EUCAST subcommittee on resistance mechanisms

1. Introduction
2. Carbapenemase-producing Enterobacteriaceae
3. Extended-spectrum β-lactamase-producing Enterobacteriaceae
4. Acquired AmpC β-lactamase-producing Enterobacteriaceae
5. Methicillin resistant Staphylococcus aureus
6. Glycopeptide non-susceptible Staphylococcus aureus
7. Vancomycin resistant Enterococcus faecium and Enterococcus faecalis
8. Penicillin non-susceptible Streptococcus pneumoniae
9. Transparency declaration

Clinical response to carbapenems

- Susceptible (S)
- Intermediate (I)
- Resistant (R)
EUCAST subcommittee on resistance mechanisms

Screening cut-off for carbapenemase producing Enterobacteriaceae

<table>
<thead>
<tr>
<th>Carbapenem</th>
<th>MIC (mg/L)</th>
<th>Disk diffusion zone diameter (mm) with 10 µg disks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S/I breakpoint</td>
<td>Screening cut-off</td>
</tr>
<tr>
<td>Meropenem&lt;sub&gt;1&lt;/sub&gt;</td>
<td>≤2</td>
<td>&gt;0.12</td>
</tr>
<tr>
<td>Imipenem&lt;sub&gt;3&lt;/sub&gt;</td>
<td>≤2</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Ertapenem&lt;sub&gt;4&lt;/sub&gt;</td>
<td>≤0.5</td>
<td>&gt;0.12</td>
</tr>
</tbody>
</table>

<sup>1</sup> Best balance of sensitivity and specificity; <sup>2</sup> In some cases zone diameters for OXA-48 producers are up to 26 mm, so <27 mm may be used as a screening cut-off in countries where OXA-48 is endemic, but at the expense of lower.

Algorithm for phenotypic detection of carbapenemases

Meropenem <25 mm with disk-diffusion or MIC >0.12 mg/L in all Enterobacteriaceae

- Synergy with APBA/PBA only
  - KPC (or other class A carbapenemase)
- Synergy with APBA/PBA AND cloxacillin
- Synergy with DPA/EDTA only
  - Metallo-beta-lactamase (MBL)
- No synergy
  - ESBL plus porin loss AND OXA-48
New EUCAST guidance documents

EUCAST Guidance Documents in susceptibility testing

- Direct susceptibility testing (16 Feb 2012)
- Oral cephalosporins and Enterobacteriaceae breakpoints (16 Feb 2012)
- Stenotrophomonas maltophilia (1 Feb 2012)
- Burkholderia cepacia group (20 July, 2013)
- Breakpoints for topical use of antimicrobial agents (29 March, 2014)
Currently, it is not possible to recommend susceptibility testing of *B. cepacia* isolates to guide patient therapy.

Susceptibility testing is problematic:
- unlike gradient MIC or disk diffusion, **ISO broth microdilution** gives reproducible MIC results
- poor correlation between different methods

Difficult to establish correlations of MICs and clinical outcomes
- no evidence to describe a relationship between MIC and outcomes
- *B. cepacia* is frequently part of a mixed infection
- MIC distributions are wide and encompass the PK/PD breakpoints
- Superficial skin and external eye and ear infections but not for bowel decontamination or inhaled agents

- EUCAST has not found a consensus to resolve different opinions
  - use ECOFFs for agents when used topically
  - use clinical breakpoints when available and ECOFF when there are not clinical breakpoints

- Acceptable distributions are not available for all topical agents

- Only specific breakpoints for nasal decolonisation of *S. aureus* with mupirocin is supported with clinical data

- If tissue is involved the use of systemic treatment and systemic breakpoints should be considered
### Topical agents guidance document

