EUCAST
EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

BrCAST
Brazilian Committee on Antimicrobial Susceptibility Testing

EUCAST 2017: Quais são as novidades e quais as diferenças em relação ao CLSI 2017?

Sao Paulo, May 27, 2017

SaludMadrid

Dr. Rafael Cantón

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SERVICIO DE MICROBIOLOGÍA Y PARASITOLOGÍA

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Departamento de Microbiología II
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EUCAST

EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases


Agenda Missão e Objetivo Documentos Versões anteriores Organização Perguntas Frequentes Links Eventos Fale Conosco
BrCAST
Brazilian Committee on Antimicrobial Susceptibility Testing
Pesquisar
Pesquisar
I Encontro Internacional BrCAST e EUCAST
Hotel Renaissance - São Paulo - SP / Dia 05 de Março de 2016, de 9h00 às 16h00
INSCRIÇÕES ONLINE ENCERRADAS
Ainda há vagas disponíveis para inscrições no local do evento. A secretaria do evento abrirá às 7:30.
O pagamento poderá ser feito em cheque, dinheiro ou cartão.

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

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search term

www.eucast.org

- Organization
- EUCAST News
- Clinical breakpoints
- Expert rules and intrinsic resistance
- Resistance mechanisms
- Guidance documents
- Consultations
- MIC distributions and ECOFFs
- Zone distributions and ECOFFs
- AST of bacteria
- AST of mycobacteria
- AST of fungi
- AST of veterinary pathogens
- Frequently Asked Questions (FAQ)
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Website changes

04 May 2017

The European Committee on Antimicrobial Susceptibility Testing - EUCAST

EUCAST is a standing committee jointly organized by ESCMID, ECDC and European national breakpoint committees. EUCAST was formed in 1997. It has been chaired by Ian Phillips (1997 - 2001), Gunnar Kahlmeter (2001 - 2012), Rafael Canton 2012 - 2016) and Christian Giske (2016 -). Its scientific secretary is Derek Brown (1997 - 2016) and John Turnidge (2016 -). Its webmaster is Gunnar Kahlmeter (2001 -). From 2016, Rafael Canton is the Clinical Data Co-ordinator and Gunnar Kahlmeter the Technical Data Co-ordinator.

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 countries, FESCI and ISC. The Steering Committee also consults on EUCAST proposals with experts within the fields of infectious diseases and microbiology, pharmaceutical companies and susceptibility testing device manufacturers.

EUCAST has several subcommittees - → see page Subcommittees.

Most antimicrobial MIC breakpoints in Europe have been harmonised by EUCAST. Breakpoints for new agents are set as part of the licensing process for new agents through EMA. EUCAST breakpoints are available in devices for automated susceptibility testing but with some limitations, depending on the system. A disk diffusion susceptibility test method → calibrated to EUCAST MIC breakpoints is also available.

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

To cite the EUCAST website or a document on the EUCAST website: List the document name, version, year and the full web adress. For example, if you want to refer to the current EUCAST breakpoint table, the citation reads The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, version 7.1, 2017, http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_7.1_Bre

Copyright

QUICK NAVIGATION

EUCAST News

04 May 2017
Posaconazole RD for Candida and Aspergillus merged and updated.

19 Apr 2017
EUCAST Posters at ECCMID 2017

18 Apr 2017
EUCAST General Co… Agenda

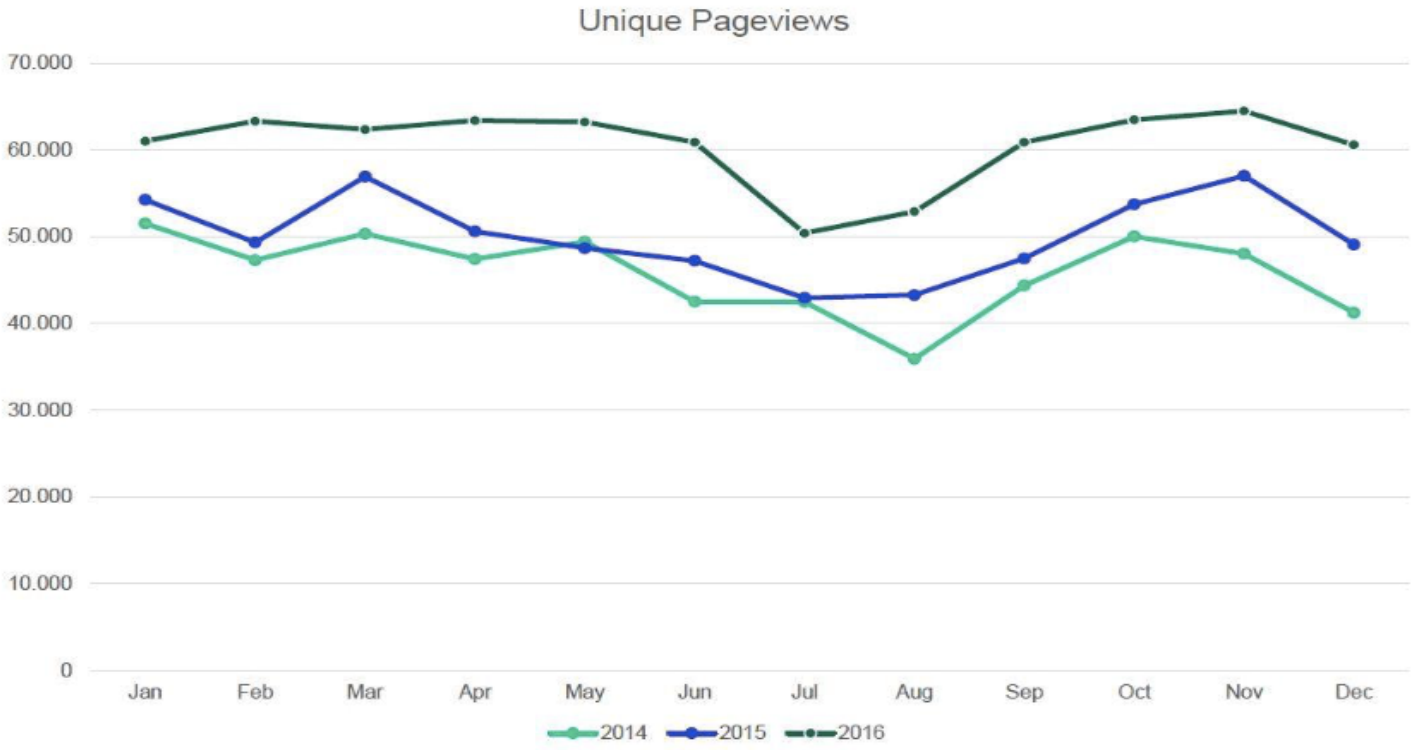
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Continuously updated
with new sections
…and freely available

Pageviews for eucast.org

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

Unique Pageviews for eucast.org – 2014 - 2016



Pageviews for mic.eucast.org

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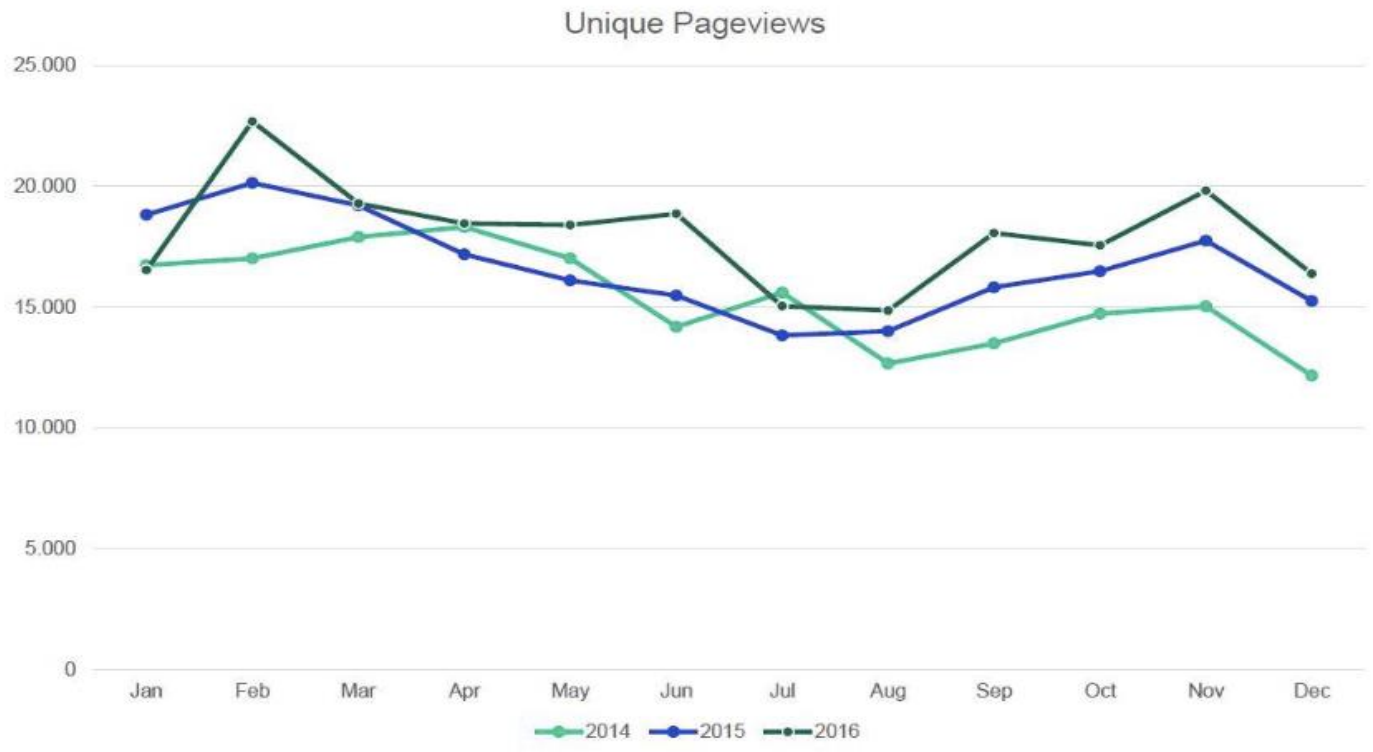
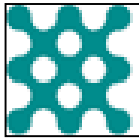
Unique Pageviews for mic.eucast.org – 2014 - 2016





ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

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

Contract 2016-19

NACs = National Antimicrobial Susceptibility Testing Committees

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, ECOFFs
Antimycobacterials

EUCAST Development and EUCAST Networks Laboratories

Experts
(ECDC Networks, ESCMID Study Groups)
Industry

EUCAST Steering Committee 2017

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European Society of Clinical Microbiology and Infectious Diseases

Executive Committee

- **Christian G. Giske**, chair
- **John Turnidge**, scientific secretary
- **Rafael Canton**, clinical data coordinator
- **Gunnar Kahlmeter**, technical data coordinator/webmaster

Representing National Breakpoints Committees

- **Sören Gatermann**, Germany
- **Christoffer Lindemann**, Norway
- **Johan Mouton**, The Netherlands
- **Alasdair MacGowan**, UK
- **Gerard Lina**, France

Representing General Committee

- **Arjana Tambic**, Croatia
- **Deniz Gur**, Turkey

- **Additionally:** visiting members from NACs (max one per meeting)

EUCAST Steering Committee 2017

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

Christian Giske (Sweeden)
Chair (2017 -)

Derek Brown (UK)
Former Scientific Secretary
(1997 – 2016)

Gunnar Kahlmeter (Sweeden)
Former Chair (2001- 2012)
Technical Data Coordinator and webmaster (2017 -)

Rafael Cantón (Spain)
Former Chair (2012 - 2016)
Clinical Data Coordinator (2017 -)

John Turnidge (Australia)
Scientific Secretary (2017 -)

Now in China
lecturing on EUCAST

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search term

Organization

... National AST Committees (NAC)

- Organization
  - EUCAST statutes
  - Steering Committee
  - General Committee
  - Subcommittees
  - National AST Committees (NAC)
  - Development Laboratories
  - Network Laboratories
- EUCAST News
- Clinical breakpoints
- Expert rules and intrinsic resistance
- Resistance mechanisms
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- AST of bacteria
- AST of mycobacteria

The European Committee on Antimicrobial Susceptibility Testing – EUCAST

National Antimicrobial Susceptibilty Testing Committees (NACs)

EUCAST recommends that countries institute a "National Antimicrobial Susceptibility Testing Committee" (or a committee corresponding to this description). Countries in the process of adopting EUCAST antimicrobial susceptibility testing guidelines will find this particularly useful during the implementation process. The chairperson, or another committee officer, should represent the country on the EUCAST General Committee.

This document presents EUCAST suggestions on
How to organise and form a NAC.

NACs are invited to provide a link to their website for EUCAST to post here.

List of and brief information on National breakpoint committees and NACs:

Australia

The EUCAST NAC SOP

- **Structure:**
  - independent committee or a subcommittee of a group with a wider antimicrobial remit
- **Membership:**
  - experts and stakeholders in antimicrobial susceptibility testing:
    - Individual experts
    - Representatives of professional organisations/societies Representatives of government
    - Representatives of antibiotic use, resistance surveillance committees
    - Representatives of quality assurance agencies

EUCAST committees and subcommittees. European Committee on Antimicrobial Susceptibility Testing. EUCAST SOP 4.2, 2016. http://www.eucast.org

NAC objectives

- **To formulate strategy at a national level**
  - Action through government, professional organisations or societies
  - Inclusive decision to follow EUCAST breakpoints
- **To implement breakpoints and methods**
  - Identify stakeholders and provide information
  - Communicate with device manufacturers to ensure no practical limitations
  - Communicate with laboratory staff to ensure that all are informed
  - Communicate with clinicians on consequences of breakpoint changes
  - Communicate with government to ensure that they are on board
  - Communicate with professional organisations/societies
  - Communicate with quality assurance agencies to ensure that they use
- **EUCAST breakpoints**
  - Provide guidance and support to clinical laboratories.
  - Provide practical guidelines for introducing methods
  - Provide breakpoint tables, method descriptions

EUCAST committees and subcommittees. European Committee on Antimicrobial Susceptibility Testing. EUCAST SOP 4.2, 2016. http://www.eucast.org

NACs can influence the EUCAST process

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European Society of Clinical Microbiology and Infectious Diseases

- By direct participation in the Steering Committee
- By communicating with the Steering Committee and influencing in the agenda
- By responding to consultations
- By fostering colleagues in AST issues and thus influencing the future recruitment to the EUCAST Steering Committee
- By active participation in General Committee
- By influencing in their respective countries in the implementation of EUCAST guidelines

NACs can influence the EUCAST process

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NAC and EUCAST SC interaction

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vs

Buffet dinner **Fixed menu**

- National exceptions do occur, but should be few
- NACs should present the rationale for the decision for publication on the EUCAST website

Overview of NACs, April 2016

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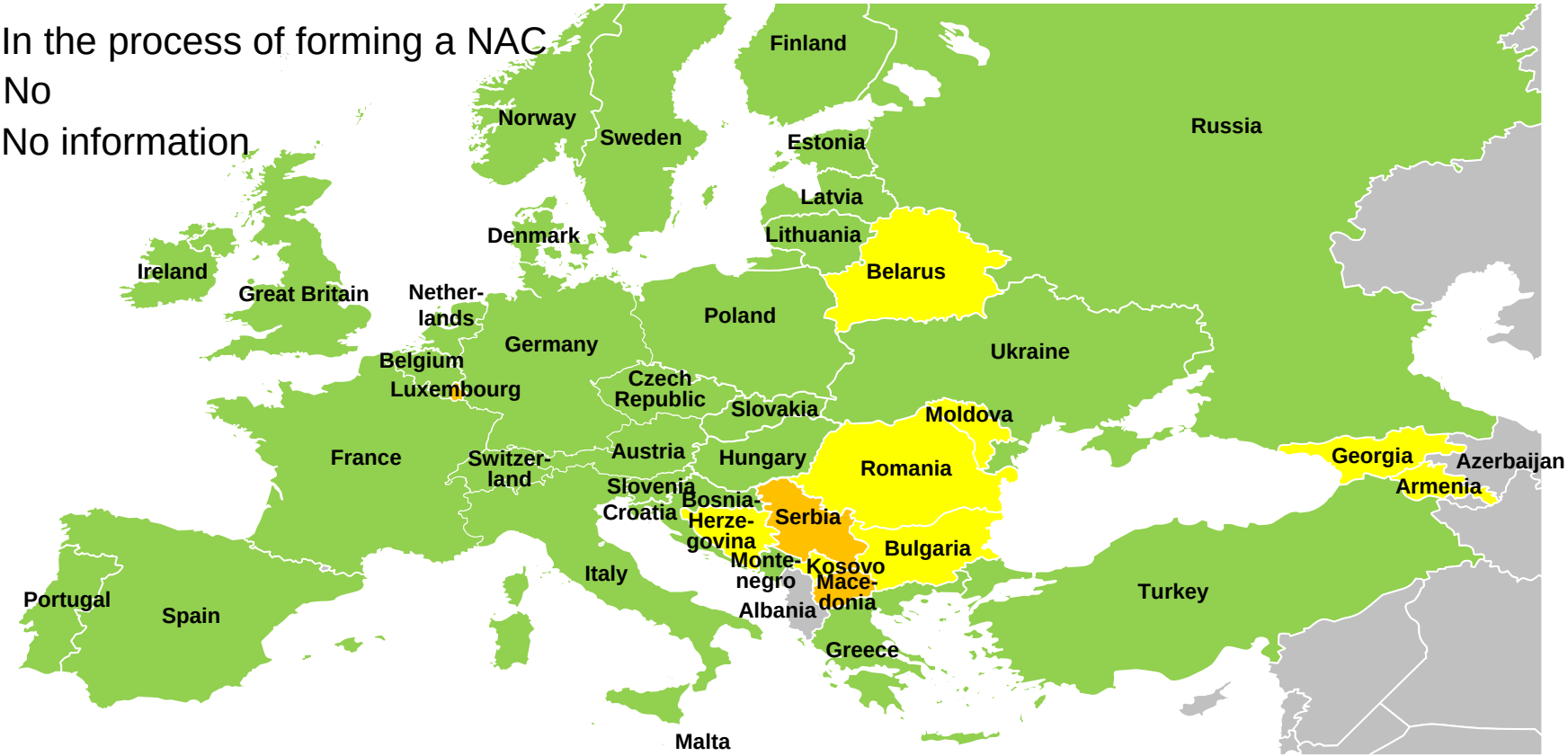
European Society of Clinical Microbiology and Infectious Diseases

