



# EUCAST (Comité europeo del antibiograma): armonización en Europa con el acuerdo del ECDC y la EMA

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**EUCAST CHAIRMAN**



**EUCAST**

EUROPEAN COMMITTEE  
ON ANTIMICROBIAL  
SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

# Antibiograma (estudio de sensibilidad a los antibióticos)

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## *Algunas cifras ...*

- 5,7% de los pacientes hospitalizados en **Europa** tiene al menos una infección nosocomial ( $\approx 80.000/\text{día}$ ), la mayoría por bacterias multirresistentes
  - 45,9% con estudio microbiológico y etiología documentada
    -  **85.0% ( $\approx 31.200$ ) con estudio de sensibilidad**
- En **España** se emiten cerca de  $3 \times 10^6$  informes de sensibilidad por año ( $\approx 8.000$  al día)\*
  - infecciones hospitalarias:  $1.6 \times 10^6$  (55%)
  - infecciones comunitarias:  $1.4 \times 10^6$  (45%)

Point prevalence survey of HAI and antimicrobial use in European hospitals 2011-2012. ECDC surveillance report. 2 July 2013

\*cálculo a partir de la actividad de un hospital terciario del SNS con 1.200 camas y atención a 550.000 habitantes

# Antibiograma: objetivos

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Evalúa la respuesta *in vitro* de un microorganismo a la acción de uno o varios antibióticos



- Predecir el **éxito o fracaso** del tratamiento antimicrobiano de forma individual (tratamiento dirigido) o empírico



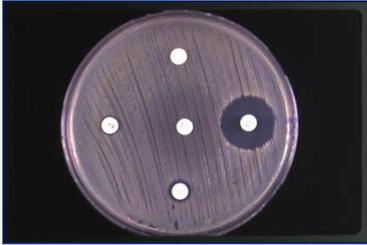
***Trascendencia para el paciente (seguridad)***

- Proporcionar **alertas epidemiológicas** para establecer medidas de control y de prevención de infección
- Conocer la **epidemiología de la resistencia** a los antibióticos (emergencia, evolución y dispersión de los mecanismos de resistencia) y evaluar las medidas establecidas para su control



***Trascendencia en Salud Pública***

# Antibiograma: interpretación de los datos de sensibilidad



↓  
CMI (mg/L); halos de inhibición (mm)

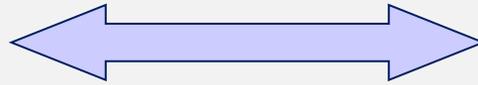
↓  
Puntos de corte (*breakpoints*)

↓  
CATEGORIAS CLINICAS  
Sensible (**S**); Intermedio (**I**); Resistente (**R**)