- 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>Ofloxacin&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 (framycepin)</th>
<th>Bacitracin</th>
<th>Mupirocin</th>
<th>Retapamulin</th>
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<tr>
<td><strong>Enterobacteriaceae</strong></td>
<td>ECOFF</td>
<td>2</td>
<td>0.12</td>
<td>0.25</td>
<td>0.5</td>
<td>16</td>
<td>2</td>
<td>-</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Systemic clinical breakpoint</td>
<td>2/4</td>
<td>0.5/1</td>
<td>1/2</td>
<td>0.5/1</td>
<td>8/8</td>
<td>2/2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Acinetobacter spp.</strong></td>
<td>ECOFF</td>
<td>4</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>ND</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Systemic clinical breakpoint</td>
<td>4/4</td>
<td>1/1</td>
<td>1/2</td>
<td>1/2</td>
<td>2/2</td>
<td>-</td>
<td>ND</td>
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<td>-</td>
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<tr>
<td><strong>P. aeruginosa</strong></td>
<td>ECOFF</td>
<td>8</td>
<td>0.5</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>ND</td>
<td>-</td>
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<tr>
<td>Systemic clinical breakpoint</td>
<td>4/4</td>
<td>0.5/1</td>
<td>1/2</td>
<td>1/2</td>
<td>4/4</td>
<td>-</td>
<td>ND</td>
<td>-</td>
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<tr>
<td><strong>S. aureus</strong></td>
<td>ECOFF</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>16</td>
<td>-</td>
<td>0.5</td>
<td>1</td>
<td>ND</td>
<td>1/1&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.5</td>
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<tr>
<td>Systemic clinical breakpoint</td>
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<td>1/1</td>
<td>1/2</td>
<td>1/2</td>
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<td>-</td>
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<tr>
<td><strong>S. pneumoniae</strong></td>
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<td>-</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>8</td>
<td>-</td>
<td>32</td>
<td>ND</td>
<td>ND</td>
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<td>Systemic clinical breakpoint</td>
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<td>0.12/2</td>
<td>2/2</td>
<td>0.12/4</td>
<td>8/8</td>
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<tr>
<td><strong>β-haemolytic streptococci</strong></td>
<td>ECOFF</td>
<td>-</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>8</td>
<td>-</td>
<td>32</td>
<td>ND</td>
<td>ND</td>
<td>0.5</td>
<td>0.12</td>
</tr>
<tr>
<td>Systemic clinical breakpoint</td>
<td>-</td>
<td>-</td>
<td>1/2</td>
<td>-</td>
<td>8/8</td>
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<td>-</td>
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<tr>
<td><strong>H. influenzae</strong></td>
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<td>4</td>
<td>0.06</td>
<td>0.06</td>
<td>0.12</td>
<td>1</td>
<td>-</td>
<td>ND</td>
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</tr>
<tr>
<td>Systemic clinical breakpoint</td>
<td>IE</td>
<td>0.5/0.5</td>
<td>1/1</td>
<td>0.5/0.5</td>
<td>2/2</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
</tr>
<tr>
<td><strong>Moraxella spp.</strong></td>
<td>ECOFF</td>
<td>0.25</td>
<td>0.12</td>
<td>0.12</td>
<td>0.25</td>
<td>2</td>
<td>-</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>-</td>
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<tr>
<td>Systemic clinical breakpoint</td>
<td>IE</td>
<td>0.5/0.5</td>
<td>1/1</td>
<td>0.5/0.5</td>
<td>2/2</td>
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</tbody>
</table>

- = inappropriate combination; IE = insufficient evidence to set a clinical breakpoint; ND = No ECOFF defined on EUCAST MIC distribution website  
  1Agents also available for systemic use  
  2Breakpoints for nasal decontamination S≤1, R>256 mg/l.
New and ongoing **breakpoints (BP)** with
- EMA ceftobiprole, β-lactam-β-lactamase inhibitor combinations
  macrolides, tetracyclines, glycopeptides, oxazolidinones
  delamanid and other antimicobacterial agent
- CLSI colistin (under TATFAR initiative)
- NACs temocillin, nitroxoline, spiramycin, tigecycline, aztreonam
- Ciprofloxacin and *N. meningitidis*
- *N. gonorrhoeae* and various antimicrobials
- Daptomycin and enterococci
- Organisms-agent combinations lacking clinical data supporting BP

**New RD documents** (new agents and new RD due to revised BP)

**New documents, technical notes / guidance documents**
- new version of expert rules (v3)
- dissociated clindamycin resistance (staphylococci and streptococci)
- SOPs (format and revision of EUCAST documents, …)
### Latest Changes

<table>
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<tr>
<th>Title</th>
<th>Description</th>
<th>Major</th>
<th>Minor</th>
<th>Date</th>
</tr>
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<tr>
<td>EUCAST AFST membership changes</td>
<td>The description of the EUCAST AFST Subcommittee has been updated.</td>
<td>✔</td>
<td>✔</td>
<td>2014/04/21</td>
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<tr>
<td>Consultation on MIC determination of conferring mutants</td>
<td>See EUCAST news-flow for consultation document and response form.</td>
<td>✔</td>
<td></td>
<td>2014/04/16</td>
</tr>
<tr>
<td>Czech translations of EUCAST documents</td>
<td>Czech translations of EUCAST documents available on the Czech NAC homepage.</td>
<td>✔</td>
<td>✔</td>
<td>2014/03/19</td>
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<tr>
<td>The EUCAST Disk Diffusion Test published</td>
<td>The EUCAST Disk diffusion test published in CMI.</td>
<td>✔</td>
<td>✔</td>
<td>2014/03/14</td>
</tr>
<tr>
<td>New FAQ (updated from March 2013 to February 2014)</td>
<td>The FAQ document has undergone a major revision. New questions and answers have been added and other Q&amp;As have been revised.</td>
<td>✔</td>
<td>✔</td>
<td>2014/02/26</td>
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<tr>
<td>EUCAST SOP 7.0 Preparation and handling of samples</td>
<td>Another EUCAST SOP published. This describes how minutes are prepared and handled inside the organisation of EUCAST.</td>
<td>✔</td>
<td>✔</td>
<td>2014/01/22</td>
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</table>
Acknowledgements

More information:

- Next lecturers at this workshop!
- **Monday 12 May, 07.45 - 8.45 Hall D**
  Meet the Experts: EUCAST frequently asked questions
- **Monday 12 May, 12.45 - 14.15 CCIB/Room 122/123**
  EUCAST General Committee meeting
- **Monday 12 May, 16.30 - 18:00, CCIB/Room 122/123**
  EUCAST Subcommittee on Antifungal Susceptibility Testing (ASFT) General Committee meeting
- **Saturday 10 May – Tuesday 13 May**
  EUCAST at the ESCMID Booth. EUCAST presentations