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

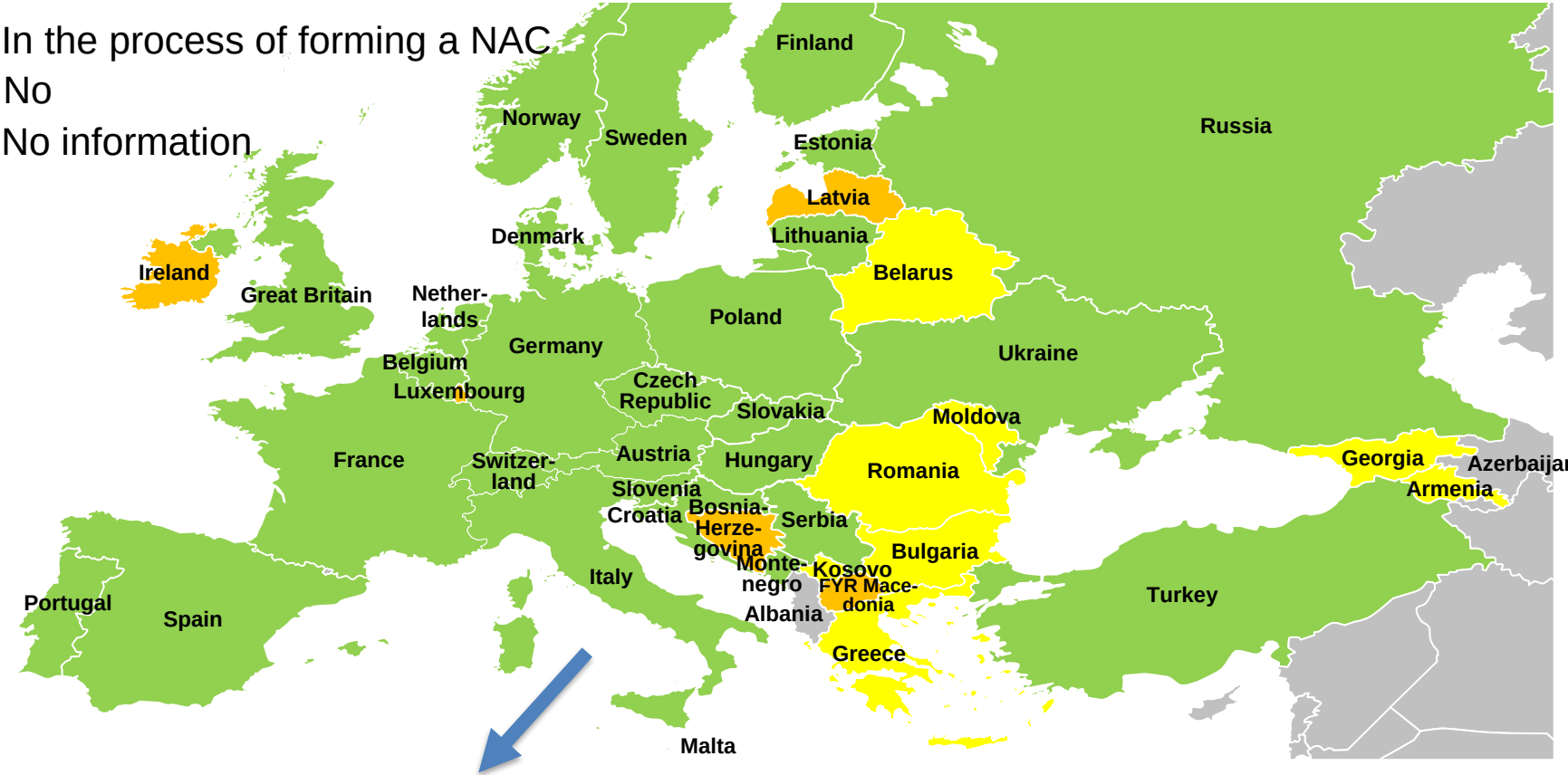


Countries not on this map: Australia | Brazil | Canada | Iceland | Israel | Morocco | New Zealand | South Africa | USA

Overview of NACs, April 2017

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

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



Other countries: Australia | Brazil | China | Canada | Iceland | Israel | Morocco | New Zealand | South Africa | USA

NACs outside Europe

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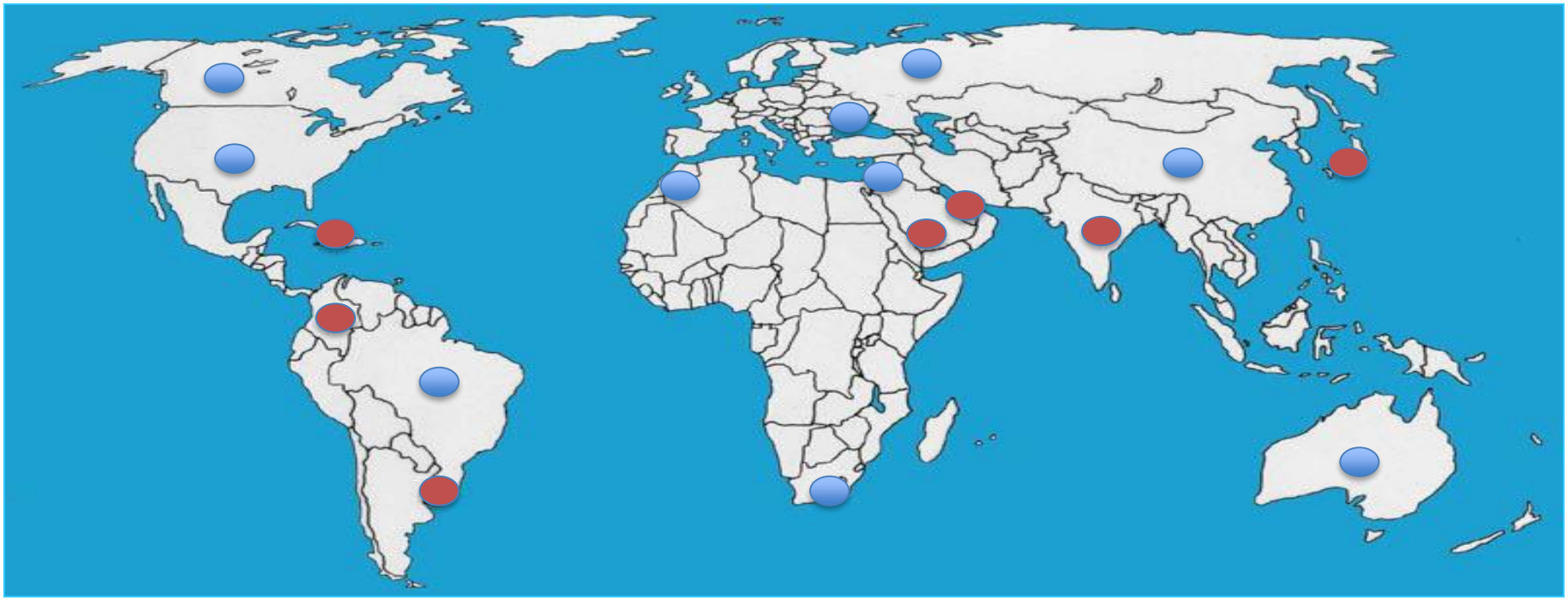

- Countries with a NAC operating under EUCAST standards
- Countries with interest to establish a NAC under EUCAST standards

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04 May 2017

The European Comm
Susceptibility Testin

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European national breakpoint comm
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Derek Brown (1997 - 2016) and Joh
Kahlmeter (2001 -). From 2016, Ra
and Gunnar Kahlmeter the Technica

EUCAST deals with breakpoints an
antimicrobial susceptibility testing a
EMA and ECDC. EUCAST does not
containment of resistance or infectio
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representatives from European and
Committee also consults on EUCAS
infectious diseases and microbiolog
testing device manufacturers.

EUCAST has several subcommittee

Most antimicrobial MIC breakpoints
Breakpoints for new agents are set
through EMA. EUCAST breakpoints
susceptibility testing but with some
diffusion susceptibility test method
also available.

EUCAST invites anyone with an inte
antimicrobial breakpoints in particul
National Breakpoint Committees.

To cite the EUCAST website or a
document name, version, year and
to refer to the current EUCAST brea
Committee on Antimicrobial Suscep
interpretation of MICs and zone dian
http://www.eucast.org/fileadmin/src/

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Website changes

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EUCAST documents translated to other languages

Documents in Czech
Documents in German
Documents in Italian
Documents in Scandinavian languages
Documents in Spanish
Documents in Turkish
Documents in French
Documents in Chinese

The translation to Chinese of the EUCAST guidelines was initiated by Dr Yuqing Liu at Shandong Academy of Agricultural Sciences within the framework of the Sino-Swedish IMPACT project, funded by the Swedish Research Council (grant D0879801) and National Natural Science Foundation of China (grant 81361138021)

→ Documents in Austrian

EUCAST takes full responsibility for the english versions of all EUCAST documents available on the website. These are dated and assigned a version number.

National AST Committees (NACs) take responsibility for translating and updating the EUCAST national documents.

Most documents are "locked" and can not be edited. "Unlocked" versions, suitable for those responsible for translations, can be obtained from the ✉ **EUCAST Development Laboratory**.

EUCAST documents, whether in English or any other language, shall be freely available to users.

Copyright

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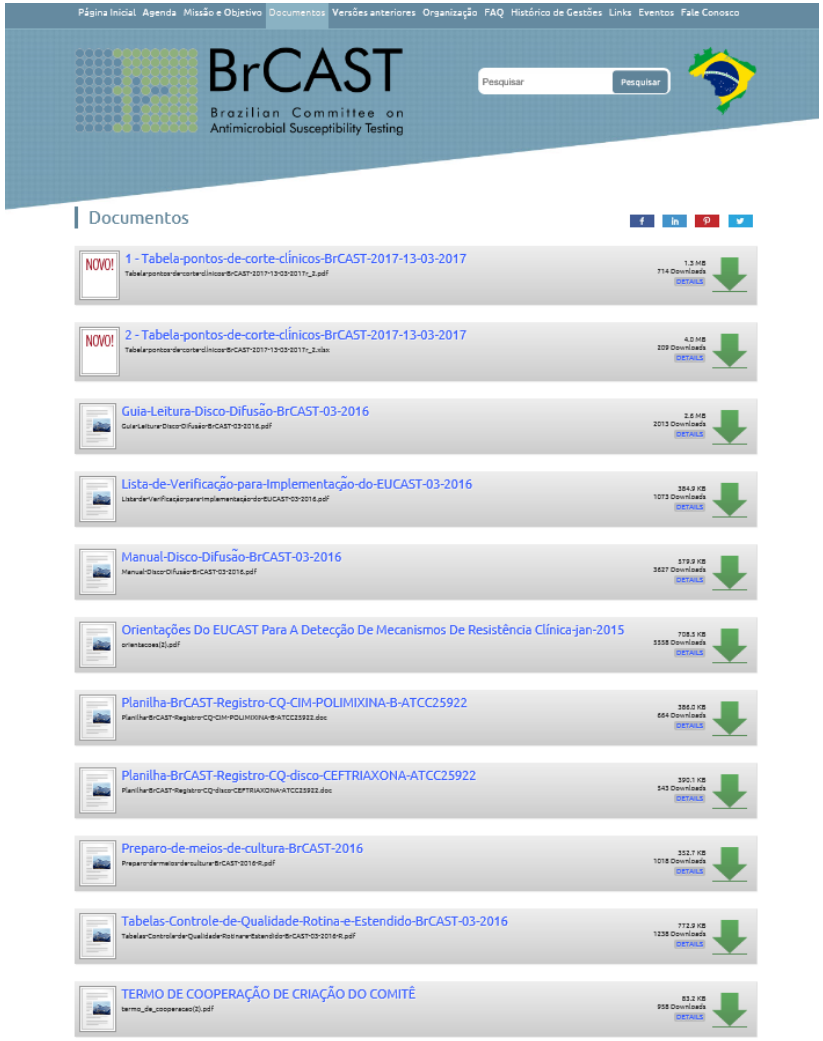
Updated EUCAST translations and new translations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Brazilian Committee on Antimicrobial Susceptibility Testing
Pesquisar
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Documentos
NOVO!
1 - Tabela-pontos-de-corte-clínicos-BrCAST-2017-13-03-2017
Tabela-pontos-de-corte-clinicos-BrCAST-2017-13-03-2017r_E.pdf
1.3 MB
714 Downloads
DETAILS
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2 - Tabela-pontos-de-corte-clínicos-BrCAST-2017-13-03-2017
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DETAILS
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termo_de_cooperacao(2).pdf
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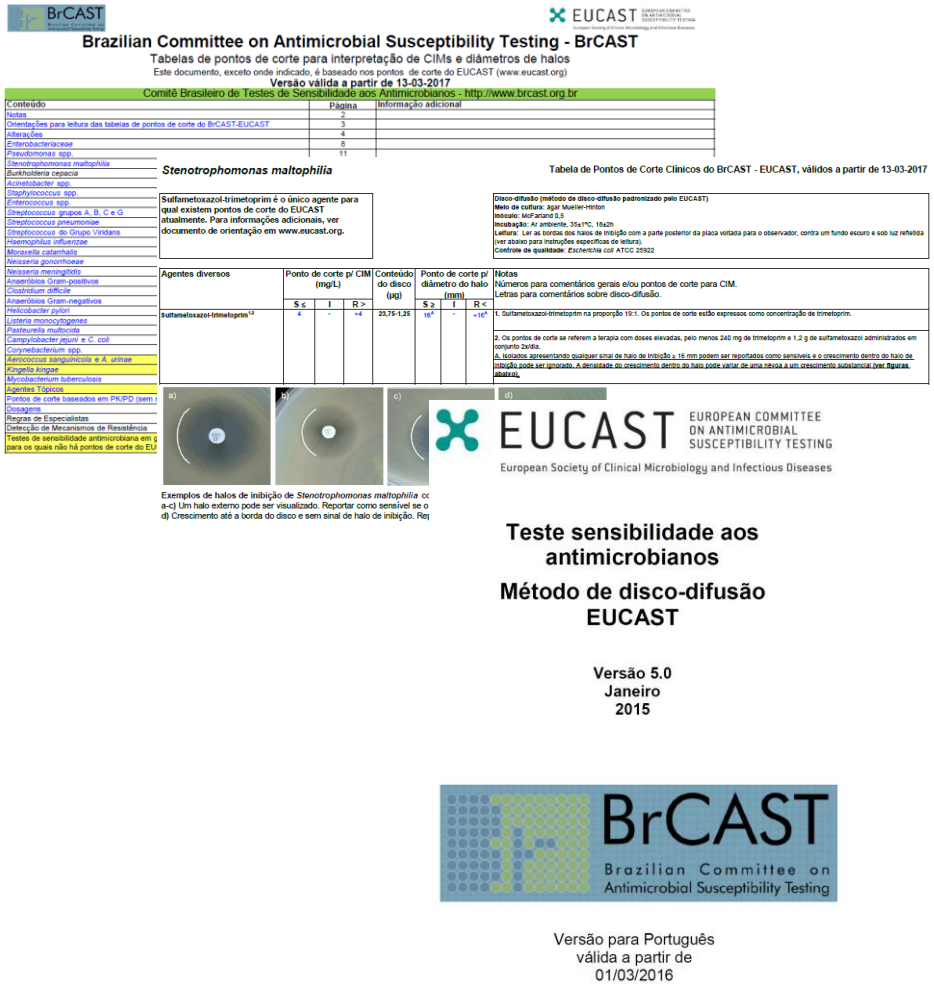
BrCAST
EUCAST
Brazilian Committee on Antimicrobial Susceptibility Testing - BrCAST
Tabelas de pontos de corte para interpretação de CIMs e diâmetros de halos
Este documento, exceto onde indicado, é baseado nos pontos de corte do EUCAST (www.eucast.org)
Versão válida a partir de 13-03-2017
Comitê Brasileiro de Testes de Sensibilidade aos Antimicrobianos - http://www.brcast.org.br
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Enterobacteriaceae 6
Pseudomonas spp. 11
Stenotrophomonas maltophilia
Burkholderia cepacia
Acinetobacter spp.
Staphylococcus spp.
Enterococcus spp.
Streptococcus grupos A, B, C e G
Streptococcus pneumoniae
Streptococcus do Grupo Viridans
Haemophilus influenzae
Moraxella catarrhalis
Neisseria gonorrhoeae
Neisseria meningitidis
Anaeróbios Gram-positivos
Clostridium difficile
Anaeróbios Gram-negativos
Helicobacter pylori
Listeria monocytogenes
Pasteurella multocida
Campylobacter jejuni e C. coli
Corynebacterium spp.
Aerococcus sanguinicola e A. urinae
Kingella kingae
Mycobacterium tuberculosis
Agentes Tópicos
Pontos de corte baseados em PK/PD (sem
Dosagens
Regras de Especialistas
Detecção de Mecanismos de Resistência
Testes de sensibilidade antimicrobiana em
para os quais não há pontos de corte do EU
Stenotrophomonas maltophilia
Tabela de Pontos de Corte Clínicos do BrCAST - EUCAST, válidos a partir de 13-03-2017
Sulfametoxazol-trimetoprim é o único agente para qual existem pontos de corte do EUCAST atualmente. Para informações adicionais, ver documento de orientação em www.eucast.org.
Disco-difusão (método de disco-difusão padronizado pelo EUCAST)
Meio de cultura: ágar Mueller-Hinton
Inóculo: McFarland 0,5
Incubação: Ar ambiente, 35±1°C, 16±2h
Leitura: Ler as bordas dos halos de inibição com a parte posterior da placa voltada para o observador, contra um fundo escuro e sob luz refletida (ver abaixo para instruções específicas de leitura).
Controle de qualidade: Escherichia coli ATCC 25922
Agentes diversos
Ponto de corte p/ CIM (mg/L)
Conteúdo do disco (µg)
Ponto de corte p/ diâmetro do halo (mm)
Notas
Números para comentários gerais e/ou pontos de corte para CIM.
Letras para comentários sobre disco-difusão.
S ≤
I
R >
S ≥
I
R <
Sulfametoxazol-trimetoprim[1,2]
4
-
>4
23,75-1,25
16[A]
-
<16[A]
1. Sulfametoxazol-trimetoprim na proporção 19:1. Os pontos de corte estão expressos como concentração de trimetoprim.
2. Os pontos de corte se referem a terapia com doses elevadas, pelo menos 240 mg de trimetoprim e 1,2 g de sulfametoxazol administrados em conjunto 2x/dia.
A. Isolados apresentando qualquer sinal de halo de inibição ≥ 16 mm podem ser reportados como sensíveis e o crescimento dentro do halo de inibição pode ser ignorado. A densidade do crescimento dentro do halo pode variar de uma nessa a um crescimento substancial (ver figuras abaixo).
a)
b)
c)
d)
Exemplos de halos de inibição de Stenotrophomonas maltophilia
a-c) Um halo externo pode ser visualizado. Reportar como sensível se o
d) Crescimento até a borda do disco e sem sinal de halo de inibição. Re
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European Society of Clinical Microbiology and Infectious Diseases
Teste sensibilidade aos antimicrobianos
Método de disco-difusão EUCAST
Versão 5.0
Janeiro
2015
BrCAST
Brazilian Committee on Antimicrobial Susceptibility Testing
Versão para Português
válida a partir de
01/03/2016

… also in Chinese!

