EUCAST update

Christian G. Giske, MD/PhD
Chair of EUCAST
Professor/Chief consultant physician
Karolinska Institutet and
Karolinska University Hospital
April 2020
Johan W. Mouton 1956-2019

Obituary Prof. dr. Johan Willem Mouton

Johan Mouton died in the evening of July 9th, 2019, at the age of 62. Johan was a passionate and inspiring microbiologist who played a leading role in pharmacokinetics and pharmacodynamics on the international scene. He was a husband, a father, a friend, a colleague, a fellow scientist and to us, a brother in arms. Only once did he give up – on the evening of the 9th of July.

Completing his medical studies he graduated in 1988, and then started his training in Medical Microbiology at the Erasmus University in Rotterdam. He completed a PhD in pharmacokinetics and what in those days was a new field of pharmacodynamics (PK/PD). He was soon fascinated by the art of mathematical modeling. In his capacity as a clinical microbiologist he worked in Nijmegen at both the Canisius-Wilhelmina Hospital and Radboud University Medical Centre and in Rotterdam at the Erasmus MC.

To Johan research was a passion and together with fellow scientists he published many articles. He also enjoyed teaching and lecturing and early on became an asset both in national Dutch societies and committees and on the international scene. His role in the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and its yearly congress, ECCMID, cannot be overestimated. In the finest ESCMID tradition Johan involved himself in study groups, guidelines writing, summer school and postgraduate courses and he allowed ESCMID and ECCMID to occupy much of his thoughts and his spare time. He was one of the original members of the European Committee of Antimicrobial Susceptibility Testing (EUCAST) and shared the success of bringing EUCAST to all European countries and to many outside Europe. He missed only one steering committee meeting between joining in 2002 and 2019 - he could not make the last one, he wanted to, he tried to but could not – he died on the evening of the last day of the 90th committee meeting. But even so, he needed to talk to us on the phone during the meeting. Johan was very important to EUCAST, and EUCAST was very important to Johan.

Our thoughts are with Anouk, Jaap, his parents and relatives.

Johan’s friends and colleagues in ESCMID and EUCAST.

Johan Willem Mouton

Johan Mouton was a world leader in pharmacokinetics and pharmacodynamics and antimicrobial resistance. He died on July 9, 2019.

Johan Mouton liked to keep moving. The start of the week might find him in Stockholm, giving a lecture. On Tuesday, back to Rotterdam, where he ran a research unit at the Department of Medical Microbiology and Infectious Diseases at Erasmus University Medical Centre. You knew he was there from his laugh, spilling...
New EUCAST PK-PD experts

Joseph Meletiadis, Greece

Shampa Das, UK
EUCAST SC 2019

• Christian G. Giske, chair
• John Turnidge, scientific secretary
• Rafael Canton, clinical data coordinator
• Gunnar Kahlmeter, technical data coordinator/webmaster
• Shampa Das, PK-PD expert
• Joseph Meletiadis, PK-PD expert
• Sören Gatermann, Germany
• Christoffer Lindemann, Norway
• Alasdair MacGowan, UK
• Gerard Lina, France
• Efi Petinaki, Greece
• Cidália Pina Vaz, Portugal
• Two new will be recruited in 2020
Implementation of EUCAST breakpoints/guidelines, February 2020

% Laboratories on EUCAST guidelines:
- >90%
- 50-90%
- 10-50%
- <10%
- Information lacking

Countries not on the map: Australia, Brazil, China, Canada, Iceland, Israel, Malta, Morocco, New Zealand, South Africa, USA.
**Disk diffusion as main AST method, February 2020**

% Laboratories on disk diffusion as main method

- **>90%**
- **50-90%**
- **10-50%**
- **<10%**
- **Information lacking**

Other countries: Australia, Brazil, China, Canada, Iceland, Israel, Malta, Morocco, New Zealand, South Africa, USA
EUCAST Subcommittees