Comités técnicos del antibiograma

# Estudio de sensibilidad a los antimicrobianos



**CLSI (NCCLS)**



- **Puntos de corte clínicos**

$S \leq ; R \geq$

**EUCAST**



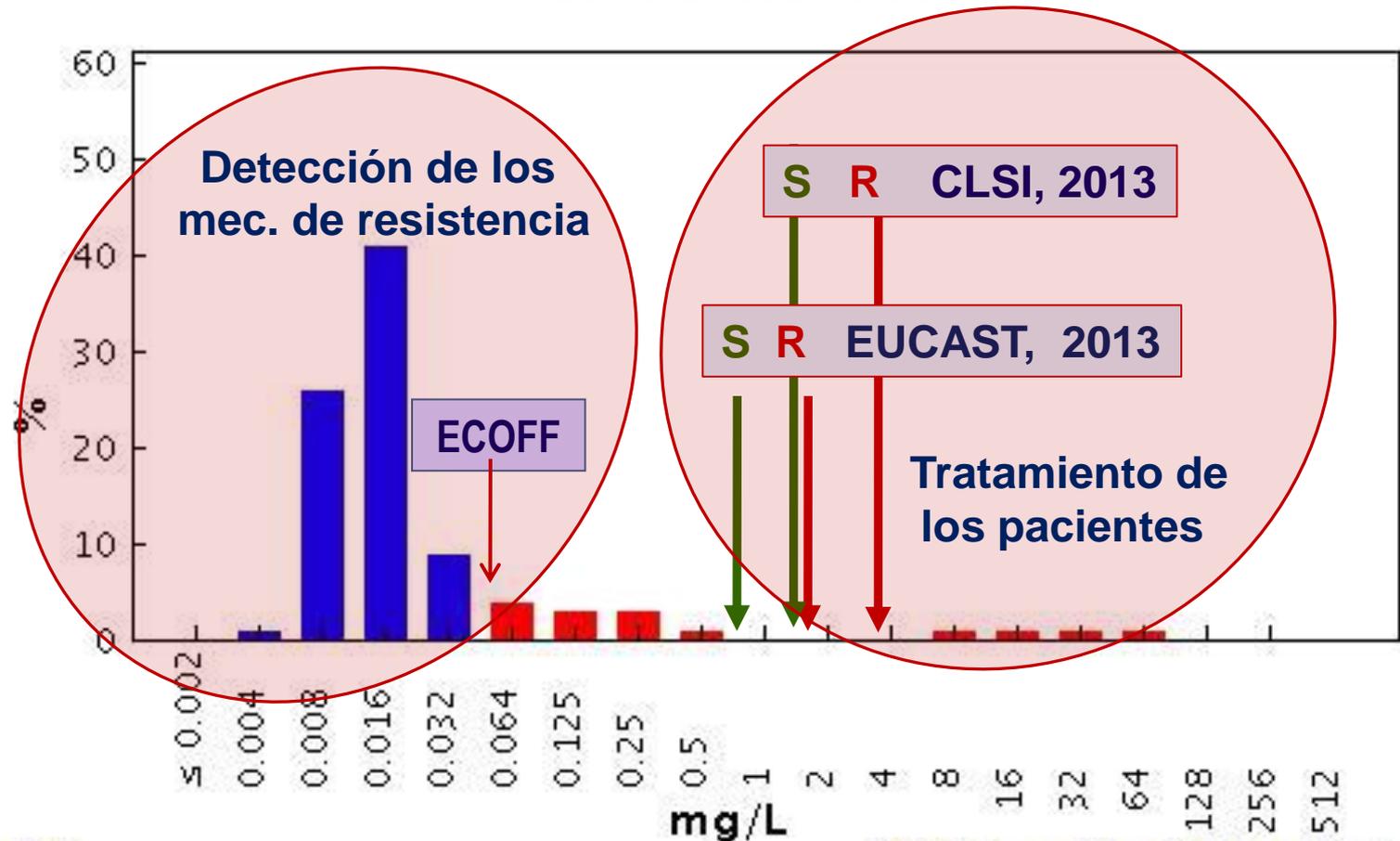
- **Puntos de corte clínicos y epidemiológicos (ECOFFs)**

$ECOFF \leq \quad S \leq ; R >$

# Ciprofloxacin / Escherichia coli

Antimicrobial wild type distributions of microorganisms - reference database

## EUCAST MIC Distribution



MIC

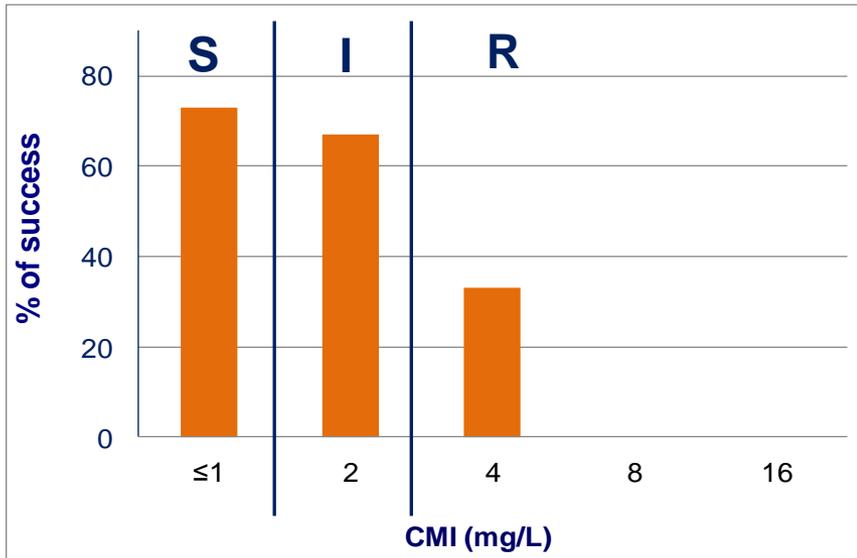
Epidemiological cut-off: WT ≤ 0.032 mg/L