嗜麦芽窄食单胞菌

EUCAST 折点中，甲氧苄啶-磺胺甲噁唑是唯一一个针对嗜麦芽窄食单胞菌的药物。要想获取更多的信息，请参考 www.eucast.org 中的指南目录。

纸片扩散法（EUCAST 标准的纸片扩散法方法）

培养基：MH 琼脂

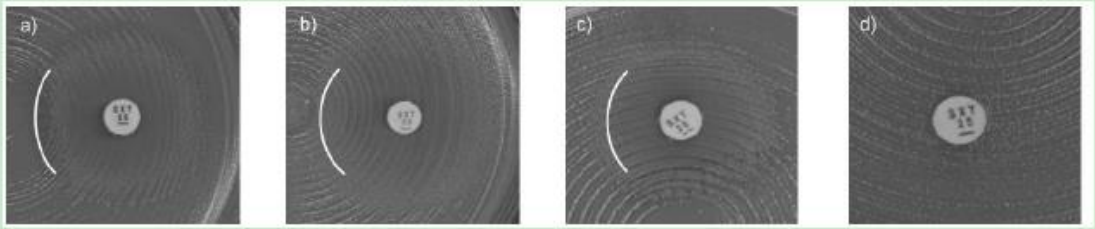
接种：0.5 麦氏浊度

孵育：空气，35±1℃，18±2 h

阅读：在黑色背景下，通过反射光，在细菌完全不生长的区域测量抑菌圈直径

质量控制：大肠杆菌 ATCC 25922

其它抗生素	MIC 折点（mg/L）		纸片含量（μg）	抑菌圈直径折点（mm）		注释 数字注释针对 MIC 折点 字母注释针对纸片扩散法
	S≤	R>		S≥	R<	
甲氧苄啶-磺胺甲噁唑 [1]	4	4	1.25-23.75	16[A]	16[A]	1.甲氧苄啶和磺胺甲噁唑的比例是 1:19.折点是依据甲氧苄啶的浓度制定的。 A.忽略抑菌圈制备的薄雾状生长或完全生长（见下面图片）。



甲氧苄啶-磺胺甲噁唑对嗜麦芽窄食单胞菌的抑菌圈直径的示例

a-c）可以看到一个外部的圈。如果抑菌圈直径≥16 mm，则报告为敏感。

d）平板上完全生长，并且看不到抑菌圈。报告为耐药。

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- MIC distributions and ECOFFs
- Zone distributions and ECOFFs
- AST of bacteria
- AST of mycobacteria
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Website changes

04 May 2017

The European Committee on Antimicr
Susceptibility Testing - EUCAST

EUCAST is a standing committee jointly organized by ESCMID, E
European national breakpoint committees. EUCAST was formed
been chaired by Ian Phillips (1997 - 2001), Gunnar Kahlmeter (20
Rafael Canton 2012 - 2016) and Christian Giske (2016 -). Its scie
Derek Brown (1997 - 2016) and John Turnidge (2016 -). Its webm
Kahlmeter (2001 -). From 2016, Rafael Canton is the Clinical Dat
and Gunnar Kahlmeter the Technical Data Co-ordinator.

EUCAST deals with breakpoints and technical aspects of phenoty
antimicrobial susceptibility testing and functions as the breakpoint
EMA and ECDC. EUCAST does not deal with antibiotic policies, s
containment of resistance or infection control. The Steering Comm
decision making body. It is supported by a General Committee wi
representatives from European and other countries, FESCI and IS
Committee also consults on EUCAST proposals with experts with
infectious diseases and microbiology, pharmaceutical companies
testing device manufacturers.

EUCAST has several subcommittees - → see page Subcommitte

Most antimicrobial MIC breakpoints in Europe have been harmoni
Breakpoints for new agents are set as part of the licensing proces
through EMA. EUCAST breakpoints are available in devices for a
susceptibility testing but with some limitations, depending on the s
diffusion susceptibility test method → calibrated to EUCAST MIC
also available.

EUCAST invites anyone with an interest in antimicrobial agents in
antimicrobial breakpoints in particular to contact EUCAST, ESCM
National Breakpoint Committees.

To cite the EUCAST website or a document on the EUCAST w
document name, version, year and the full web adress. For exam
to refer to the current EUCAST breakpoint table, the citation reads
Committee on Antimicrobial Susceptibility Testing. Breakpoint tab
interpretation of MICs and zone diameters, version 7.1, 2017,
http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/B

Copyright

Videos from EUCAST

- Organization
- EUCAST News
- Clinical breakpoints
- Expert rules and intrinsic resistance
- Resistance mechanisms
- Guidance documents
- Consultations
- MIC distributions and ECOFFs
- Zone distributions and ECOFFs
- AST of bacteria
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Instruction videos from EUCAST

In collaboration with the World Health Organisation (WHO), EUCAST publishes instruction videos on how to perform antimicrobial susceptibility testing (AST) using EUCAST recommended methods and interpretation. During 2016, five videos have been completed and 5 more are under construction in 2017.

The videos are published on Youtube™ and have an English speaker voice and English subtitles. There is a mechanism by which subtitles can be translated to other languages.

1. **Preparation of inoculum (English).**
2. **Inoculation of agar plates for disk diffusion (English).**
3. **Application of antibiotic disks and incubation of plates (English).**
4. **Reading of inhibition zone diameters (English).**
5. **Guidance on the use of the breakpoint table (English).**

Instruction videos on EUCAST susceptibility testing with subtitles in other languages than English:

Instruction videos in German.
Instruction videos in Russian.
Instruction videos in Turkish.
Instruction videos in French.
Instruction videos in Spanish.
Instruction videos in Portuguese.
Instruction videos in Arabic.
Instruction videos in Czech.

Instruction videos in ...(more to follow shortly)

Acknowledgements

The instruction videos from EUCAST on how to perform antimicrobial susceptibility disk diffusion testing was produced by a project team from EUCAST and WHO:

Erika Matuschek, Jenny Åhman and Gunnar Kahlmeter, EUCAST Development Laboratory
Christopher Oxenford, Danilo Lo Fo Wong and Nienke van de Sande, WHO
Jonas Ljungdahl, photographer and editor, Växjö, Sweden.

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European Society of Clinical Microbiology and Infectious Diseases

Disk diffusion instruction videos

EUCAST project – 10 videos (5 finalized) financed by WHO

Subtitles in “other” languages

YouTube, WHO webpage, EUCAST webpage

Implementation of EUCAST breakpoints, April 2016

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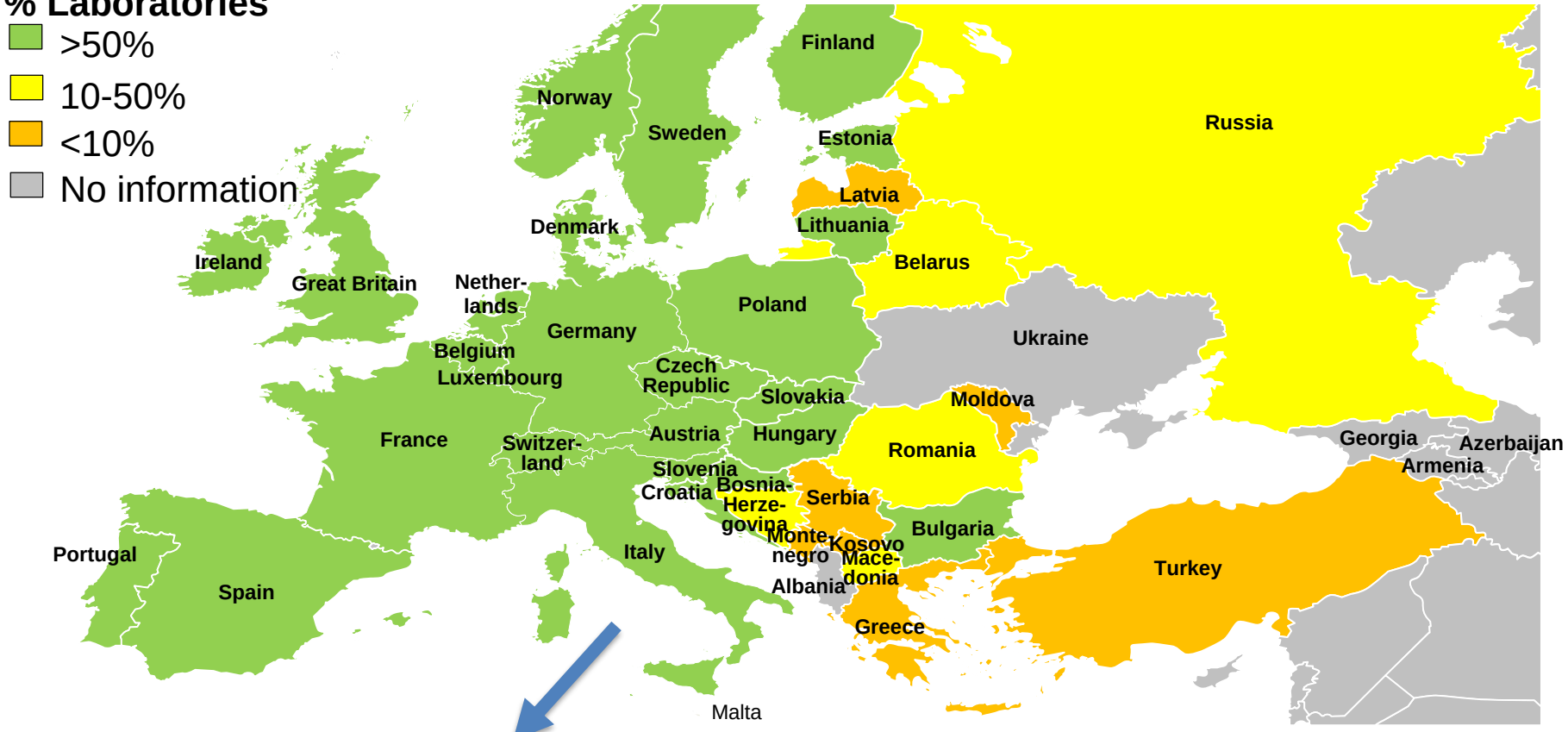
European Society of Clinical Microbiology and Infectious Diseases



Countries not on this map: Australia | Brazil | Canada | Iceland | Israel | Morocco | New Zealand | South Africa | USA

Implementation of EUCAST breakpoints, April 2017

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European Society of Clinical Microbiology and Infectious Diseases

Other countries: Australia | Brazil | China | Canada | Iceland | Israel | Morocco | New Zealand | South Africa | USA

Implementation of EUCAST disk diffusion, April 2016

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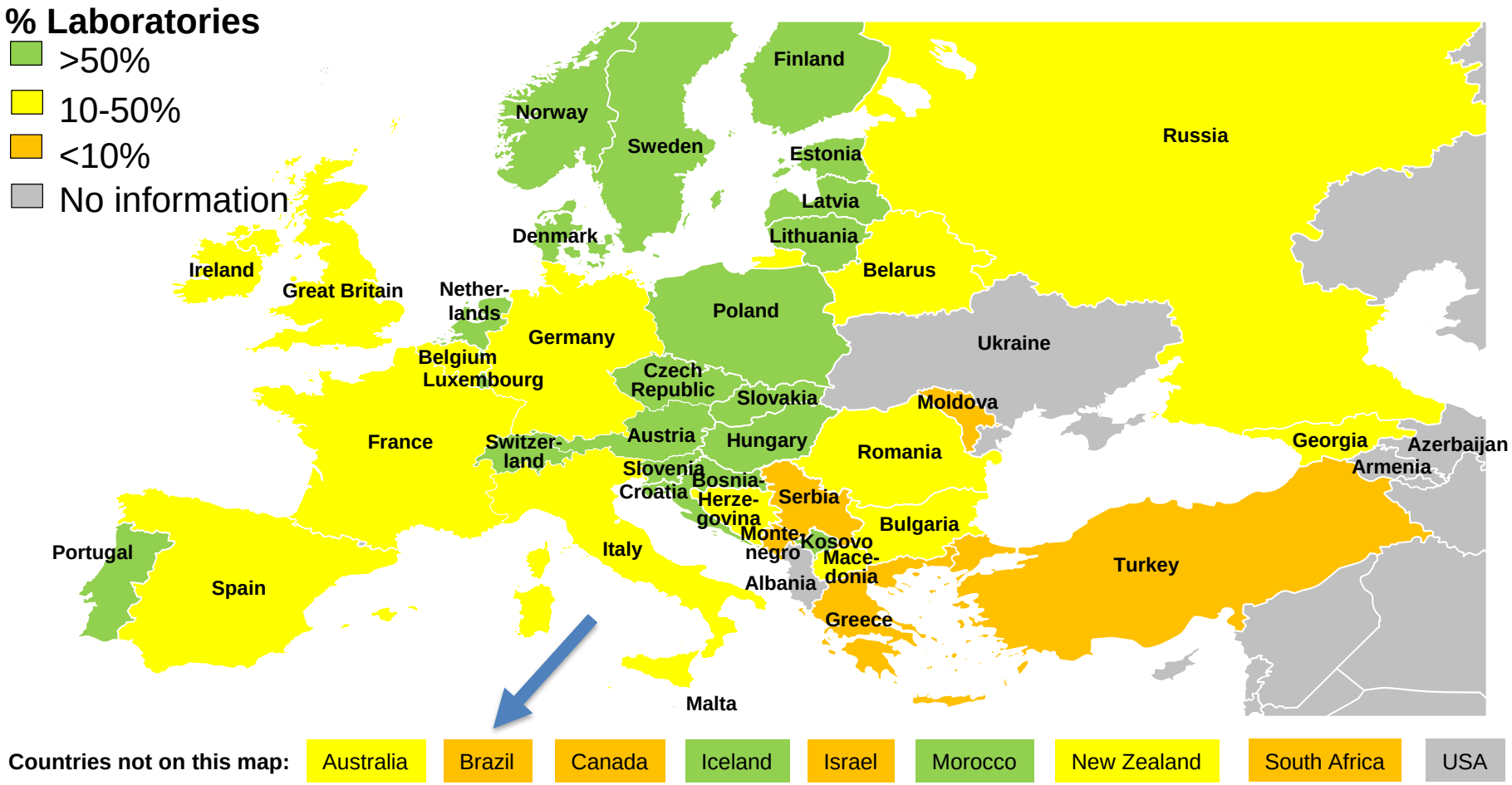

Countries not on this map: Australia | Brazil | Canada | Iceland | Israel | Morocco | New Zealand | South Africa | USA

Implementation of EUCAST disk diffusion, April 2017

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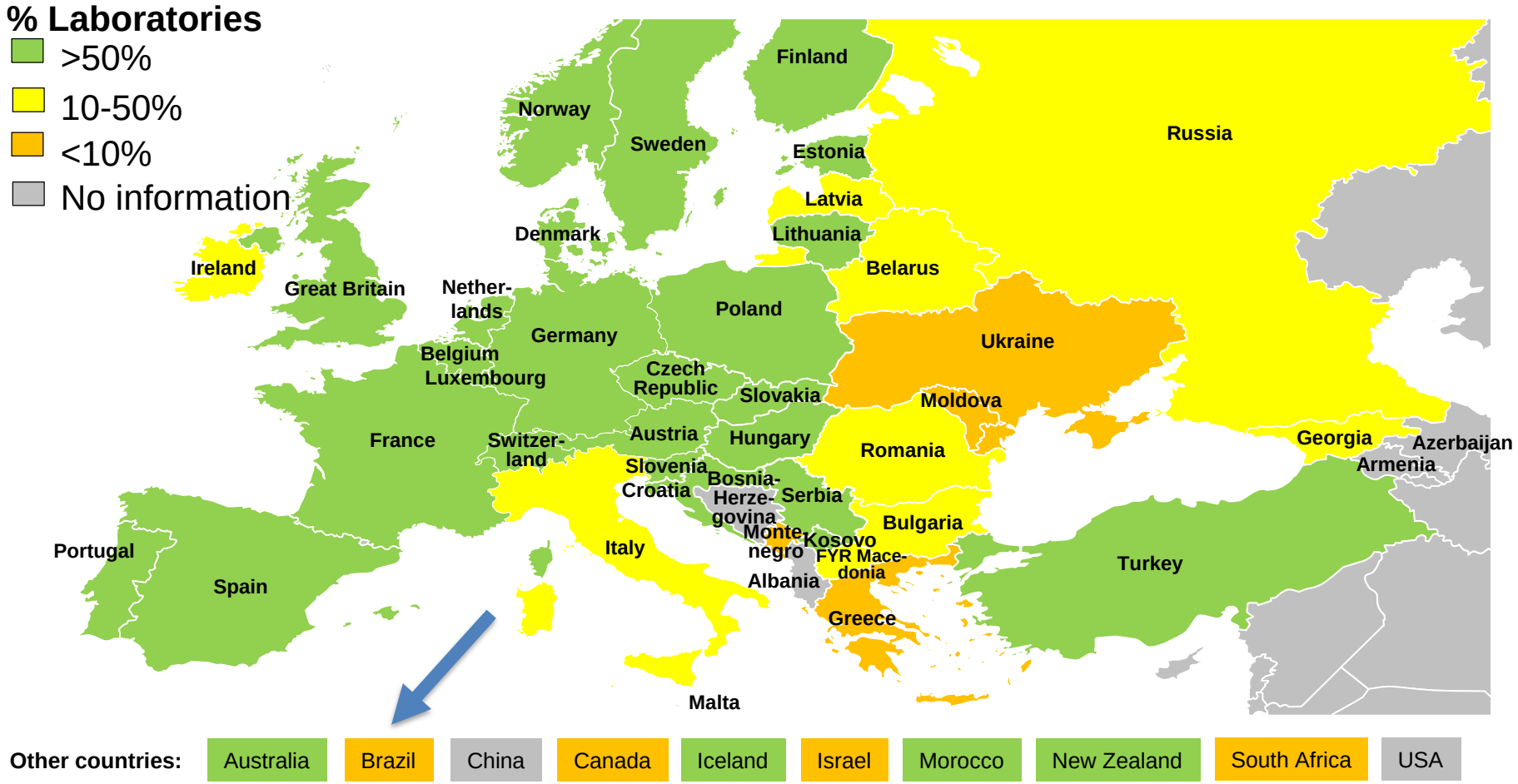

EUCAST Subcommittees

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

- **STANDING**
  - Antifungal susceptibility testing
  - Veterinary susceptibility testing
- **AD HOC**
  - Intrinsic Resistance and Expert Rules
  - MIC distributions and ECOFFs
  - Polymyxins breakpoints and methods (joint with CLSI)
  - Antimycobacterial Susceptibility testing
  - Detection of resistance mechanisms
  - Relationship between WGS (NGS) and phenotypic susceptibility testing
- **INACTIVE**
  - Anaerobes

Clinical Microbiology and Infection 23 (2017) 2–22

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Review

The role of whole genome sequencing in antimicrobial susceptibility testing of bacteria: report from the EUCAST Subcommittee

M.J. Ellington [1, †], O. Ekelund [2, †], F.M. Aarestrup [3], R. Canton [4], M. Doumith [1], C. Giske [5], H. Grundman [6], H. Hasman [7], M.T.G. Holden [8], K.L. Hopkins [1], J. Iredell [9], G. Kahlmeter [2], C.U. Köser [10], A. MacGowan [11], D. Mevius [12, 13], M. Mulvey [14], T. Naas [15], T. Peto [16], J.-M. Rolain [17], Ø. Samuelsen [18], N. Woodford [1, *]

…**the MIC**… reflects more than gene presence / absence; … multiple and complex interplays between different systems including cellular permeability, influx/efflux, target availability and binding as well as enzymatic expression levels and activities.