• **STANDING**
  – Antifungal susceptibility testing
  – Veterinary susceptibility testing
  – Antimycobacterial susceptibility testing

• **AD HOC**
  – Intrinsic resistance and expert rules
  – MIC distributions and ECOFFs
  – Joint working group with CLSI on disk mass development and QC criteria
  – Relationship between WGS (NGS) and phenotypic susceptibility testing
  – Anaerobic AST
  – Detection of resistance mechanisms
  – Polymyxins breakpoints and methods (joint with CLSI)
Breakpoint consultations 2019

**Finalised**

1. Aminoglycoside breakpoints
2. Moving WT of some species (mainly *P. aeruginosa*) into the I-group
3. Update of expert rules
4. *B. pseudomallei* breakpoints
5. Temocillin
6. Mecillinam – expansion of species with breakpoints for UTI

**Upcoming (2020)**

1. Fosfomycin
2. Piperacillin-tazobactam and Enterobacterales
3. Oral aminopenicillin breakpoints for Enterobacterales
4. Breakpoints for endocarditis
5. Meningitis breakpoints
The EUCAST Development Laboratory

- Developing EUCAST breakpoint table v 10.0 (published January 2020)
- Developing disk diffusion criteria for novel agents
- AST for *B. pseudomallei* (completed), *Nocardia* spp. and *Vibrio* spp.
- Rapid AST directly from blood culture bottles – continued work with more antimicrobials and species (*Acinetobacter* spp.)
- Disk diffusion methodology for rapidly growing anaerobes ongoing
- AST for fosfomycin, temocillin, beta-lactams vs *H. influenzae*
- Colistin gradient tests with addition of Ca²⁺
- *S. pneumoniae* and benzylpenicillin gradient tests
Rapid AST directly from blood culture bottles

EUCAST has published recommendations for short incubation (4, 6 and 8 hours) AST directly from positive blood culture bottles:

- direct inoculation of disk diffusion plates (MH, MH-F) using 100 - 150 μL directly from a positive blood culture bottle (BD, bioMérieux and Thermo Fisher).
- no centrifugation or dilution of the inoculum - streak plates as for standard EUCAST disk diffusion.
- shortened incubation - 4, 6 and 8 hours with breakpoints adapted to each incubation time.
- zone diameters are read from the front of the plate after removal of the lid.
- breakpoints for each species and each reading time.
- identity of species must be known prior to interpretation of AST results.
- the method is currently validated for the following species.
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Pseudomonas aeruginosa*
  - *Staphylococcus aureus*
  - *Streptococcus pneumoniae*
  - *Enterococcus faecalis and Enterococcus faecium*
  - Acinetobacter baumannii (added 2 May, 2019)
PCG gradient tests underestimate MICs

Comparison of gradient test MICs from Swedish laboratories with BMD from EDL

<table>
<thead>
<tr>
<th>Comparison reference MIC</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2 dilutions lower</td>
<td>3</td>
<td>4.4</td>
</tr>
<tr>
<td>2 dilutions lower</td>
<td>10</td>
<td>14.7</td>
</tr>
<tr>
<td>1 dilution lower</td>
<td>32</td>
<td>47.1</td>
</tr>
<tr>
<td>Identical</td>
<td>18</td>
<td>26.5</td>
</tr>
<tr>
<td>1 dilution higher</td>
<td>3</td>
<td>4.4</td>
</tr>
<tr>
<td>2 dilutions higher</td>
<td>2</td>
<td>2.9</td>
</tr>
<tr>
<td>&gt;2 dilutions higher</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Within Essential Agreement</td>
<td>53</td>
<td>77.9</td>
</tr>
</tbody>
</table>

Preliminary conclusion: Etest (other gradient tests are being evaluated) underestimates benzylpenicillin MICs. This seems to be most pronounced with higher MICs.
### Example Enterobacterales