16247 observations (81 data sources)

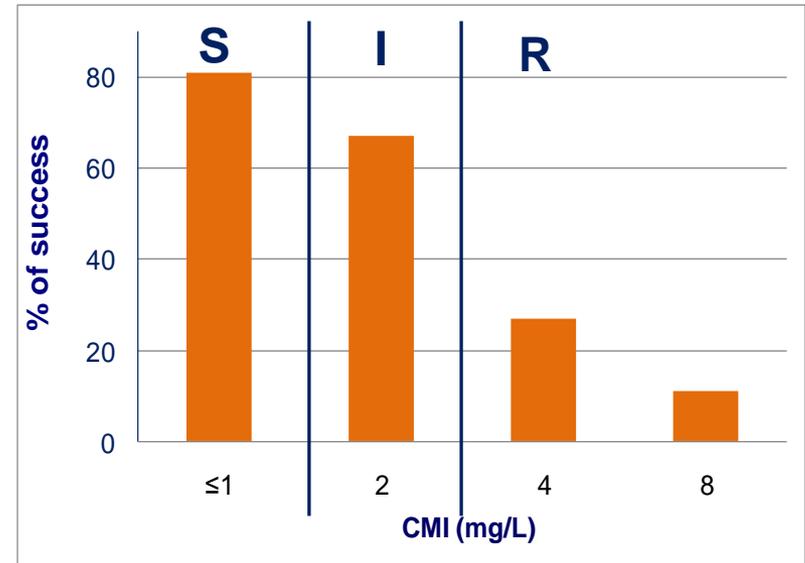
Clinical breakpoints: S ≤ 0.5 mg/L, R > 1 mg/L

# Relevancia clínica de los puntos de corte

Éxito terapéutico en pacientes con bacteriemia por cepas de *Klebsiella* spp. y *E. coli* productoras de BLEE y tratados con cefalosporinas de 3 gen. en monoterapia



Paterson et al. JCM 2001; 39:2206-12



Andes & Craig. CMI 2005; 11 (Suppl. 6):10-7



Los puntos de corte para establecer las categorías clínicas (S, I y R) se realizan utilizando **criterios microbiológicos, farmacológicos (PK/PD) y clínicos**

# Puntos de corte (*clinical breakpoints*)

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Punto de corte = punto de rotura

Tomado de UNE-EN ISO 20776-1:2006. Junio 2007

Valores específicos de parámetros, tales como valores de CMI, según los cuales las bacterias se pueden asignar a las categorías clínicas de sensible (S), intermedio (I) y resistente (R)

**Sensible:** cepa bacteriana inhibida *in vitro* por una concentración de un agente antimicrobiano que se asocia con una alta probabilidad de *éxito terapéutico*

**Intermedio:** cepa bacteriana inhibida *in vitro* por una concentración de un agente antimicrobiano que se asocia con un efecto terapéutico incierto

**Resistente:** cepa bacteriana inhibida *in vitro* por una concentración de un agente antimicrobiano que se asocia con una alta probabilidad de *fracaso terapéutico*



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## Objetivos principales

- Armonizar los puntos de corte existentes en Europa
- Definir los puntos de corte para los nuevos antimicrobianos



- Colaboración con la EMA (*European Medicines Agency*) a través de procedimientos estándares de actuación\*
- Acuerdo de colaboración (contrato) con el ECDC (*European Centre for Diseases Prevention and Control*)
- Aceptado por la industria farmacéutica y del diagnóstico