- … the primary AST comparator for WGS-based prediction should be **the ECOFF**, wherever possible, in order to assess WGS-inferred ‘antibiograms’ (based on gene positivity) against phenotypically-defined categories of wild-type or non-wild-type.

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Warnings!
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Rationale Documents

... Consultations

EUCAST Consultations

Current consultations

- **Consultation - letter of invitation** 3 March, 2017 - 14 April, 2017: Revision of **"EUCAST guidelines for detection of resistance mechanisms and specific resistances of Clinical and/or epidemiological importance"**.
  Form to be used for comments (no later than 14 April, 2017)

- **Consultation - letter of invitation** 9 March, 2017 - 14 May, 2017:
  "EUCAST discussion document (v 3) on MIC distributions and the determination of epidemiological cut-off values (ECOFFs)"
  - from the EUCAST Subcommittee on MIC distributions and ECOFFs.
  Form to be used for comments (no later than 14 May, 2017)

Consultations with comments and responses:

- **Proposed breakpoints for Aerococcus spp and Kingella kingae - comments and responses.**
- **Proposed revision of fluoroquinolone breakpoints. - Comments and responses.**
- **Proposed revision of the colistin breakpoint for *Pseudomonas aeruginosa*. - Comments and responses.**
- **Report from the EUCAST Subcommittee on the role of whole genome sequencing (WGS) in antimicrobial susceptibility testing. - Comments and responses.**
- **Wide consultation the EUCAST proposed changes in the definition of the intermediate category.**

Recent consultations

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

1. EUCAST guidelines for **detection of resistance mechanisms** and specific resistances of Clinical and/or epidemiological importance
2. MIC distributions and the **determination of ECOFFs** *(EUCAST Subcommittee on MIC distributions and ECOFFs)*
3. Breakpoints for ***Aerococcus* spp and *Kingella kingae*** *(in breakpoint table 2017, v7.1)*
4. **Fluoroquinolone** breakpoints *(in breakpoint table 2017, v7.1)*
5. **Colistin breakpoint for *P. aeruginosa*** *(in breakpoint table 2017, v7.1)*
6. **Nitroxoline** breakpoints *(in breakpoint table 2017, v7.1)*
7. Role of **WGS in antimicrobial susceptibility testing** *(EUCAST Subcommittee on the WGS)*
8. EUCAST proposed changes in the definition of the **intermediate category**
9. Revision of Expert rules (v 3.0). **Intrinsic resistance and exceptional phenotypes tables**

Breakpoint table v7.0

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European Committee on Antimicrobial Susceptibility Testing

Breakpoint tables for interpretation of MICs and zone diameters

Version 7.0, valid from 2017-01-01

This document should be cited as "The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 7.0, 2017. http://www.eucast.org."

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
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AST - when there is no breakpoint?

EUCAST SOP 2016

- The breakpoint is “IE”
- The breakpoint is “—”
- The agent is not in the table
- The species is not in the table

When there are no breakpoints…

- Do not report “S”, “I” or “R”
  - These are susceptibility categories based on evidence for or against favorable clinical outcome.
- Report an MIC with a comment or only a comment
  - MIC is below or above the PK/PD breakpoint if available;
  - Compare MIC with breakpoints of a closely related organism if possible.

Use common sense!!

PK-PD breakpoints, “–” and IE

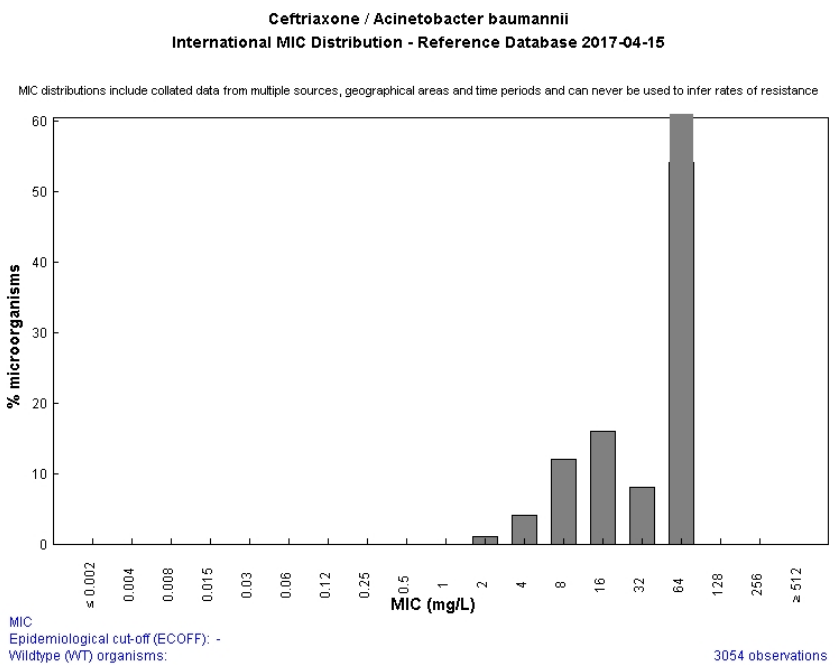
- **PK-PD (non species related) breakpoints** are used only when there are no species-specific breakpoints or other recommendations (a dash or a note) in the species-specific tables.

“–” indicates that susceptibility testing is not recommended as the species is a poor target for therapy with the agent: isolates may be reported as R without prior testing and PK-PD breakpoints should not be used

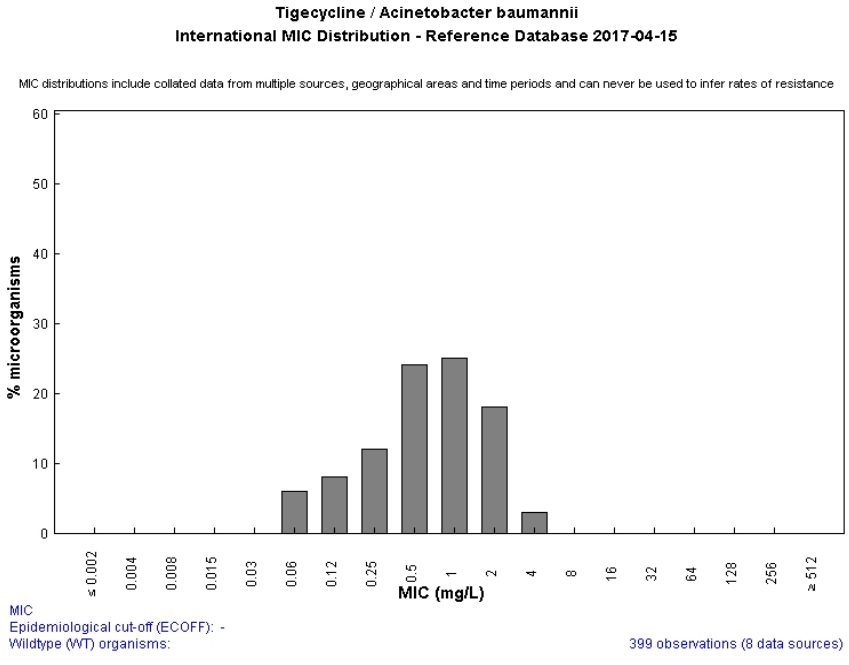
“**IE**” indicates that there is **insufficient evidence** that the organism or group is a good target for therapy with the agent:

- An MIC with a comment but without categorisation may be reported
- Eventually, PK-PD breakpoints can be used but, if available, also taking into account ECOFFs

PK-PD breakpoints, “–” and IE



	mg/L	
	S (≤)	R (>)
A.baumanii ceftriaxone	–	–
PK-PD	1	2



	mg/L	
	S (≤)	R (>)
A.baumanii tigecycline	IE	IE
PK-PD	0.25	0.5

EUCAST breakpoints: new and reviewed/revised

Antibiotic	Breakpoints
Ceftazidime-avibactam	**New:** Enterobacteriaceae, *P. aeruginosa*, PK/PD
Floroquinolones	**Revised:** Enterobacteriaceae, *P. aeruginosa*, *Acinetobacter* spp., *Staphylococcus* spp. , β-haemolitic and viridans streprococci, *S. pneumoniae*, *H. influenzae*
Colistin (together with CLSI)	**Revised:** *P. aeruginosa*

Ongoing 2017: Temocillin (pending regulatory decisions), carbapenems (close to finalized), aminoglycosides and tigecycline

CEFTAZIDIME-AVIBACTAM *vs* CEFTAZIDIME

- CAZ-AVI: CAZ + β-lactamase inhibitor (AVI) which inhibits Ambler class A, class C and some class D enzymes but not metallo-β-lactamases (class B)

- Indications for treatment in adults[1]:
  - complicated intra-abdominal infections
  - complicated urinary tract infections, including pyelonephritis
  - nosocomial pneumonia, including ventilator associated pneumonia
  - infections caused by aerobic Gram-(-) organisms in patients with limited treatment options

- Dosage of CAZ-AVI: 2 g CAZ + 0.5 g AVI x 3 iv over 2 h

[1]Summary of product characteristics. EMA

CEFTAZIDIME-AVIBACTAM *vs* CEFTAZIDIME

Organisms	Antibiotic	MIC breakpoints (mg/L)	
		S ≤	R >
Enterobacteriaceae	CAZ	1	4
	CAZ-AVI	8	8
P. aeruginosa	CAZ	8	8
	CAZ-AVI	8	8
PK-PD breakpoints	CAZ	4	8
	CAZ-AVI	8	8
For susceptibility testing, avibactam is fixed at 4 mg/L			

- Dosages CAZ: 1 g (standard) -2 g (high) x 3 IV

  CAZ-AVI: 2 g CAZ + 0.5 g x 3 IV over 2h

CEFTAZIDIME-AVIBACTAM *vs* CEFTAZIDIME

- Probability of target attainment (PTA) of T>MIC was 50% (1-log kill) for both drugs, but **for CAZ-AVI, unlike CAZ, 2 h extended infusion was considered**

- For **Enterobacteriaceae**

  - CAZ PK-PD breakpoints (≤4 / >8 mg/L) were reduced to ≤1 / 4 mg/L to avoid ESBL producers with MICs of 2-4 mg/L reported as S and with 8 mg/L reported as "I" due to clinical data of failure

  - CAZ/AVI is doubling CAZ dose, additionally extended infusion (2 h) is used

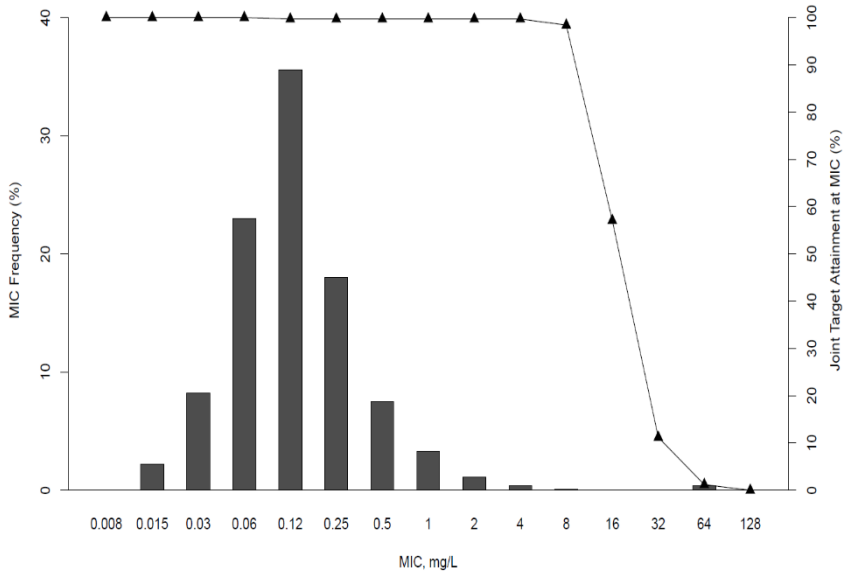
- For ***P. aeruginosa***

  - CAZ "S" breakpoint (4 mg/l) was increased one dilution (8 mg/L) to avoid dividing the wild type distribution and was the same for CAZ-AVI (8 mg/L)

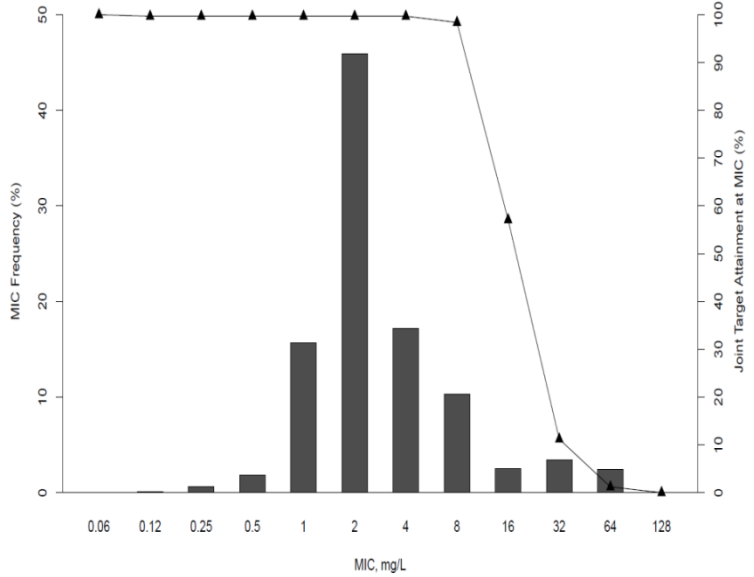
CEFTAZIDIME-AVIBACTAM *vs* CEFTAZIDIME

PTA analysis overlaying MIC distributions (global surveillance data*) against *Enterobacteriaceae* and *P. aeruginosa*

***Enterobacteriaceae* (N=13,949)**



***P. aeruginosa* (N=2,208)**



Global Surveillance Study, AZ. 2013

FLUOROQUINOLONE BREAKPOINTS

- **Previous breakpoints** established during **harmonization process** with a compromise of microbiological, PK-PD and clinical data available

- **New breakpoints** established according to

  - Pharmacodynamic targets for fluoroquinolones as a class[1]
  - Monte Carlo simulations for each compound[1]
  - Probability of target attainments[1]
  - PK-PD breakpoints with recommended doses
  - Requirements to avoid splitting wild type distributions
  - Clinical data relating MIC to outcome (if available)

Approved (Sept 2016) after consultation (June 2016) and **published Jan 2017**, also discussed at CLSI and approved in Jan 2017 (they will be published in 2018)

[1]USCAST. Quinolone In Vitro Susceptibility Test Interpretive Criteria Evaluations. Version 1.2, 2017. http://www.uscast.org

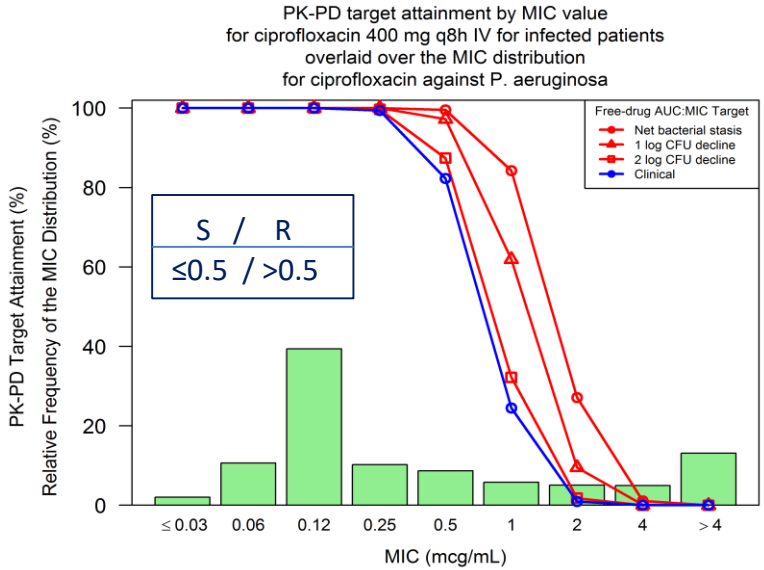
FLUOROQUINOLONE BREAKPOINTS

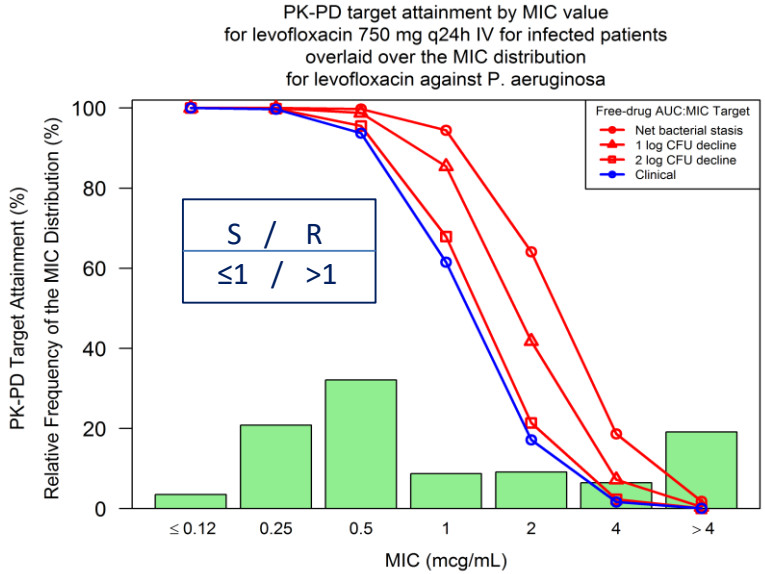
		MIC breakpoints (mg/L)			
		≤2016		≥2017	
		S ≤	R >	S ≤	R >
PK-PD breakpoints	CIP	0.5	1	0.25	0.5
	LVF	1	2	0.5	1
E. coli	CIP	0.5	1	0.25	0.5
	LVF	1	2	0.5	1
P. aeruginosa	CIP	0.5	1	0.5[1]	0.5[1]
	LVF	1	2	1[1]	1[1]
S. aureus	CIP	1	1	1[1]	1[1]
	LVF	1	2	1[1]	1[1]
S. pneumoniae	CIP	0.5	1	-	-
	LVF	2	2	2[1]	2[1]