<table>
<thead>
<tr>
<th>Aminoglycosides</th>
<th>MIC breakpoints (mg/L)</th>
<th>Disk content (µg)</th>
<th>Zone diameter breakpoints (mm)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S ≤ R &gt; ATU</td>
<td>S ≥ R &lt; ATU</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amikacin (systemic infections)</td>
<td>(8)²</td>
<td>30</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Amikacin (UTI only)</td>
<td>8</td>
<td>30</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Gentamicin (systemic infections)</td>
<td>(2)²</td>
<td>10</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Gentamicin (UTI only)</td>
<td>2</td>
<td>10</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Netilmicin</td>
<td>E</td>
<td>10</td>
<td>E</td>
<td>E</td>
</tr>
<tr>
<td>Tobramycin (systemic infections)</td>
<td>(2)²</td>
<td>10</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Tobramycin (UTI only)</td>
<td>2</td>
<td>10</td>
<td>17</td>
<td>17</td>
</tr>
</tbody>
</table>

**Dosages**

<table>
<thead>
<tr>
<th>Aminoglycosides</th>
<th>Standard dose</th>
<th>High dose</th>
<th>Special situations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>30 mg/kg x 1 iv</td>
<td></td>
<td>Enterobacterales: High dose only.</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>7 mg/kg x 1 iv</td>
<td></td>
<td>Enterobacterales: High dose only.</td>
</tr>
<tr>
<td>Netilmicin</td>
<td>7 mg/kg x 1 iv</td>
<td></td>
<td>Enterobacterales: High dose only.</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>7 mg/kg x 1 iv</td>
<td></td>
<td>Enterobacterales: High dose only.</td>
</tr>
</tbody>
</table>
Debate on the new definition of "I"

Point-Counterpoint: Differences between the European Committee on Antimicrobial Susceptibility Testing and Clinical and Laboratory Standards Institute Recommendations for Reporting Antimicrobial Susceptibility Results

Gunnar Kahlmeter, Christian G. Giske, Thomas J. Kirn, Susan E. Sharp

TABLE 1 Definitions of the I group

<table>
<thead>
<tr>
<th>Interpretive category (abbreviation)</th>
<th>Status</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate (I)</td>
<td>EUCAST previous definition (in common with CLSI)</td>
<td>A microorganism is defined as intermediate by a level of antimicrobial agent activity associated with uncertain therapeutic effect. It implies that an infection due to the isolate may be appropriately treated in body sites where the drugs are physically concentrated or when a high dosage of the drug can be used; it also indicates a buffer zone that should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations.</td>
</tr>
<tr>
<td>Susceptible, increased exposure* (I)</td>
<td>EUCAST new definition (not shared with CLSI)</td>
<td>A microorganism is categorized as &quot;susceptible, increased exposure*&quot; when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.</td>
</tr>
</tbody>
</table>

*Exposure is a function of how the mode of administration, dose, dosing interval, and infusion time as well as the distribution and excretion of the antimicrobial agent will influence the infecting organism at the site of infection.
For several agents, in v. 10.0 of the breakpoint tables, EUCAST has introduced breakpoints which categorise wild-type organisms (organisms without phenotypically detectable acquired resistance mechanisms to the agent) as "Susceptible, increased exposure (I)" instead of "Susceptible, standard dosing regimen (S)". In v. 9.0, these are listed as agent\textsuperscript{HE} to emphasize the need for high exposure (HE). Following efforts to explain and inform colleagues in clinical microbiology, colleagues involved in treatment and in forming antimicrobial policies and stewardship, laboratories are encouraged to implement the new standard as soon as possible but no later than at the end of 2020. During the transition, it is possible to continue to use breakpoints in table v. 9.0 for breakpoints highlighted in light green in v. 10.0.