\*SOP = *standard operation procedure*

# www.eucast.org

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[Clinical breakpoints](#)

[Expert rules](#)

[Setting breakpoints](#)

[MIC distributions](#)

[Zone diameter distributions](#)

[Antimicrobial susceptibility testing](#)

[Antifungal susceptibility testing \(AFST\)](#)

[Frequently Asked Questions \(FAQ\)](#)

[Meetings](#)

[EUCAST Presentations](#)

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## The European Committee on Antimicrobial Susceptibility Testing - EUCAST

EUCAST is a standing committee jointly organized by ESCMID, ECDC and European national breakpoint committees. 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 a subcommittee on antifungal susceptibility testing and on methods for detection of resistance mechanisms of clinical and/or epidemiological importance.

### EUCAST News

30 Aug 2013  
**French translations updated!**

19 Aug 2013  
**EUCAST SOP 4 updated**

17 Aug 2013  
**USNAC formed**

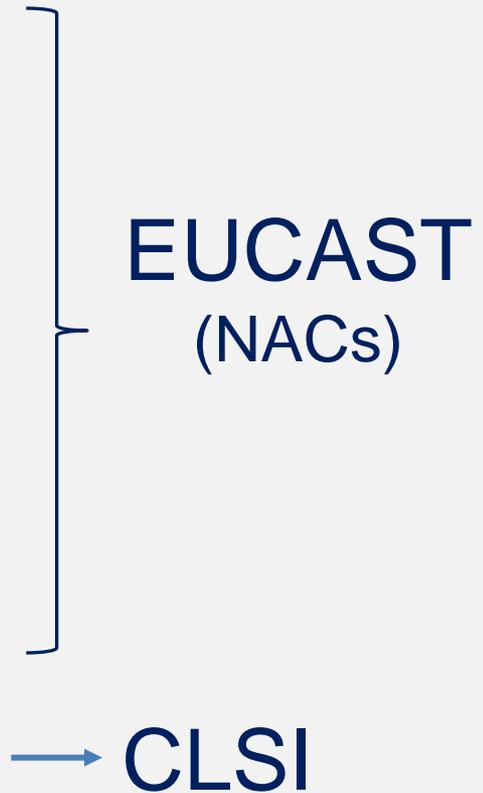
12 Aug 2013  
**Templates for contributing MIC-distributions available**

... [descarga libre de la información y los documentos](#)

# Comités de puntos de corte (antibiograma)

1997 → 2001 → 2013

Comité		País
BSAC		Reino Unido
CA-SFM		Francia
CRG		Holanda
DIN		Alemania
NWGA		Noruega
SRGA		Suiza
NCCLS		EEUU



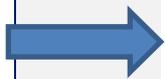
- EUCAST fue fundado en 1997 y remodelado en 2001

Comité		País	Acuerdo con las agencia reguladoras
EUCAST <sup>1</sup>		Europe	SI <sup>2</sup>
CLSI		USA	No

<sup>1</sup>EUCAST es el paraguas para los comite nacionales de puntos de corte en Europa [BSAC, CA-SFM, CRG, (DIN), NWGA & SRGA]

<sup>2</sup>EUCAST funciona como comité de expertos de la EMA y con acuerdos de colaboración con el ECDC

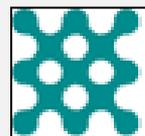
**2013**



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**ESCMID**  
EUROPEAN SOCIETY  
OF CLINICAL MICROBIOLOGY  
AND INFECTIOUS DISEASES