[1]high dose should always be used

FLUOROQUINOLONE BREAKPOINTS

Percent probabilities of CIP and LVF PK-PD target attainments based on free-drug AUC:MIC ratio targets relative to the MIC distribution for *P. aeruginosa*





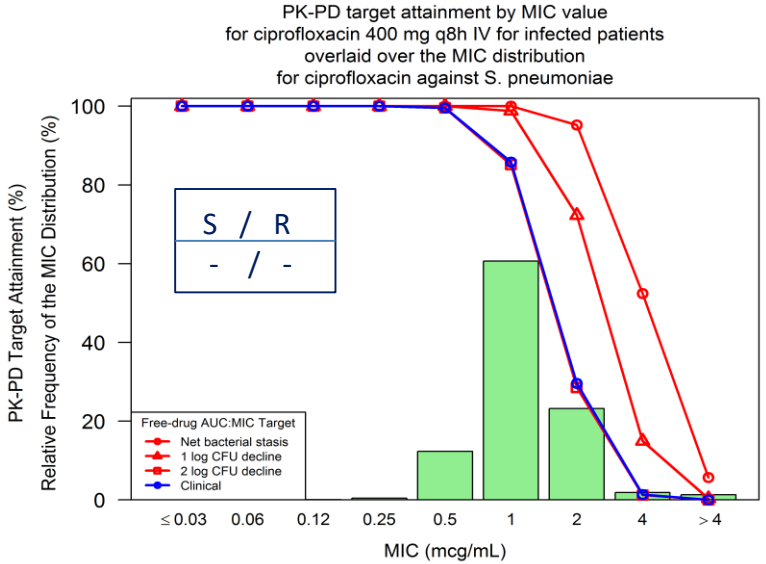
PK-PD breakpoint indicates S ≤0.5 mg/L.
R (>0.5 mg/L) is based on a high dose

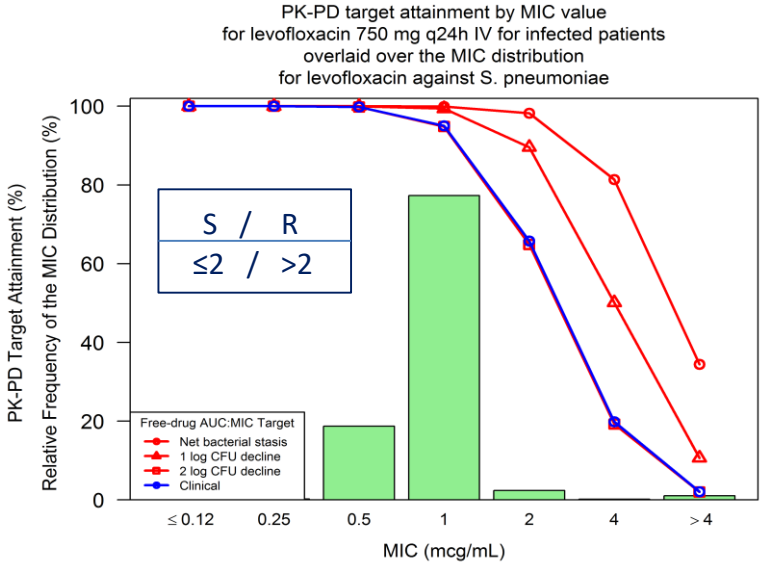
S breakpoint (>0.5 mg/L), based on a high dose, was increased (>1 mg/l) to avoid spliting WT distribution

[1]USCAST. Quinolone In Vitro Susceptibility Test Interpretive Criteria Evaluations. Version 1.2, 2017. http://www.uscast.org

FLUOROQUINOLONE BREAKPOINTS

Percent probabilities of CIP and LVF PK-PD target attainments based on free-drug AUC:MIC ratio targets relative to the MIC distribution for *S. pneumoniae*





CIP is a por agent for *S. pneumonae*. PTA is too low even when a high dose is used

R breakpoint (>1 mg/L), based on a high dose, was increased (>2 mg/l) to avoid spliting WT distribution

[1]USCAST. Quinolone In Vitro Susceptibility Test Interpretive Criteria Evaluations. Version 1.2, 2017. http://www.uscast.org

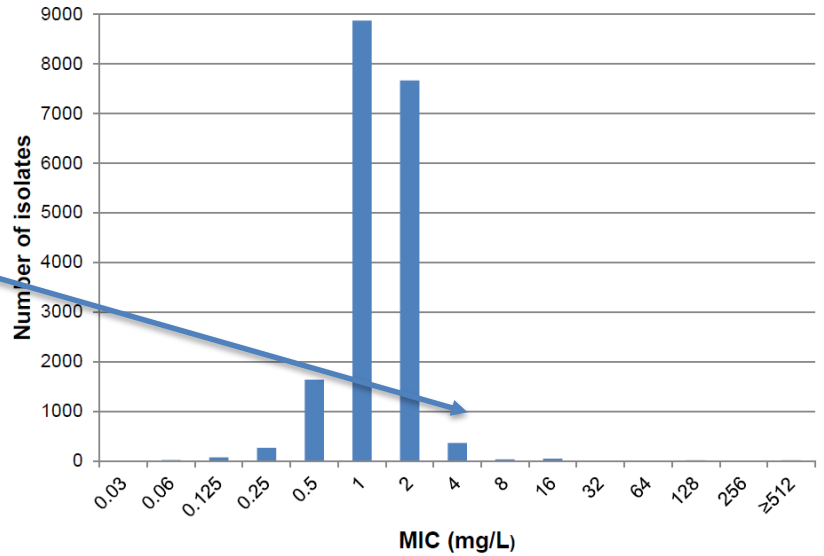
COLISTIN BREAKPOINTS IN *P. aeruginosa*

- Joint **EUCAST-CLSI Working Group** to review breakpoints for polymyxins (2013 -)
- **2016:** colistin breakpoints for **Enterobacteriaeae** (S ≤2 mg/L, R >2 mg/L)
- **2017:** Reduction of colistin breakpoints in *P. aeruginosa* from S ≤4 mg/L, R >4 mg/L to S ≤2 mg/L, R >2 mg/L

  - MIC distributions data:

    - ECOFF = 4 mg/L
    - 3% of isolates >2 mg/L

  - PK/PD data



COLISTIN BREAKPOINTS IN *P. aeruginosa*

- **Colistin PK/PD data:**
  - ***f*AUC24/MIC** represents the PK/PD parameter
  - **target *f*AUC24/MIC for efficacy** based on the thigh infection model is equal to **12**
    - includes most of the individual *f*AUC24/MIC values observed for stasis and 1-log kill (it also approximates to the average values for 2-log kill)
  - **target attainment rates exceeded 90% for strains with MICs of 0.5 mg/L**, and similarly for strains with MICs of 1 mg/L except at the highest creatinine clearances observed, i.e. greater than 121 mL/min
  - **target attainment for strains with MICs of 2 mg/L**, EMA dosing recommendations perform satisfactorily in patients with creatinine clearances ≤76 mL/min, but drops steeply in highest renal function groups and exposures is not adequate for strains with MICs of ≥4 mg/L

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Another examples of changes

Enterobacteriaceae	**General** • Pictures with reading examples for the fosfomycin disk diffusion test added **New breakpoints** • Temocillin (information added, see note) • Ceftazidime-avibactam (MIC and zone diameter) • Fosfomycin iv and oral (zone diameter) • Nitroxoline (MIC and zone diameter) **Revised breakpoints** • Cefepime (zone diameter) • Ceftriaxone (zone diameter) • Cefuroxime iv and oral (zone diameter) • Aztreonam (zone diameter) • Ciprofloxacin (MIC and zone diameter) • Levofloxacin (MIC and zone diameter) • Moxifloxacin (MIC and zone diameter) • Norfloxacin (valid for uncomplicated UTI only) • Ofloxacin (MIC and zone diameter) • Trimethoprim-sulfamethoxazole (zone diameter) **New comments** • Penicillins comments 5 and 6 • Cephalosporins comment 3 • Miscellaneous agents comment 1 • Miscellaneous agents comments B, C and D **Revised comments** • Miscellaneous agents comment 2
***Pseudomonas* spp.**	**New breakpoints** • Ceftazidime-avibactam (MIC and zone diameter for *P. aeruginosa*) **Revised breakpoints** • Ciprofloxacin (MIC and zone diameter) • Levofloxacin (MIC and zone diameter) • Colistin (MIC) **New comments** • Cephalosporins comment 3 • Fluoroquinolones comments 1-2 • Miscellaneous agents comment 1
Streptococcus pneumoniae	**Revised comments**

EUCAST Breakpoint Table v 7.1, 2017

Enterobacteriaceae

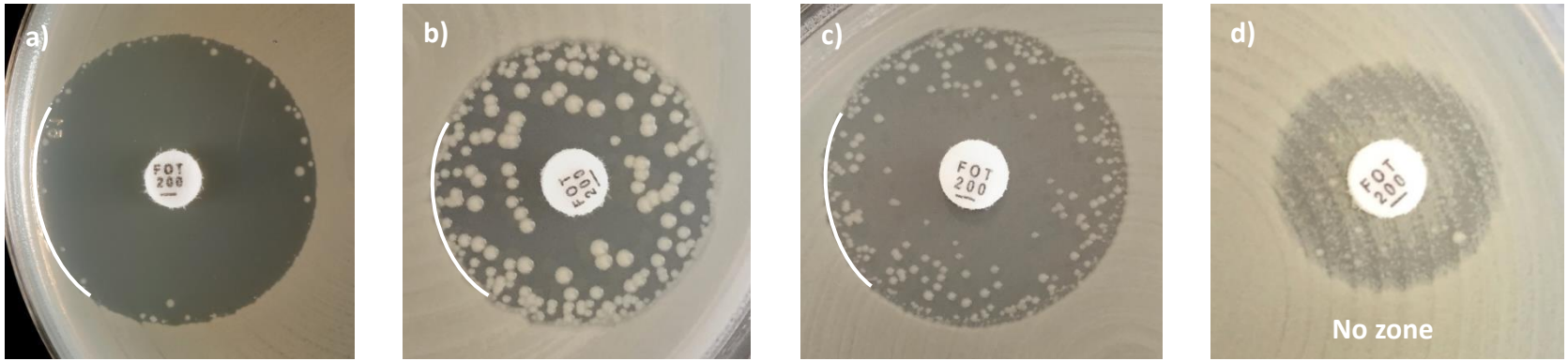
Miscellaneous agents	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)	
	S ≤	R >		S ≥	R <
Fosfomycin iv	32[2]	32[2]	200[B]	24[C,D]	24[C,D]
Fosfomycin oral (uncomplicated UTI only)	32[2]	32[2]	200[B]	24[C,D]	24[C,D]

2. Agar dilution is the reference method for fosfomycin. MICs must be determined in the presence of glucose-6-phosphate (25 mg/L in the medium). Follow the manufacturers' instructions for commercial systems.

B. Fosfomycin 200 µg disks must contain 50 µg glucose-6-phosphate.
C. Zone diameter breakpoints apply to *E. coli* only. For other Enterobacteriaceae, use an MIC method.
D. Ignore isolated colonies within the inhibition zone.

Reading of fosfomycin zones

Ignore isolated colonies within the inhibition zone and read the outer zone edge.



a-c) Ignore all colonies and read the outer zone edge

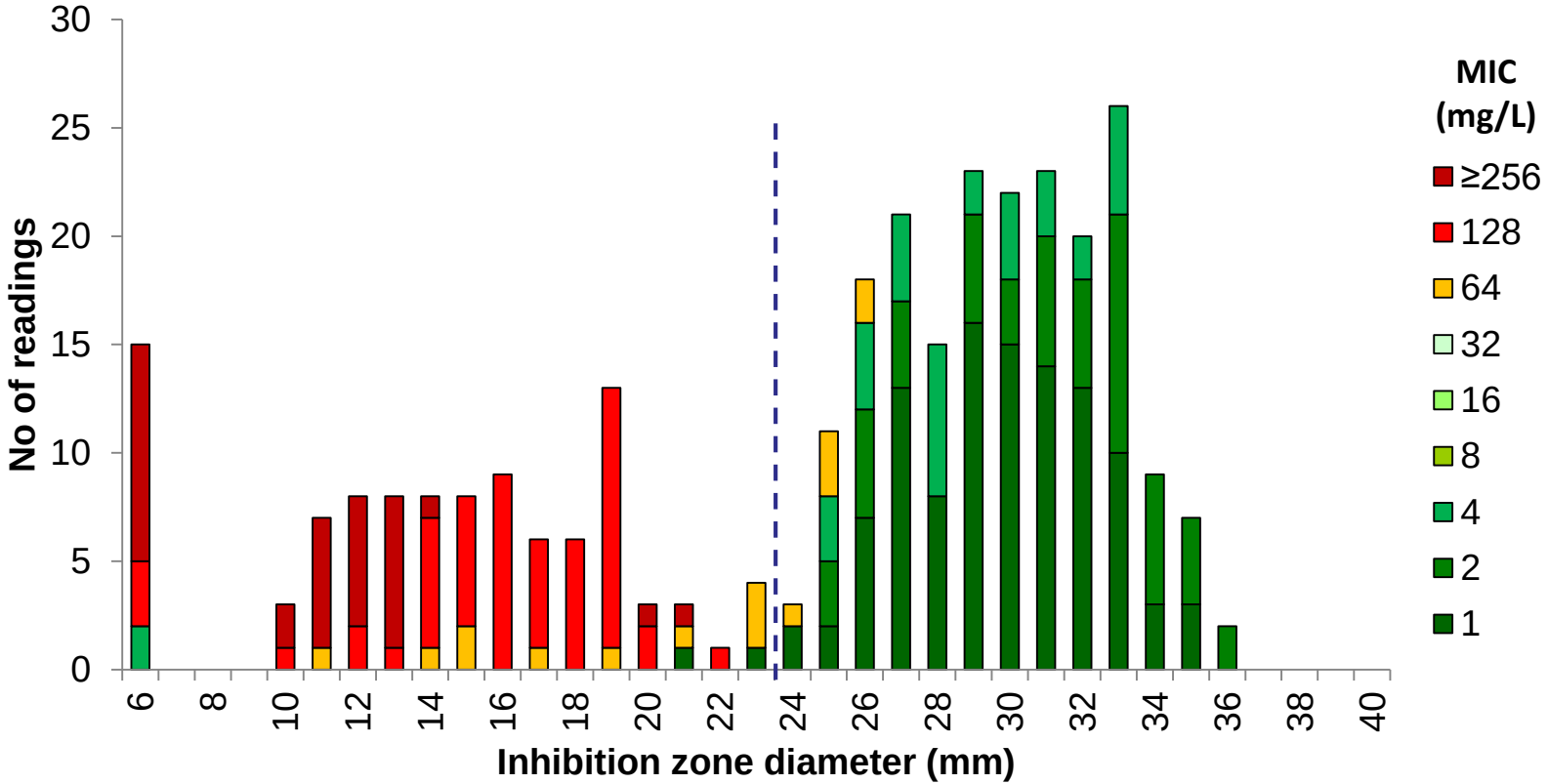
d) Record as no inhibition zone

Calibration of fosfomycin disk diffusion test

- Agar dilution MICs were used as reference
  - All isolates with *fosA* genes according to WGS had fosfomycin MICs ≥128 mg/L

- Ignoring colonies within the inhibition zones (fosfomycin 200 µg disks with 50 µg G6P) for *E. coli*:
  - Reproducible results
  - Good correlation with agar dilution
- The reading instructions were validated at 9 laboratories