- It won’t get better than I for \textit{P. aeruginosa} vs:
  - Piperacillin-tazobactam
  - Ceftazidime
  - Cefepime
  - Imipenem
  - Ciprofloxacin
  - Levofloxacin

- The following drugs can still be reported as S:
  - Ceftazidime-avibactam
  - Ceftolozane-tazobactam
  - Meropenem
  - Meropenem-vaborbactam

- Logical consequence of redefinition of the I-group (with stewardship challenges)
## The new *B. pseudomallei* breakpoints

### Burkholderia pseudomallei

**Expert Rules and Intrinsic Resistance Tables**

**Burkholderia pseudomallei EUCAST Clinical Breakpoint Tables v. 10.0, valid from 2020-01-01**

<table>
<thead>
<tr>
<th>Penicillins</th>
<th>MIC breakpoints (mg/L)</th>
<th>Disk content (µg)</th>
<th>Zone diameter breakpoints (mm)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amoxicillin-clavulanic acid</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>S ≤ R &gt; ATU</td>
<td>20-10</td>
<td>50 ≥ R &lt; ATU</td>
<td>Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>MIC breakpoints (mg/L)</td>
<td>Disk content (µg)</td>
<td>Zone diameter breakpoints (mm)</td>
<td>Notes</td>
</tr>
<tr>
<td><strong>Cefazidime</strong></td>
<td>S ≤ R &gt; ATU</td>
<td>19</td>
<td>50 ≥ R &lt; ATU</td>
<td>Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>MIC breakpoints (mg/L)</td>
<td>Disk content (µg)</td>
<td>Zone diameter breakpoints (mm)</td>
<td>Notes</td>
</tr>
<tr>
<td><strong>Imipenem</strong></td>
<td>S ≤ R &gt; ATU</td>
<td>19</td>
<td>29 ≥ R &lt; ATU</td>
<td>Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.</td>
</tr>
<tr>
<td><strong>Meropenem</strong></td>
<td>S ≤ R &gt; ATU</td>
<td>19</td>
<td>24 ≥ R &lt; ATU</td>
<td>Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>MIC breakpoints (mg/L)</td>
<td>Disk content (µg)</td>
<td>Zone diameter breakpoints (mm)</td>
<td>Notes</td>
</tr>
<tr>
<td><strong>Doxycycline</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>S ≤ R &gt; ATU</td>
<td>Note&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.</td>
</tr>
<tr>
<td><strong>Tetracycline (screen)</strong></td>
<td>NA</td>
<td>30</td>
<td>50 ≥ R &lt; 25</td>
<td>1. Occasionally used in the treatment of melioidosis (consult with an expert before starting therapy, as dosing is critical). 2. For susceptibility testing purposes, the concentration of clavulanic acid is fixed at 2 µg/L.</td>
</tr>
</tbody>
</table>

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<sup>1</sup> Numbers relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.

---

1. Occasionally used in the treatment of melioidosis (consult with an expert before starting therapy, as dosing is critical).
2. For susceptibility testing purposes, the concentration of clavulanic acid is fixed at 2 µg/L.

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**EUCAST Clinical Breakpoint Tables v. 10.0, valid from 2020-01-01**

**Medium:** Mueller-Hinton broth

**Inoculum:** 5x10<sup>8</sup> CFU/mL

**Incubation:** Air, 35±1°C, 18±2h

**Reading:** Unless otherwise stated, read MICs at the lowest concentration of the agent that completely inhibits visible growth.

**Quality control:** Pseudomonas aeruginosa ATCC 27853. For agents not covered by this strain, see EUCAST QC Tables.
Temocillin breakpoints

EUCAST General Consultation on breakpoints for Temocillin

Consultation period 11 October 2019 – 30 November 2019

This is a general consultation on proposed breakpoints for temocillin. Breakpoints are proposed for a limited range of species of Enterobacterales, namely those commonly associated with urinary tract infection. Temocillin is registered in a small number of European countries for the following indications: complicated urinary tract infection, bacteraemia, lower respiratory tract infections and wound infections. It is often considered as a non-carbapenem option for treating infections caused by Enterobacterales harbouring extended-spectrum beta-lactamases.