- Other Enterobacteriaceae and *P. aeruginosa* to be evaluated during 2017


Fosfomycin 200 µg vs. MIC (agar dilution)
E. coli, 17 clinical isolates tested at 9 sites (x 2 disks)
No of readings
0
5
10
15
20
25
30
6
8
10
12
14
16
18
20
22
24
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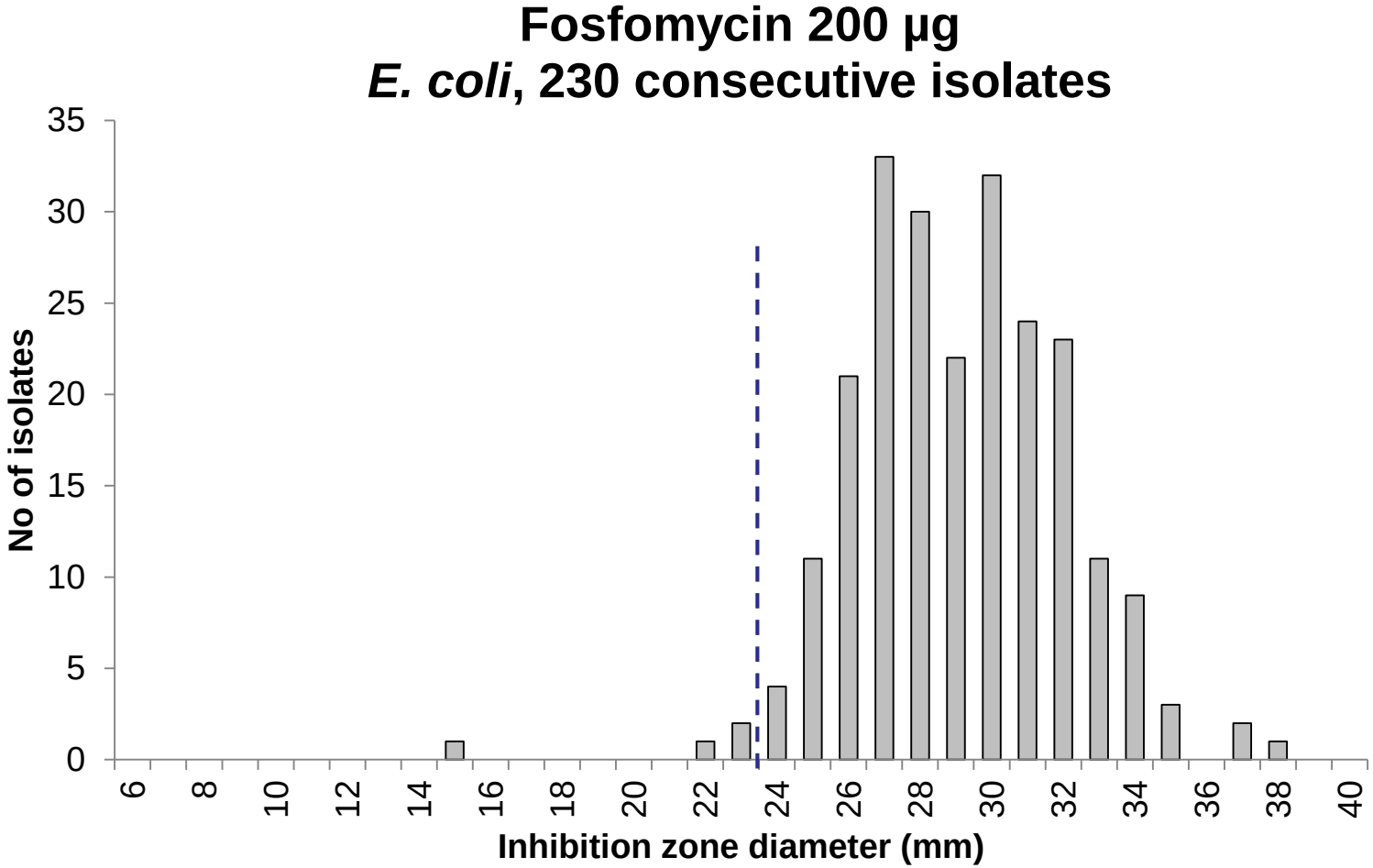
38
40
Inhibition zone diameter (mm)
MIC (mg/L)
≥256
128
64
32
16
8
4
2
1


Fosfomycin 200 µg
E. coli, 230 consecutive isolates
No of isolates
0
5
10
15
20
25
30
35
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
Inhibition zone diameter (mm)

Changes in cefoxitin breakpoint for staphylococci

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Cephalosporins[1]	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes
	S ≤	R >		S ≥	R <	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Cefaclor[2]	Note[1]	Note[1]		Note[A]	Note[A]	1/A. Susceptibility of staphylococci to cephalosporins is inferred from the cefoxitin susceptibility except for cefixime, ceftazidime, ceftazidime-avibactam, ceftibuten and ceftolozane-tazobactam, which do not have breakpoints and should not be used for staphylococcal infections. Some methicillin-resistant *S. aureus* are susceptible to ceftaroline and ceftobiprole, **see Notes 5/C and 6/D.**
Cefadroxil	Note[1]	Note[1]		Note[A]	Note[A]	
Cefalexin	Note[1]	Note[1]		Note[A]	Note[A]	
Cefazolin	Note[1]	Note[1]		Note[A]	Note[A]	
Cefepime	Note[1]	Note[1]		Note[A]	Note[A]	
Cefixime	-	-		-	-	
Cefotaxime	Note[1]	Note[1]		Note[A]	Note[A]	
Cefoxitin (screen), *S. aureus* and coagulase-negative staphylococci other than *S. epidermidis*	Note[3,4]	Note[3,4]	30	22[A,B]	22[A,B]	2. Breakpoints are based on a minimum dose of 500 mg x 3.
Cefoxitin (screen), *S. epidermidis*	Note[4]	Note[4]	30	28[A,B]	28[A,B]	3. *S. aureus* and *S. lugdunensis* with cefoxitin MIC values >4 mg/L and *S. saprophyticus* with cefoxitin MIC values >8 mg/L are methicillin resistant, mostly due to the presence of the *mecA* or *mecC* gene. Disk diffusion reliably predicts methicillin resistance.
Cefoxitin (screen), *S. pseudintermedius*	Note[4]	Note[4]	30	35[A]	35[A]	4. For staphylococci other than *S. aureus*, *S. lugdunensis* and *S. saprophyticus*, the cefoxitin MIC is a poorer predictor of methicillin resistance than the disk diffusion test.
Cefpodoxime	Note[1]	Note[1]		Note[A]	Note[A]	5/C. Methicillin-susceptible isolates can be reported susceptible to ceftaroline without further testing.
Ceftaroline, *S. aureus*	1[5]	1[5]	5	20[C]	20[C]	6/D. Methicillin-susceptible isolates can be reported susceptible to ceftobiprole without further testing.
Ceftazidime	-	-		-	-	
Ceftazidime-avibactam	-	-		-	-	B. If coagulase-negative staphylococci are not identified to species level use zone diameter breakpoints S≥25, R<22 mm. Isolates with zone diameter 22–24 mm should be reported resistant or the presence of *mecA*/*mecC* determined.
Ceftibuten	-	-		-	-	
Ceftobiprole, *S. aureus*	2[6]	2[6]	5	17[D]	17[D]	
Ceftolozane-tazobactam	-	-		-	-	
Ceftriaxone	Note[1]	Note[1]		Note[A]	Note[A]	
Cefuroxime iv	Note[1]	Note[1]		Note[A]	Note[A]	
Cefuroxime oral	Note[1]	Note[1]		Note[A]	Note[A]	

Breakpoint table 7.1 released later

Staphylococcus spp. - Cefoxitin screen for *S. epidermidis* (zone diameter) revised

Staphylococcus spp. - Cefoxitin screen for *S. pseudintermedius* replaced with oxacillin (DD)

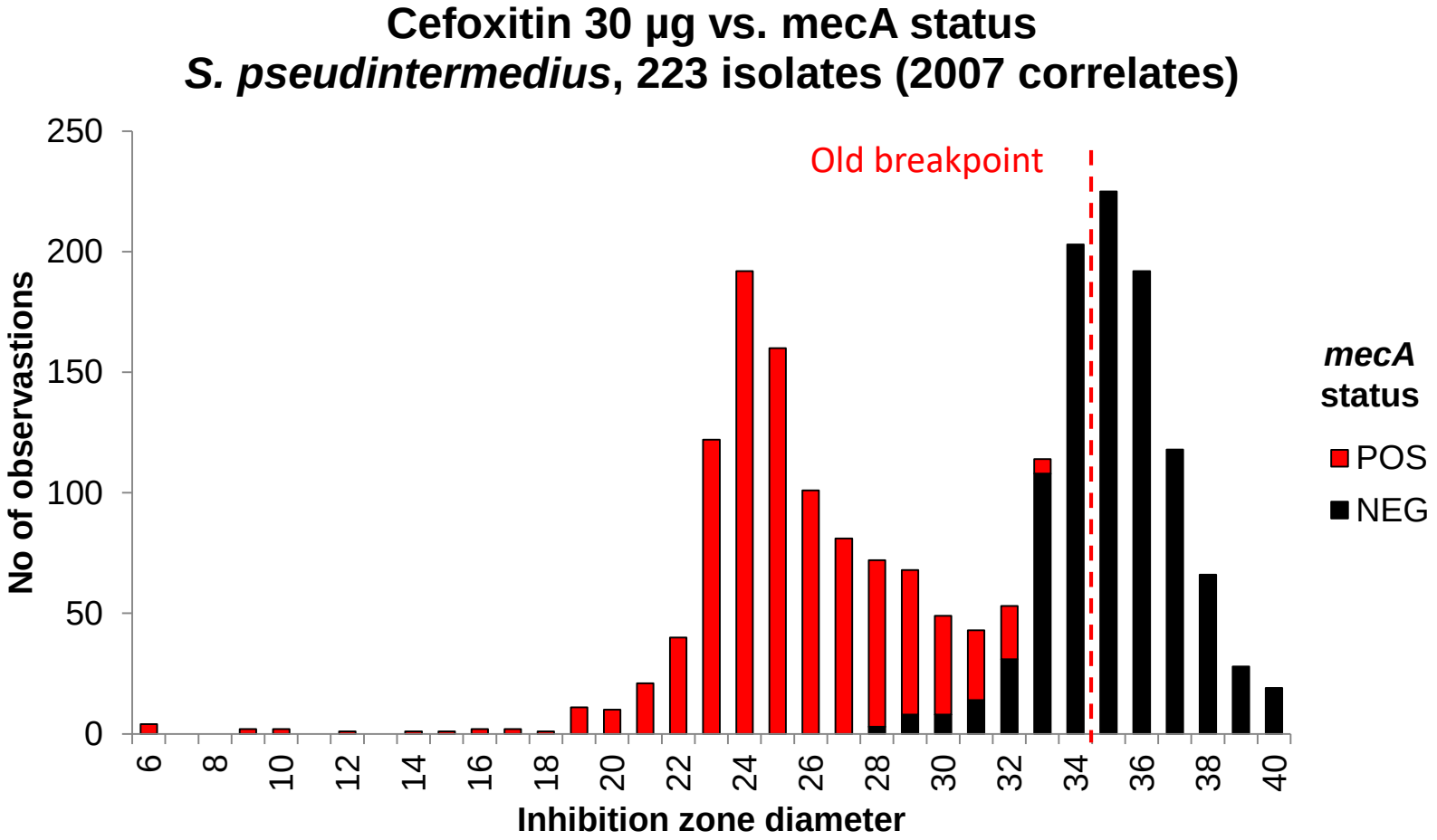
Screen for methicillin resistance in staphylococci

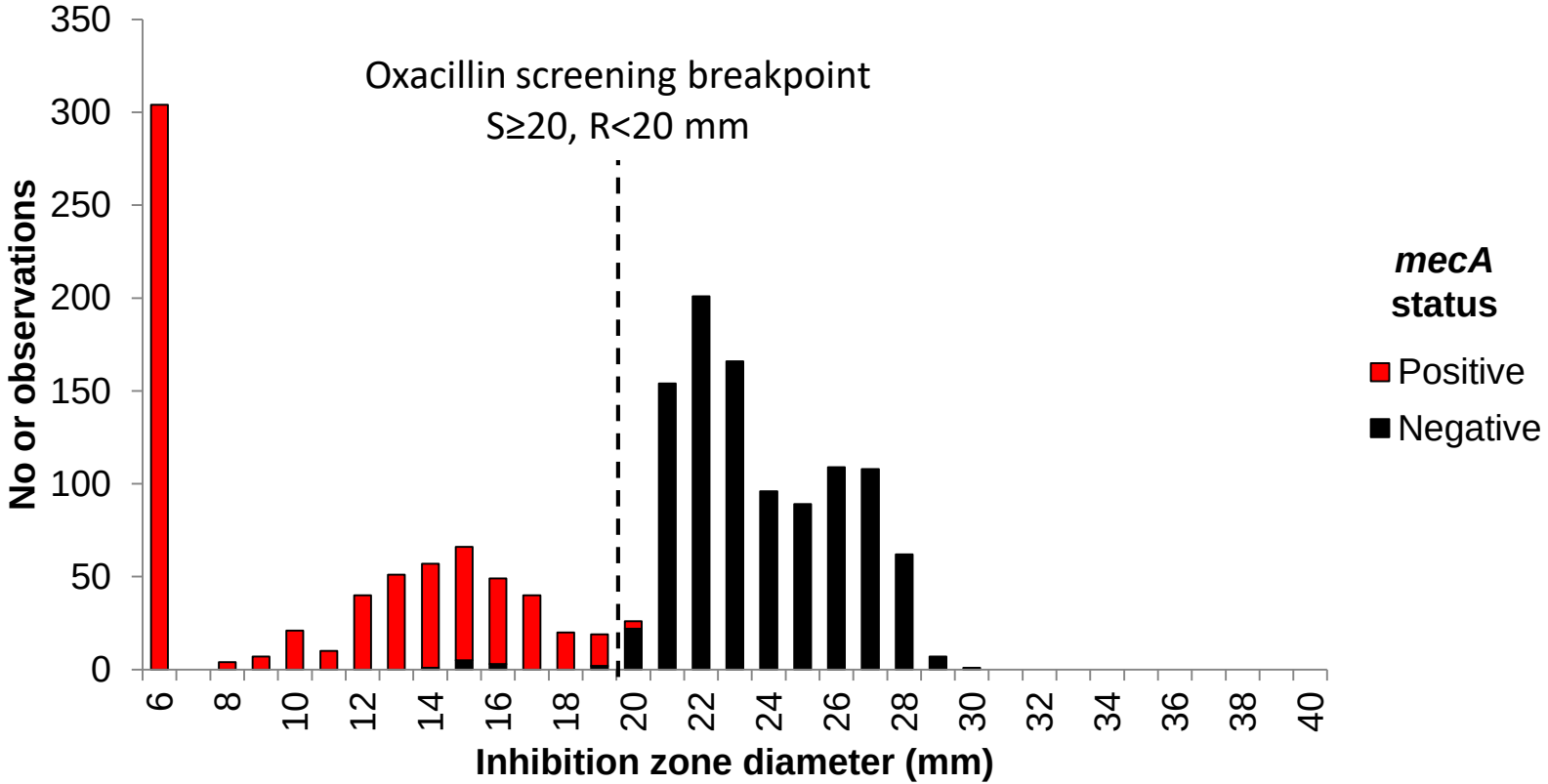
EUCAST breakpoint table v 7.1

Cefoxitin (screen), *S. aureus* and coagulase-negative staphylococci other than *S. epidermidis*	Note[3,4]	Note[3,4]	**30**	22[A,B]	22[A,B]
Cefoxitin (screen), *S. epidermidis*	Note[4]	Note[4]	**30**	25[A,B]	25[A,B]
Cefoxitin (screen), *S. pseudintermedius*	NA	NA	**30**	Note[E]	Note[E]

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

E. Cefoxitin screen for methicillin resistance in ***S. pseudintermedius*** is less predictive of the presence of *mecA* than in other staphylococci. **Use the oxacillin 1 µg disk** with zone diameter breakpoints S≥20, R<20 mm to screen for methicillin resistance.


Cefoxitin 30 µg vs. mecA status
S. pseudintermedius, 223 isolates (2007 correlates)
Old breakpoint
No of observastions
250
200
150
100
50
0
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
Inhibition zone diameter
mecA status
POS
NEG


Oxacillin 1 µg vs. mecA status
S. pseudintermedius, 223 isolates (2007 correlates)
Oxacillin screening breakpoint
S≥20, R<20 mm
No or observations
350
300
250
200
150
100
50
0
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
Inhibition zone diameter (mm)
mecA status
Positive
Negative

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Breakpoints for *Aerococcus*

Aerococcus sanguinicola and *urinae*

EUCAST Clinical Breakpoint Tables v. 7.0, valid from 2017-01-01

Disk diffusion (EUCAST standardised disk diffusion method)
Medium: Mueller-Hinton agar + 5% defibrinated horse blood and 20 mg/L β-NAD (MH-F)
Inoculum: McFarland 0.5
Incubation: 5% CO_2, 35±1°C, 18±2h. Isolates with insufficient growth after 16-20h incubation are reincubated immediately and inhibition zones read after a total of 40-44h incubation.
Reading: Read zone edges as the point showing no growth viewed from the front of the plate with the lid removed and with reflected light.
Quality control: *Streptococcus pneumoniae* ATCC 49619

Penicillins	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes
	S ≤	R >		S ≥	R <	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Benzylpenicillin	0.125	0.125	1 unit	21	21	1/A. Infer susceptibility from amicillin susceptibility.
Ampicillin	0.25	0.25	2	26	26	
Amoxicillin	Note[1]	Note[1]		Note[A]	Note[A]	

Carbapenems	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes
	S ≤	R >		S ≥	R <	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Meropenem	0.25	0.25	10	31	31	

Fluoroquinolones	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes
	S ≤	R >		S ≥	R <	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Ciprofloxacin (uncomplicated UTI only)	2	2	5	21[A]	21[A]	1. Susceptibility can be inferred from ciprofloxacin susceptibility.
Levofloxacin (uncomplicated UTI only)	2[1]	2[1]	5	Note[B]	Note[B]	
Norfloxacin (screen)	NA	NA	10	17[C]	17[C]	A. Susceptibility can be inferred from norfloxacin susceptibility. **See Note C.** B. Susceptibility can be inferred from ciprofloxacin or norfloxacin susceptibility. **See Note C.** C. The norfloxacin disk diffusion test can be used to screen for fluoroquinolone resistance.

Glycopeptides	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes
	S ≤	R >		S ≥	R <	Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.
Vancomycin	1	1	5	16	16	

AST of colistin – dilution methods

- Broth microdilution (BMD)
  - International reference method (ISO 20776-1)
  - Sulphate salts
  - Standard polystyrene trays
  - No additives or pre-treatment of plates

  - In-house prepared or commercial plates

- Agar dilution
  - To be evaluated

For BMD, see EUCAST Guidance Documents
www.eucast.org/guidance_documents/

AST of colistin – diffusion methods

- Gradient tests?
  - Etest, bioMérieux
  - MIC Test Strip (MTS), Liofilchem
  - Poor correlation with reference BMD
  - Warning on www.eucast.org

- Disk diffusion?
  - Poor separation between resistant and susceptible isolates

- The poor performance of diffusion tests is probably due to poor diffusion of colistin in agar.