The proposed breakpoints apply only in the setting of maximum dosing (2g 8-hourly iv) and therefore isolates with MICs less than or equal to 16 mg/L will be reported as “I”, Susceptible – Increased exposure.

The draft rationale document below outlines the reasons for the selection of proposed breakpoints. Also appended are recent MIC and zone diameter data from the EUCAST Development Laboratory, which also support the proposals.

<table>
<thead>
<tr>
<th>Enterobacterales</th>
<th>Current MIC Breakpoint (mg/L)</th>
<th>Proposed MIC Breakpoint (mg/L)</th>
<th>Current ZD Breakpoint (mm)</th>
<th>Proposed ZD Breakpoint (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S ≤</td>
<td>R &gt;</td>
<td>S ≤</td>
<td>R &gt;</td>
</tr>
<tr>
<td><strong>Temocillin</strong></td>
<td>-</td>
<td>-</td>
<td>&lt;0.001</td>
<td>16</td>
</tr>
</tbody>
</table>

*Zone diameter correlates will be made available in the EUCAST breakpoint table v 10.0 (2020)
EUCAST-AFST Activities
Chairman’s report

April 2020
Full subcommittee report available online
Comments and Qs welcomed

Chairman Maiken Cavling Arendrup (maiken.c.arendrup@escmid.org)
Scientific Secretary Jesus Guinea Ortega (jesusguineaortega@escmid.org)
Clinical Data Coordinator Joseph Meletiadis (joseph.meletiadis@escmid.org)
Chairman’s report: Meetings

• AFST General Committee Meetings
  – Sunday 14/4 at 16:00 to 18:00, RAI Amsterdam, NL

• AFST Steering Committee Meetings
  – 21st April 2019 during ECCMID RAI Amsterdam, NL
  – 15th-16th July 2019, Copenhagen, DK
  – 16th-17th January 2020, Malmö, SE
Chairman’s report: Organisation

AFST SC organisation 2019-20 (SOP 4.3)

<table>
<thead>
<tr>
<th>Role</th>
<th>Appointed by</th>
<th>Appointed for</th>
<th>Name and year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chairman</td>
<td>EUCAST SC</td>
<td>3 y with possible reappointment</td>
<td>Maiken Cavling Arendrup 2017-20</td>
</tr>
<tr>
<td>Secretary</td>
<td>EUCAST SC + AFST Chair</td>
<td>3 y with possible reappointment</td>
<td>Jesús Guinea (ES) 2019-22</td>
</tr>
<tr>
<td>Data coordinator</td>
<td>EUCAST SC + AFST Chair</td>
<td>3 y with possible reappointment</td>
<td>Joseph Meletiadis 2017-20</td>
</tr>
<tr>
<td>NAC representative 1</td>
<td>EUCAST SC + AFST</td>
<td>2 y (even years) new countries have priority</td>
<td>Mihai Mares (RO) (end of term 2020)</td>
</tr>
<tr>
<td>NAC representative 2</td>
<td>EUCAST SC + AFST</td>
<td>2 y (odd years) new countries have priority</td>
<td>Nathalie Friberg (FI) (end of term 2021)</td>
</tr>
<tr>
<td>EUCAST SC representative</td>
<td>EUCAST SC</td>
<td>Not defined</td>
<td>Johan Mouton → Gunnar Kahlmeter</td>
</tr>
</tbody>
</table>

MC Arendrup (chair), J Guinea (secretary), J Meletiadis (data coordinator), G Kahlmeter (EUCAST SC repr.), M Mares & N Friberg (NACs)
Chairman’s report: Organisation

EUCAST Network Laboratories document

• 11 EUCAST Network Laboratories contact persons:
  – Jesús Guinea (Spain), Eric Dannaoui (France), Caroline Moore (UK), Manuel Cuenca-Estrella (Spain), Oliver Kurzai (Germany), Wendy van de Sande (Netherlands), Joseph Meletiadis (Greece), Aristeia Velegraki (Greece), Paul E. Verweij (Netherlands), Cornelia Lass-Flörl (Austria), Mihai Mares (Romania), Francesco Barchiesi (Italy), Michela Paolucci (Italy), Katrien Lagrou (Belgium).