EXPERT RULES DOCUMENT PARTIALLY UPDATED

- Intrinsic resistance tables
- Exceptional resistance phenotypes tables
- Expert rules tables

EXPERT RULES DOCUMENT PARTIALLY UPDATED

- The new **intrinsic resistance** & **exceptional resistance phenotypes** tables **(v3.1)** have invalidated these tables in the **expert rules document (v2.0)**

- Although **expert rules tables (IF… THEN…) (v2.0)** are presently being reviewed, they still be applied unless there is arguments against using them

  - aminoglycoside rules (12.7 to 12.10) might be deleted as clinical evidence is scarce. They can be used for “interpretive reading” (inference of resistance mechanisms)

12.7	All *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*	Tobramycin, gentamicin, and amikacin	Amikacin	IF intermediately resistant or resistant to tobramycin and susceptible to gentamicin and amikacin, THEN report amikacin as intermediate for *Enterobacteriaceae* or resistant for *Pseudomonas* spp. and *Acinetobacter* spp.	Production of acquired AAC(6′)-I enzyme may not confer phenotypic resistance despite modification of amikacin
12.8	All *Enterobacteriaceae*	Gentamicin and other aminoglycosides	Gentamicin	IF intermediately resistant to gentamicin and susceptible to other aminoglycosides, THEN report as resistant to gentamicin	Expression of AAC(3)-I enzyme may be low, and isolates may have decreased susceptibility to gentamicin
12.9	All *Enterobacteriaceae*	Tobramycin, gentamicin, and amikacin	Tobramycin	IF intermediately resistant to tobramycin, resistant to gentamicin and susceptible to amikacin, THEN report as resistant to tobramycin	Expression of the ANT(2″) enzyme may be low and isolates may have decreased susceptibility to tobramycin
12.10	All *Enterobacteriaceae*	Netilmicin and gentamicin	Netilmicin	IF intermediately resistant to netilmicin and intermediately resistant or resistant to gentamicin and tobramycin, THEN report as resistant to netilmicin	Expression of the AAC(3″)-II or AAC(3″)-IV enzyme may be low and isolates may appear with decreased susceptibility to netilmicin

EXPERT RULES: INTRINSIC RESISTANCE

- **Intrinsic resistance tables from Expert rules** were reviewed by EUCAST-SC, approved after general consultation an published Sept-2016 (v3.1)
- **Intrinsic resistance**, as opposed to acquired and/or mutational resistance, is a characteristic of all or almost all isolates of the bacterial species
- For a clinical point of view, the drug is considered clinically useless, they can be reported as “R” and susceptibility testing is unnecessary
- Absence of detectable resistance when intrinsic resistance should be present suggests misidentification or an error on susceptibility testing

  Exceptions might occur due to rare mutations, insertions and or/deletions affecting gene expression rendering susceptibility to the drug in question
  Even if a ‘susceptible' result is confirmed, the drug use is not recommended

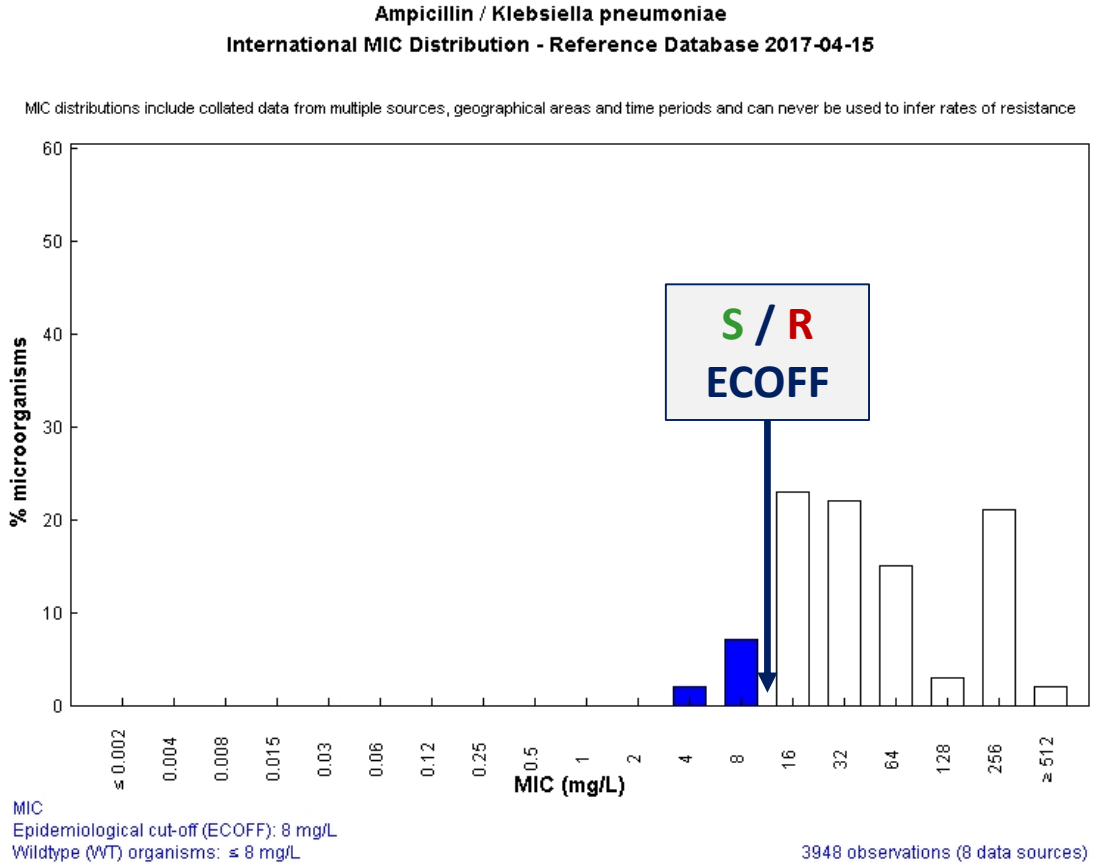
INTRINSIC RESISTANCE

Rule no.	Organisms	Ampicillin	Amoxicilin-Clavulanic acid	Ampicillin-sulbactam	Ticarcillin	Cefazolin, Cefalotin Cefalexin, Cefadroxil	Cefoxitin[2]	Cefuroxime	Tetracyclines	Tigecycline	Polymyxin B, Colistin	Nitrofurantoin
1.1	*Citrobacter koseri,Citrobacter amalonaticus*[3]	R			R							
1.2	*Citrobacter freundii*[4]	R	R	R		R	R					
1.3	*Enterobacter cloacae* complex	R	R	R		R	R					
1.4	*Enterobacter aerogenes*	R	R	R		R	R					
1.5	*Escherichia hermannii*	R			R							
1.6	*Hafnia alvei*	R	R	R		R	R					
1.7	*Klebsiella pneumoniae*	R			R							
1.8	*Klebsiella oxytoca*	R			R							
1.9	*Morganella morganii*	R	R	R		R			R		R	R
1.10	*Proteus mirabilis*								R	R	R	R
1.11	*Proteus penneri*	R				R		R	R	R	R	R
1.12	*Proteus vulgaris*	R				R		R	R	R	R	R
1.13	*Providencia rettgeri*	R	R	R		R		R	R	R	R	R
1.14	*Providencia stuartii*	R	R	R		R		R	R	R	R	R
1.15	*Raoultella* spp.	R			R							
1.16	*Serratia marcescens*	R	R	R		R	R	R	R[5]		R	R
1.17	*Yersinia enterocolitica*	R	R	R	R	R	R					
1.18	*Yersinia pseudotuberculosis*										R	

R = resistant

http://www.eucast.org/expert_rules_and_intrinsic_resistance/

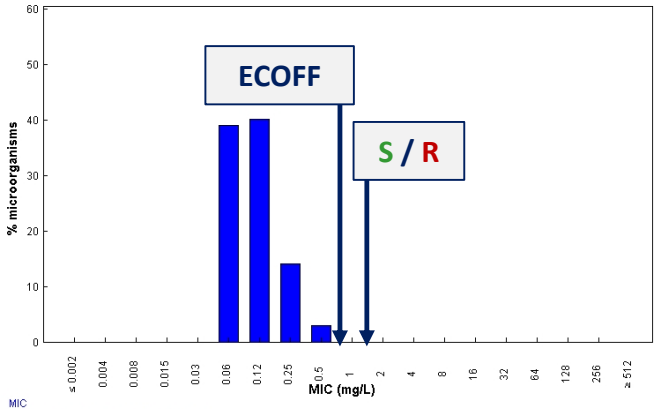
EXPERT RULES: INTRINSIC RESISTANCE



INTRINSIC RESISTANCE

Tigecycline / Escherichia coli
International MIC Distribution - Reference Database 2017-04-15

MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance

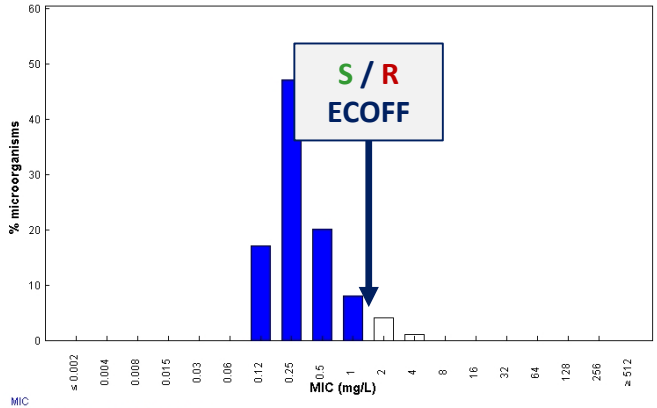


MIC
Epidemiological cut-off (ECOFF): 0.5 mg/L
Wildtype (WT) organisms: ≤ 0.5 mg/L

24146 observations (23 data sources)

Tigecycline / Klebsiella pneumoniae
International MIC Distribution - Reference Database 2017-04-15

MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance

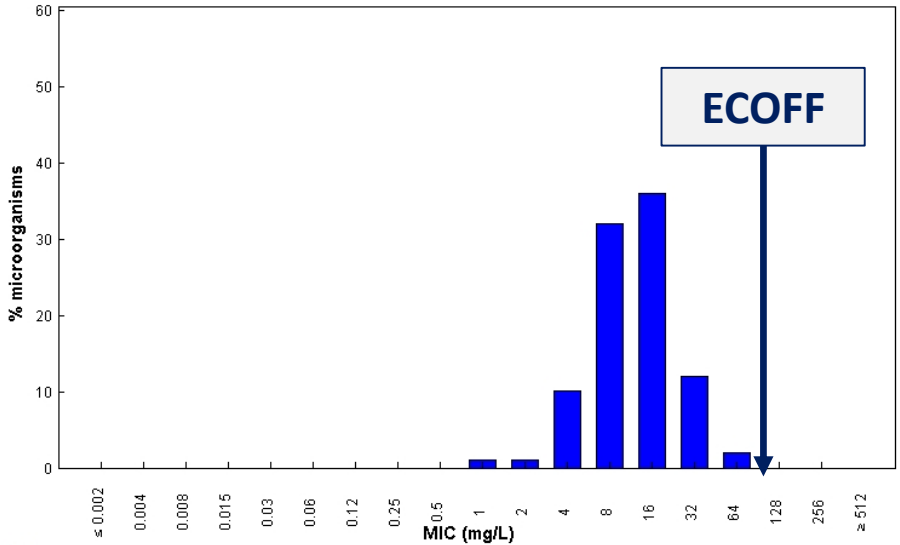


MIC
Epidemiological cut-off (ECOFF): 1 mg/L
Wildtype (WT) organisms: ≤ 1 mg/L

12534 observations (27 data sources)

Tigecycline / Pseudomonas aeruginosa
International MIC Distribution - Reference Database 2017-04-15

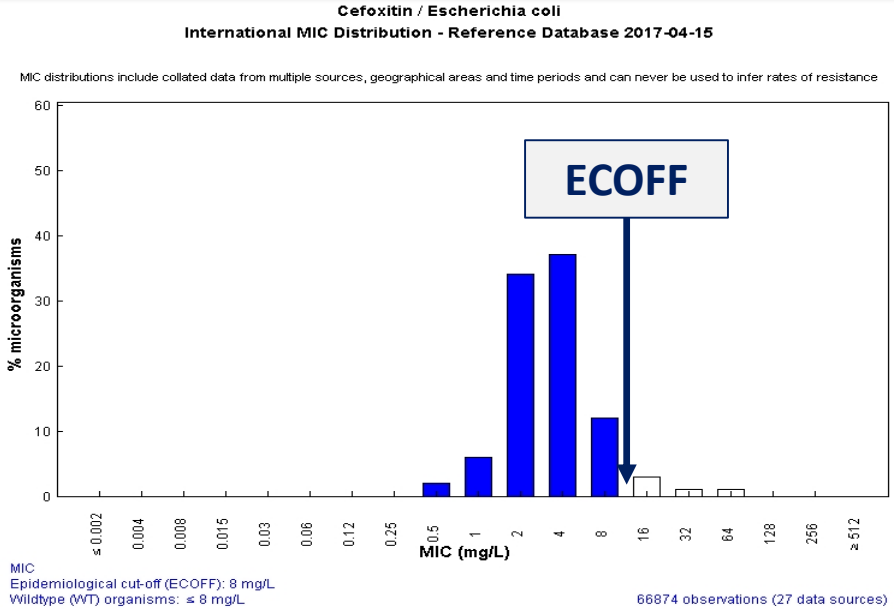
MIC distributions include collated data from multiple sources, geographical areas and time periods and can never be used to infer rates of resistance

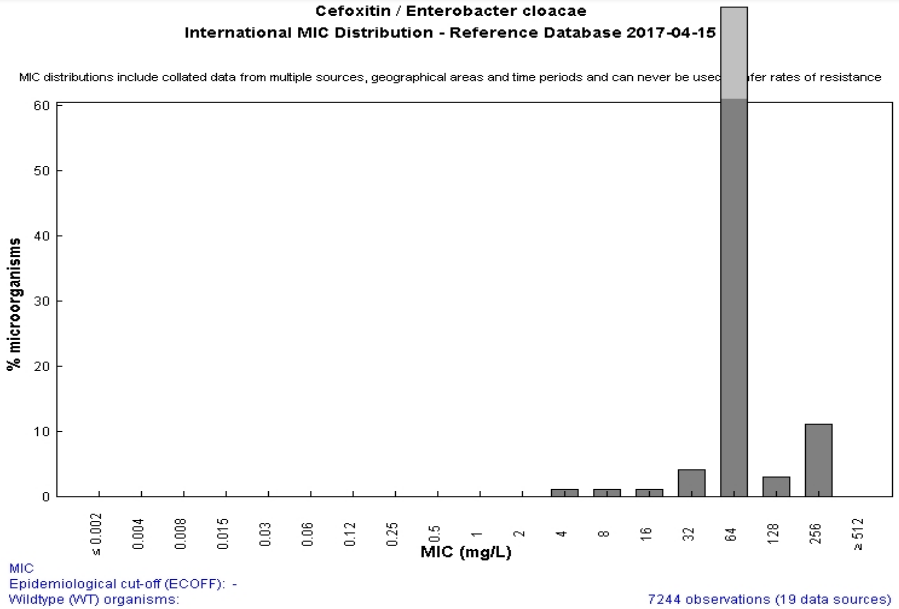


MIC
Epidemiological cut-off (ECOFF): 64 mg/L
Wildtype (WT) organisms: ≤ 64 mg/L

1120 observations (8 data sources)

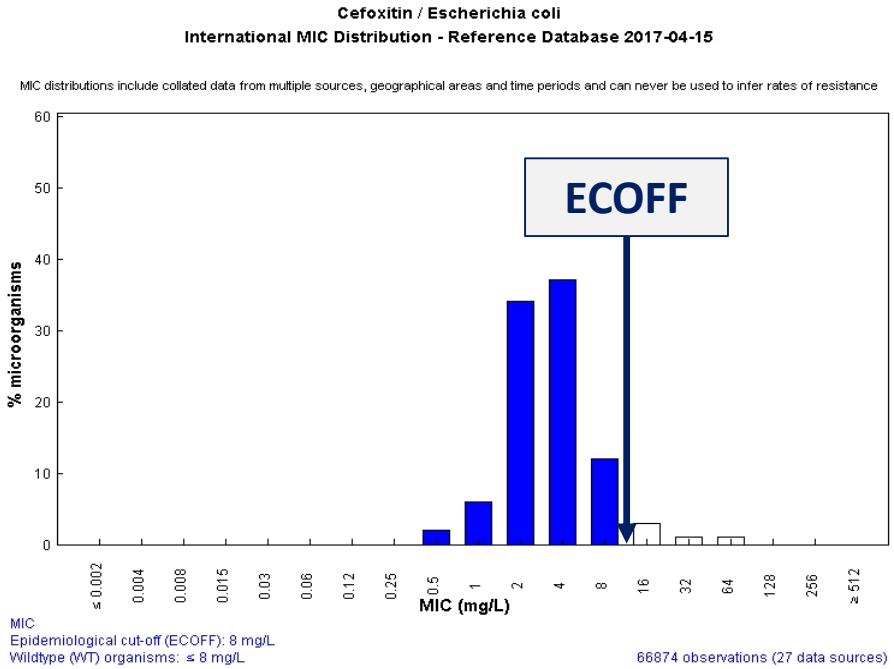
EXPERT RULES: INTRINSIC RESISTANCE

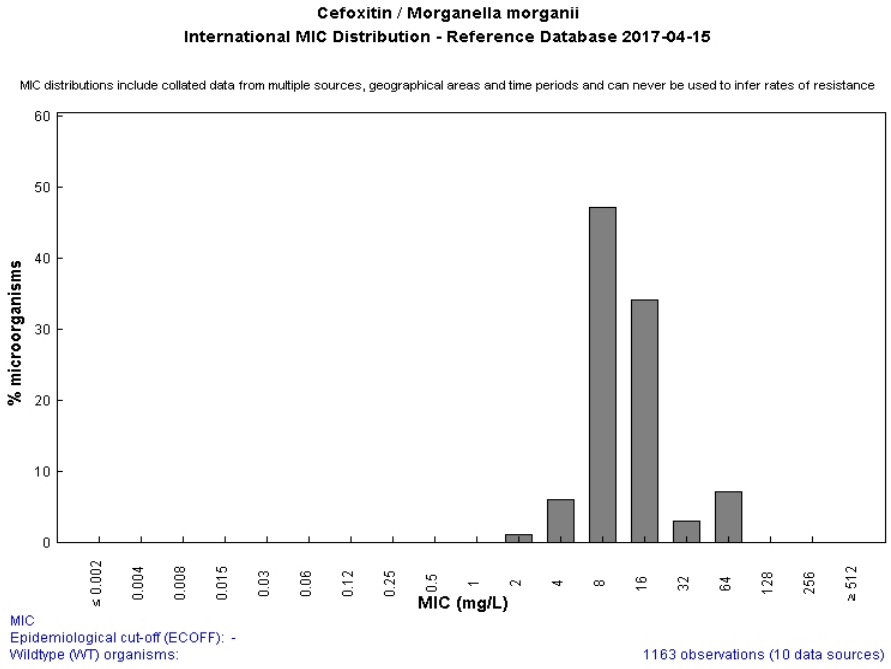




- Clinical breakpoints for FOX have not been defined. Enterobacteriaceae “intrinsically R” to FOX produce a chromosomal inducible AmpC β-lactamase (AmpC) responsible for higher FOX MICs when compared with species lacking production of this enzyme
- Some *Enterobacter* spp. lack AmpC (i.e. *E. gergoviae*) and cannot be considered “intrinsically R” to FOX

EXPERT RULES: INTRINSIC RESISTANCE





- If clinical breakpoints for FOX are stablished, an expert rule for *M. morganii* will be needed:

  - “IF susceptible to cefoxitin THEN report resistant for this antibiotic”

EXPERT RULES: INTRINSIC RESISTANCE

- Increasing use of MALDI TOFF and growing speciation will enlarge the number of species for which intrinsic resistance should be define

- For this objective, it will be needed

  - MIC distributions following EUCAST Subcommittee on MIC distributions and epidemiological cut-off values (ECOFFs)" recommendations [1]

  - Testing for resistance mechanism at molecular level

  - Clinical correlations (MIC and outcomes) if available

[1]MIC and ECOFF Subcommittee discussion document v3, http://www.eucast.org/documents/consultations/

EXPERT RULES: EXCEPTIONAL RESISTANCE PHENOTYPES

- Phenotype of resistance of a bacterial species to a particular antimicrobial agent that has **not yet been reported or are *still* very rare**
- They may change as resistance may develop and increase over time and also geographically as a very rare phenotype in one hospital/area/ country may be common in another
- New version has mostly removed “exceptional susceptible phenotypes” (i.e. *E. faecium* ampicillin susceptible) as this might vary among countries
- Exceptional resistance phenotypes should be checked, as they may also indicate an error in identification or susceptibility testing

  If confirmed locally, it should be further studied to confirm and sent to a reference laboratory (or other with expertise) or independent confirmation

EXPERT RULES: EXCEPTIONAL RESISTANCE PHENOTYPES

Exceptional resistance phenotypes for Gram-positives

Rule no.	Organisms	Exceptional phenotypes
6.1	*Staphylococcus aureus*	Resistant to vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin and/or tigecycline.
6.2	Coagulase-negative staphylococci	Resistant to vancomycin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid[1], tedizolid[1], quinupristin-dalfopristin[1] and/or tigecycline.
6.3	*Corynebacterium* spp.	Resistant to vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin and/or tigecycline.
6.4	*Streptococcus pneumoniae*	Resistant to carbapenems, vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin, tigecycline and/or rifampicin.
6.5	Group A, B, C and G β-haemolytic streptococci	Resistant to penicillin, cephalosporins, vancomycin, teicoplanin, telavancin, dalbavancin, oritavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin and/or tigecycline.
6.6	*Enterococcus* spp.	Resistant to daptomycin, linezolid and/or tigecycline. Resistant to teicoplanin but not vancomycin.
6.7	*Enterococcus faecalis*	Resistant to ampicillin
6.8	*Enterococcus faecalis, Enterococcus gallinarum, Enterococcus casseliflavus, Enterococcus avium*	Susceptible to quinupristin-dalfopristin, consider misidentification. If also resistant to ampicillin it is almost certainly *E. faecium*.