• EUCAST Development Laboratory for fungi:
  – Maiken Cavling Arendrup, Statens Serum Institute, Unit for Mycology, building 211, 1st floor, Artillerivej 5 DK-2300 Copenhagen S, Denmark

http://www.eucast.org/organization/network_laboratories/
Chairman’s report: New Methods and QC

1. Alternative methods for echinocandin versus *Aspergillus* testing
   1. Colorimetric microdilution MIC determination (JAC in press)
   2. Echinocandin agar screening (PMID: 31106352)

2. Dermatophyte testing
   1. EUCAST microdilution method established (JAC in press)

3. QC table update, available at EUCAST.org
   - Include a one-page overview
   - QC strains now deposited and available from
     - [https://ccug.se/](https://ccug.se/) (Culture Collection of Gothenburg Univ.)
     - except ATCC strains (available from [www.atcc.org](http://www.atcc.org))
New/Updated BP doc.s - Revised “I”

1. Clinical breakpoint table v 10.0
   Revised BPs, ATU explanation, new dosage table
2. Overview of antifungal ECOFFs and clinical breakpoints for yeasts and moulds v 1.0
   Including ECOFFs for species without BPs → wt versus non-wt interpretation

Rationale documents: more species included & implementation of the revised “I” .....
Chairman’s report: Publications

Methods

Arendrup, Maiken; Jørgensen, Karin Meinike; Guinea, Jesus; Lagrou, Katrien; Chryssanthou, E.; Hayette, Marie-Pierre; Barchiesi, Francesco; Lass-Flörli, Cornelie; Hamal, Pétri; Dannaoui, Eric; Chowdhary, Anuradha; Meletiadis, Joseph. Multicentre validation of an EUCAST method for the antifungal susceptibility testing of microconidia-forming dermatophytes. J Antimicrob Chemother. 2020 In press

Joseph Meletiadis; Maria Siopi; Lamprini Kanioura; Karin Meinike Jørgensen; David Perlin; Johan Mouton; Maiken C. Arendrup. A multicentre study for optimizing echinocandin susceptibility testing of Aspergillus species with the EUCAST methodology and a broth microdilution colorimetric method. J Antimicrob Chemother. 2020 In press


Breakpoints PK/PD research publications


Documents on www.eucast.org

Revised Clinical BP table
New ECOFF & BP summary table
Eight revised Rationale documents
EUCAST AFST subcommittee

Steering Committee
MC Arendrup, Chair (Denmark)
J Guinea, Secretary (Spain)
J Meletiadis, Data coordinator (Greece)
F Barchiesi (Italy)
P Hamal (Czech Republic)
J Mouton (EUCAST-SC)

General committee
MC Arendrup (Denmark)
S Arikan-Akdagli (Turkey)
F Barchiesi (Italy)
M Castanheira (The US)
E Chryssanthou (Sweden)
J Guinea (Spain)
P Hamal (Czech Republic)
H Järv (Estonia)
N Friberg (Finland)
O Kurzai (Germany)
K Lagrou (Belgium)
C Lass-Flörl (Austria)
O Lortholary (France)
M Mares (Romania)
T Matos (Slovenia)
C Moore (UK)
K Muehlethaler (Switzerland)
N Klimko (Russia)
T Rogers (Ireland)
C Torp Andersen (Norway)
A Velegraki (Greece)
?? (The Netherlands)
VetCAST status

Peter Damborg, Chair of VetCAST,
University of Copenhagen
<table>
<thead>
<tr>
<th>Drug/Species</th>
<th>ECOFF or TECOFF</th>
<th>PK/PD Cut off</th>
<th>Prot. binding</th>
<th>PK/PD index</th>
<th>Rationale document on EUCAST homepage</th>
<th>CBP on EUCAST homepage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Florfenicol / Calves</td>
<td><em>P. multocida</em></td>
<td>yes</td>
<td>yes</td>
<td>Time kill curve</td>
<td>completed</td>
<td>Awaiting method validation</td>
</tr>
<tr>
<td></td>
<td><em>M. haemolytica</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marbofloxacin / Horses</td>
<td><em>E. coli</em></td>
<td>yes</td>
<td>yes</td>
<td>literature</td>
<td>in progress</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Strep. equi</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin/ clavulanic acid in dogs</td>
<td>PK data generation</td>
<td>data generation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefazolin / dog</td>
<td><em>Staph. pseudintermedius</em></td>
<td>yes</td>
<td>yes</td>
<td>literature</td>
<td>in progress</td>
<td></td>
</tr>
<tr>
<td>Oxytetracycline / cattle</td>
<td>PK data modelling</td>
<td></td>
<td></td>
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</tbody>
</table>

- Also “side projects” on mink and sheep
- At least 3 pharmaceutical companies have provided PK data
- MIC data generated from several of our own projects – ECOFFs pending
ENOVAT

- **European Network for Optimization of Veterinary Antimicrobial Treatment**
- COST Action network involving >180 persons from almost 40 countries
- WG2 and WG3 working towards establishing CBPs
- **VetCAST will grow as** young scientists and countries in Eastern Europe shall be highly involved in ENOVAT research and training
Guideline on when to use which breakpoint

• Veterinary diagnostic labs currently use many different interpretive criteria for AST

• Aim: to help diagnostic labs choose the most appropriate interpretive criteria through a new guideline

• As a first step, a VetCAST expert group is compiling currently available interpretative criteria of specific antimicrobial/indication combinations for common pathogens of livestock and companion animals

• Deadline: guideline should be ready in 2020
Training activities

• A VetCAST workshop on clinical breakpoint determination was held in London in June 2019.

• A couple of VetCAST presentations and training events in 2020 were planned but have been postponed/cancelled due to COVID-19

• We anticipate (at least) the following joint VetCAST/ENOVAT training schools in the years to come:
  – Early 2021: Basic PK/PD concepts (RVC, London)
  – Early 2022: PK/PD modelling (likely in Bulgaria)
  – Late 2022: Basic PK/PD concepts (Toulouse)
  – Early 2023: Population PK / Monte-Carlo simulation (likely in France or Bulgaria)

• When co-arranged with ENOVAT - to fulfill COST Action rules - a main target audience must be early career investigators and people from less-resourceful countries of Europe.
Publications

2 new papers submitted on behalf of VetCAST to JVPT:


2 new papers published in the context of VetCAST:


Antimycobacterial Subcommittee
Update April 2020

Chair: Emmanuelle Cambau
Scientific Secretary: Thomas Schön
AMST (Anti-Mycobacterial Susceptibility Testing) 2019/2020

• AMST SC meetings
  • Malmö, Sweden at the same venue as EUCAST SC: 3rd of February 2020
  • Teleconferences: 3rd of September 2019 and 11th of November 2020

• Representation
  • WHO expert group meeting on breakpoints for first-line drugs, Geneva, February 2020
  • ERL-TB-network meeting, January 2020

• Workshop on the EUCAST reference method in Malmö; 3-4th of February 2020
  • AMST GC invited as well as academic and commercial stakeholders.
  • Planning for several projects initiated on setting ECOFFs in the reference method in collaboration with EUCAST AMST laboratories and EUCAST EDL.
AMST (Anti-Mycobacterial Susceptibility Testing) 2019/2020

• Publication of rationale documents for Bedaquiline and Delamanid
• Publication of the EUCAST reference method for the M. tuberculosis complex and a calibration SOP
Future activities - AMST