[1] Except in countries where linezolid, tedizolid or quinupristin-dalfopristin resistant coagulase-negative staphylococci are not rare.

http://www.eucast.org/expert_rules_and_intrinsic_resistance

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Warnings on EUCAST website

AST of bacteria

- Organization
- EUCAST News
- Clinical breakpoints
- Expert rules and intrinsic resistance
- Resistance mechanisms
- Guidance documents
- MIC distributions and ECOFFs
- Zone distributions and ECOFFs
- **AST of bacteria**
  - Media preparation
  - MIC determination
  - Disk diffusion methodology
  - Disk diffusion implementation
  - Compliance of manufacturers
  - Breakpoint tables
  - QC Tables
  - Calibration and validation
  - **Warnings!**

EUCAST warnings concerning antimicrobial susceptibility testing products or procedures.

The EUCAST disk diffusion development laboratories, a network of laboratories coordinated from the EUCAST development laboratory in Växjö, Sweden, from time to time discover products (disks, media batches, gradient tests or procedures) which are not performing to the expected standard. When this is the case we inform the manufacturer and publish a warning on this page.

We do not systematically test all products so the lack of a warning does not imply that there is no problem with the product in question.

Laboratories which experience problems with a susceptibility test method, and suspect that this may be related to a particular product, may contact EUCAST for advice.

1. Problems with piperacillintazobactam gradient tests from two manufacturers (see below).
2. Wide variation in disk quality in 16 disks from nine manufacturers (see below)

Trends on Pubmed for “EUCAST”

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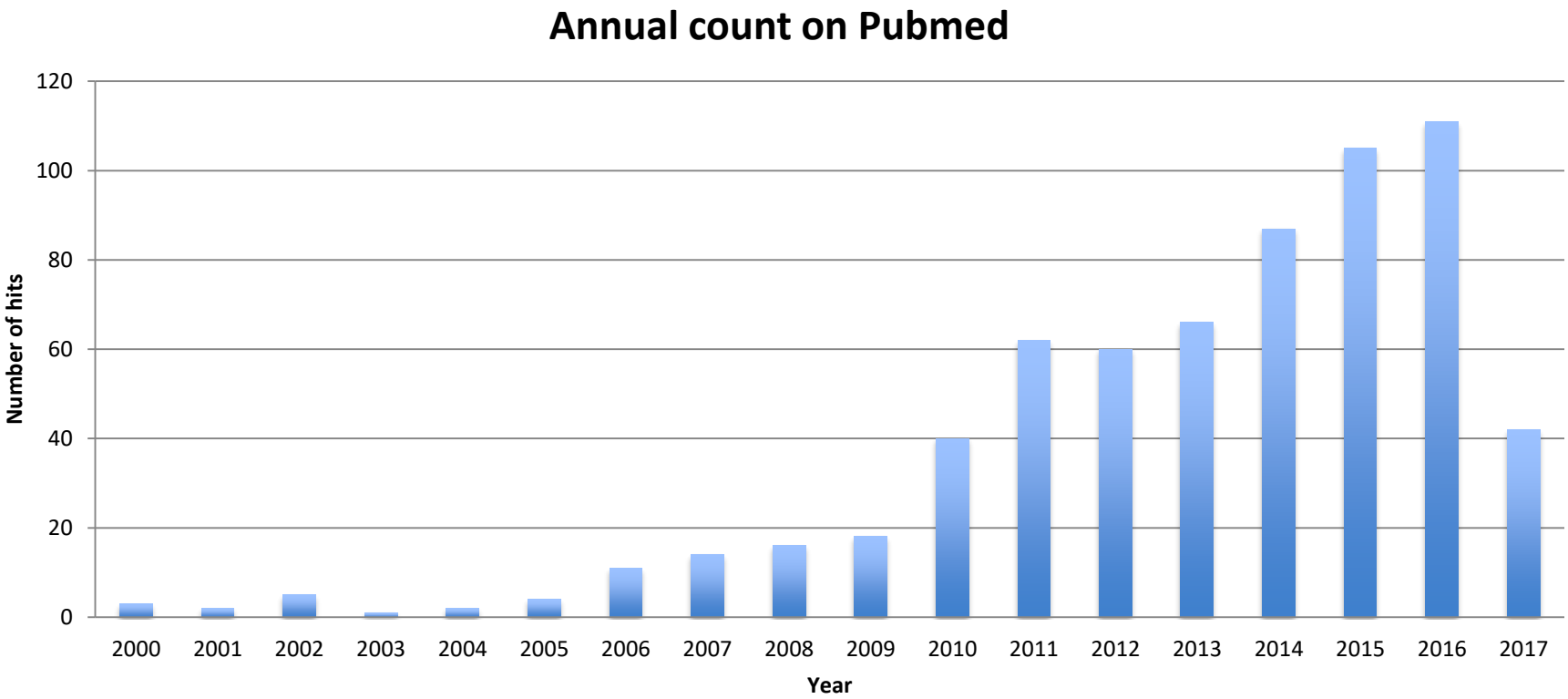

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journal homepage: www.clinicalmicrobiologyandinfection.com

Review

The role of whole genome sequencing in antimicrobial susceptibility testing of bacteria: report from the EUCAST Subcommittee

M.J. Ellington [1, †], O. Ekelund [2, †], F.M. Aarestrup [3], R. Canton [4], M. Doumith [1], C. Giske [5], H. Grundman [6], H. Hasman [7], M.T.G. Holden [8], K.L. Hopkins [1], J. Iredell [9], G. Kahlmeter [2], C.U. Köser [10], A. MacGowan [11], D. Mevius [12, 13], M. Mulvey [14], T. Naas [15], T. Peto [16], J.-M. Rolain [17], Ø. Samuelsen [18], N. Woodford [1, *]

Available published evidence does not currently support use of WGS-inferred susceptibility to guide clinical decision making. Such a paradigm shift would require large-scale education and behavioural change among microbiologists and prescribers. Gene (or mutation) absence cannot always reliably predict susceptibility, so robust evidence will be needed to show that the potential of genotypic tests for very major errors does not adversely impact on treatment outcomes. It seems likely that this may first be considered for *M. tuberculosis*, where the speed of WGS-generated results offers advantage over traditional AST methods. However, even if the evidence can be generated and expectations changed, for most bacteria and in most countries the current cost and speed of inferring antimicrobial susceptibility from WGS data remain prohibitive to wide adoption in routine clinical laboratories. Never-

AFST publications

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European Society of Clinical Microbiology and Infectious Diseases

RESEARCH NOTE

EUCAST technical note on isavuconazole breakpoints for *Aspergillus*, itraconazole breakpoints for *Candida* and updates for the antifungal susceptibility testing method documents

Keywords: Antifungal susceptibility testing, breakpoints, isavuconazole, itraconazole, QC MIC ranges
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Presented in part at the seventh Trends in Medical Mycology conference (TIMM-7), Lisbon, Portugal, 11 October 2015
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Committee members are listed in the Acknowledgements

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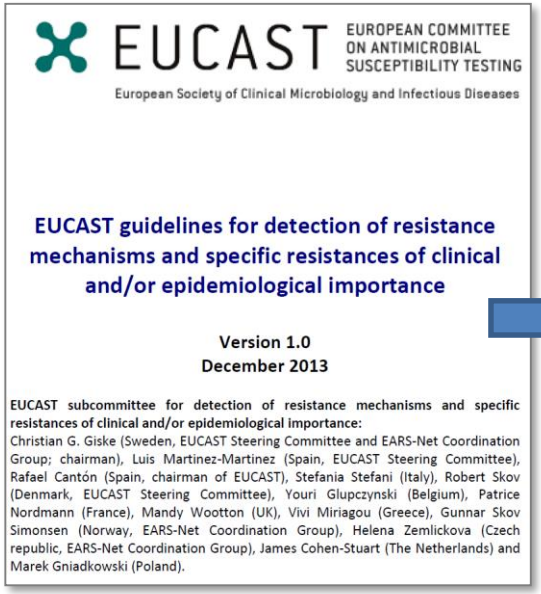
Original article

Spectrophotometric reading of EUCAST antifungal susceptibility testing of *Aspergillus fumigatus*

J. Meletiadis [1, 2, *], K. Leth Mortensen [3, 4], P.E. Verweij [5, 6], J.W. Mouton [2], M.C. Arendrup [3, 4, 7]

Resistance mechanisms guidelines update

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

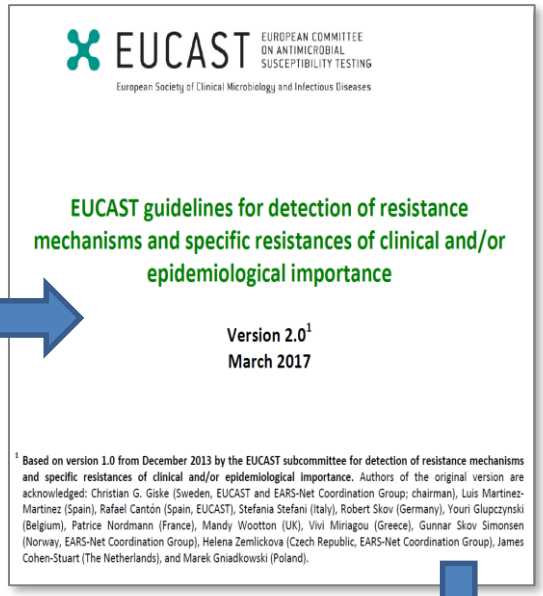


EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

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 EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance

Version 2.0[1]
March 2017

[1] **Based on version 1.0 from December 2013 by the EUCAST subcommittee for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance.** Authors of the original version are acknowledged: Christian G. Giske (Sweden, EUCAST and EARS-Net Coordination Group; chairman), Luis Martinez-Martinez (Spain), Rafael Cantón (Spain, EUCAST), Stefania Stefani (Italy), Robert Skov (Germany), 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).

www.eucast.org

also includes…

- Colistin resistance in Enterobacteriaceae
- Carbapenem resistance in *P. aeruginosa* and *Acinetobacter*

EUCAST: Detection or resistance mechanism

Resistance mechanisms of clinical and/or epidemiological importance	Required for AST categorization	Infection control	Public health
ESBL producing Enterobacteriaceae	No	Yes	Yes
Plasmid AmpC in Enterobacteriaceae	No	Yes	Yes
Carbapenemase producing Enterobacteriaceae	No	Yes	Yes
Colistin resistance in Enterobacteriaceae	Yes	Yes	Yes
Carbapenem resistance in *P. aeruginosa* and *Acinetobacter* spp.	No	Yes	Yes
Methicillin-R *S. aureus* (MRSA)	Yes	Yes	Yes
Glycopeptide non-susceptible *S. aureus*	Yes	Yes	Yes
Vancomycin resistant *E. faecium*/*E. faecalis*	Yes	Yes	Yes
Penicillin non-susceptible *S. pneumoniae*	Yes	No	Yes

http://www.eucast.org/resistance_mechanisms/

https://www.federalregister.gov/documents/2013/06/12/2013-13865/establishing-a-list-of-qualifying-pathogens-under-the-food-and-drug-administration-safety-and
http://www.who.int/medicines/publications/global-priority-list-antibiotic-resistant-bacteria/en/

M. tuberculosis AST

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Review

Mycobacterium tuberculosis drug-resistance testing: challenges, recent developments and perspectives

T. Schön [1, 2, 3], P. Miotto [4], C.U. Köser [5], M. Viveiros [3, 6], E. Böttger [3, 7], E. Cambau [3, 8, 9, 10, *]

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http://www.eucast.org

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search term

- Organization
- EUCAST News
- Clinical breakpoints
- Expert rules and intrinsic resistance
- Resistance mechanisms
- Guidance documents
- Consultations
- MIC distributions and ECOFFs
- Zone distributions and ECOFFs
- AST of bacteria
- AST of mycobacteria
- AST of fungi
- AST of veterinary pathogens
- Frequently Asked Questions (FAQ)
- Meetings
- Presentations and statistics
- Warnings!
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- Translations
- Information for industry
- Links
- Contacts

Website changes

04 May 2017

The European Committee on Antimicrobial Susceptibility Testing - EUCAST

EUCAST is a standing committee jointly organized by ESCMID, ECDC and European national breakpoint committees. EUCAST was formed in 1997. It has been chaired by Ian Phillips (1997 - 2001), Gunnar Kahlmeter (2001 - 2012), Rafael Canton 2012 - 2016) and Christian Giske (2016 -). Its scientific secretary is Derek Brown (1997 - 2016) and John Turnidge (2016 -). Its webmaster is Gunnar Kahlmeter (2001 -). From 2016, Rafael Canton is the Clinical Data Co-ordinator and Gunnar Kahlmeter the Technical Data Co-ordinator.

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 countries, FESCI and ISC. The Steering Committee also consults on EUCAST proposals with experts within the fields of infectious diseases and microbiology, pharmaceutical companies and susceptibility testing device manufacturers.

EUCAST has several subcommittees - → see page Subcommittees.

Most antimicrobial MIC breakpoints in Europe have been harmonised by EUCAST. Breakpoints for new agents are set as part of the licensing process for new agents through EMA. EUCAST breakpoints are available in devices for automated susceptibility testing but with some limitations, depending on the system. A disk diffusion susceptibility test method → calibrated to EUCAST MIC breakpoints is also available.

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

To cite the EUCAST website or a document on the EUCAST website: List the document name, version, year and the full web adress. For example, if you want to refer to the current EUCAST breakpoint table, the citation reads The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, version 7.1, 2017, http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_7.1_Br

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QUICK NAVIGATION

EUCAST News

04 May 2017
Posaconazole RD for Candida and Aspergillus merged and updated.

19 Apr 2017
EUCAST Posters at ECCMID 2017

18 Apr 2017
EUCAST General Committee 2017 Agenda

18 Apr 2017
Maps of EUCAST uptake and website stats 2017 updated.

27 Mar 2017
EUCAST instruction videos in Czech

→ About Newsfeeds

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH

htpp://brcast.org.br/

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BrCAST
Brazilian Committee on Antimicrobial Susceptibility Testing

Pesquisar Pesquisar

II ENCONTRO INTERNACIONAL BrCAST e EUCAST 2017

São Paulo – dia 27 de maio de 2017
Hotel Renaissance

BrCAST

10 de março de 2017

Prezados colegas da área de saúde,

Ratificando o compromisso assumido pelas quatro sociedades científicas que compõem o BrCAST, a Coordenação Geral, a Coordenação Clínica e o Comitê Gestor foram renovados.

Tornamos disponível em Português a versão 2017 da Tabela de Pontos de Corte, principal documento para implementação das normas BrCAST-EUCAST no laboratório clínico. Há várias atualizações importantes, como, por exemplo, os pontos de corte para fluoroquinolonas nos diferentes grupos de microrganismos, colistina e polimixina B para *Pseudomonas aeruginosa*, pontos de corte de fosfomicina para disco-difusão em *Enterobacteriaceae*, com imagens que facilitam muito a interpretação.

A apresentação oficial do documento e dos racionais das mudanças ocorrerá no dia 27 de maio de 2017, no Hotel Renaissance, na cidade de São Paulo, das 08:00 às 17:00. O evento contará com a participação do Dr. Rafael Cantón, coordenador clínico do EUCAST.

Não percam essa oportunidade de atualização, troca de experiências e interação!

Abraço a todos.

Ana Cales
Coordenador Geral do BrCAST – 2016-2018

Alexandre Zavascki
Coordenador Clínico BrCAST - 2016-2018

EUCAST
EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

BrCAST
Brazilian Committee on Antimicrobial Susceptibility Testing

EUCAST 2017: Quais são as novidades e quais as diferenças em relação ao CLSI 2017?

Sao Paulo, May 27, 2017

SaludMadrid

Dr. Rafael Cantón

Hospital Universitario Ramón y Cajal
SERVICIO DE MICROBIOLOGÍA Y PARASITOLOGÍA

instituto ramón y cajal de investigación sanitaria irycis

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