• **EUCAST reference method on MIC determination for *M. tuberculosis***
  • Facilitating the generation of MIC data in the reference method
  • Coordination of requests for generating MIC data within the AMST network
  • QC-ranges, ECOFFs and clinical breakpoints for new and existing agents
  • Technical support and development of standardized procedures to regulate COIs
  • Interaction through EMA: pretomanid

• Submission of manuscripts on the reference method and guidance on how to use it

• **ECOFF and AST reference method for non-tuberculous mycobacteria (NTM)**
  • MIC-distributions and ECOFFs from AMST laboratories
  • Oral presentation accepted for ECCMID 2020
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  • MIC-distributions and ECOFFs from AMST laboratories
  • Oral presentation accepted for ECCMID 2020
EUCAST Development Laboratory (EDL) Update April 2020

Erika Matuschek
Gunnar Kahlmeter

EUCAST General Committee Meeting 2020
Breakpoint Tables v 10.0

• New zone diameter breakpoints for
  – Eravacycline 20 µg
  – Tedizolid 2 µg

• Updated screening algorithm for beta-lactam resistance in *H. influenzae* with amoxicillin-clavulanic acid (AMC)
  – β-lactamase positive isolates with AMC 2-1 µg ≥15 mm can be reported susceptible for penicillins with beta-lactamase inhibitors (susceptible increased exposure for AMC oral), cephalosporins and carbapenems for which EUCAST breakpoints are available
RAST Breakpoint Table v. 2.0

- All breakpoint changes implemented in EUCAST Breakpoint Tables v 10.0 were implemented in RAST 2.0.

- Breakpoints for the following additional agents are introduced in RAST 2.0.
  - Ceftazidime-avibactam
  - Ceftolozane-tazobactam
  - Imipenem
  - Levofloxacin
  - Trimethoprim-sulfamethoxazole
SOP on disk potency selection

• Common criteria by EUCAST and CLSI on how to perform studies to select the optimal disk content (potency) for disk diffusion testing of new antimicrobial agents. The agreed and identical criteria will be included in EUCAST and CLSI documents.
  - EUCAST: SOP 11.0
  - CLSI: Addendum to M23

• Expected publication in June 2020.
New organisms and new agents
Finalized or ongoing

• EUCAST criteria for new organisms and agents
  – *Burkholderia pseudomallei*
    • Methods and breakpoints (EUCAST Breakpoint Tables v 10.0)
  
  – MIC and zone diameter breakpoints for new antimicrobial agents (to be published as addendums during 2020):
    • Cefiderocol
    • Temocillin
    • Lefamulin
On-going work

• Organisms currently without EUCAST breakpoints or formal method
  – *Nocardia* spp.
  – *Bacillus* spp.
  – *Achromobacter xylosoxidans*
  – *Vibrio* spp. (non-cholerae)

• Criteria for several new agents in preparation
The EUCAST rapid disc diffusion method for antimicrobial susceptibility testing directly from positive blood culture bottles

Emma Jonasson¹*, Erika Matuschek² and Gunnar Kahlmeter¹,²

¹Department of Clinical Microbiology, Central Hospital, Växjö, Sweden; ²EUCAST Development Laboratory, Växjö, Sweden

ORIGINAL ARTICLE

EUCAST evaluation of 21 brands of Mueller–Hinton dehydrated media for disc diffusion testing

J. Åhman*, E. Matuschek, G. Kahlmeter

EUCAST Development Laboratory, Växjö, Sweden
Support and educational activities

• Questions from laboratories around the world via e-mail and phone

• Visitors and Observers from laboratories and industry

• Troubleshooting for QC strains and clinical isolates

• Phenotypic confirmatory testing of unusual results
Acknowledgements

• The EDL staff: Gunnar Kahlmeter, Erika Matuschek, Jenny Åhman, Onur Karatuna, Sarah Johansson and Emma Jonasson

• EUCAST Network Laboratories (http://www.eucast.org/organization/network_laboratories/)

• Investigators contributing with isolates and data

• Clinical laboratories participating in multi-laboratory trials