EUROPEAN SOCIETY  
OF CLINICAL MICROBIOLOGY  
AND INFECTIOUS DISEASES

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

**Contract 2011-14**

**NACs = National  
Antimicrobial Susceptibility  
Testing Committees**

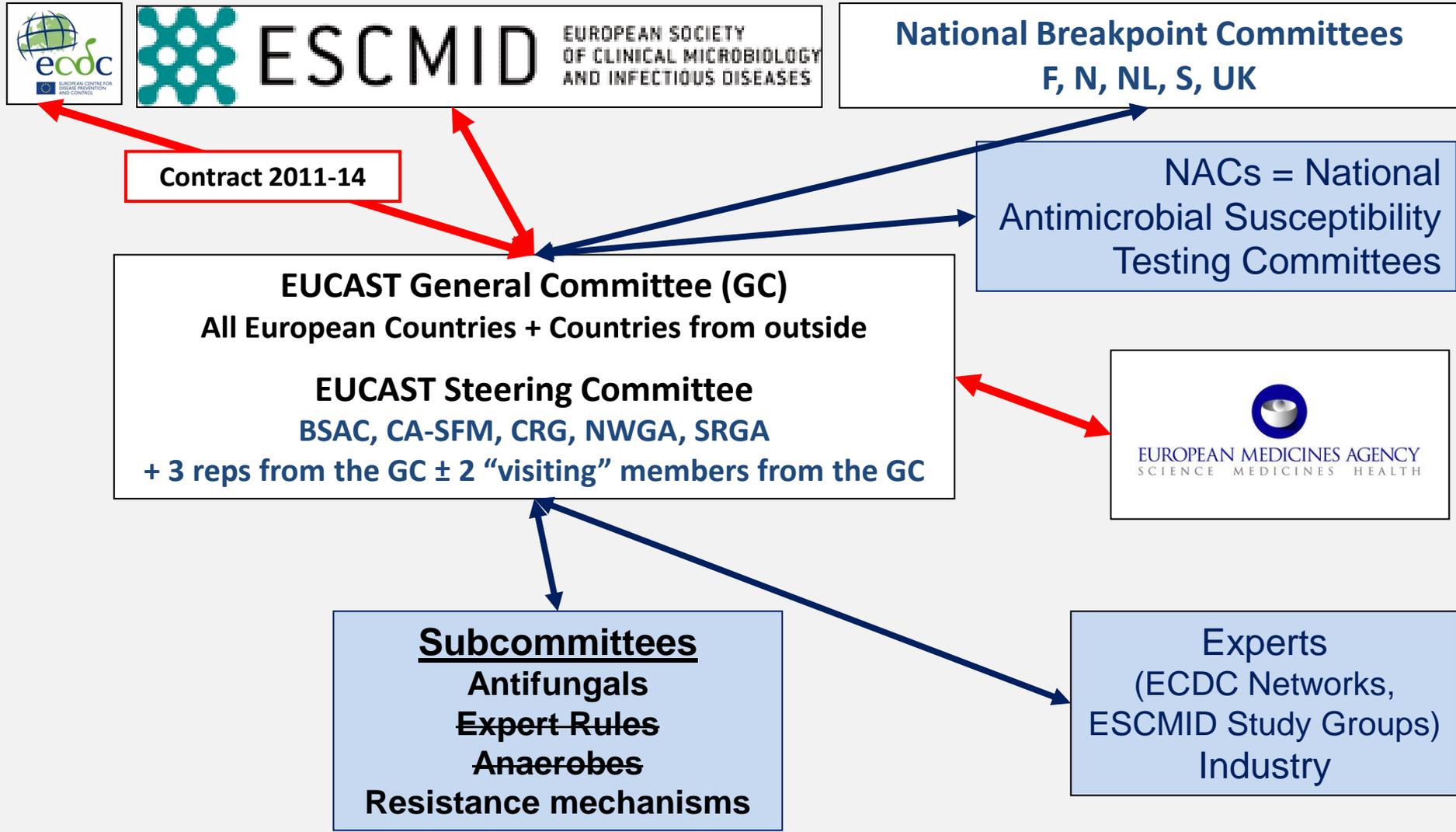
**EUCAST General Committee (GC)**  
All European Countries + Countries from outside

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



**Subcommittees**  
Antifungals  
Expert Rules  
Anaerobes  
Resistance mechanisms

**Experts**  
(ECDC Networks,  
ESCMID Study Groups)  
Industry



# Organización

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EUCAST	CLSI
<p><b>Steering Committee</b> (11) con representantes de los comités europeos de puntos de corte y 3 representantes del <i>General Committee</i> y 2 observadores de otros países</p> <p>5 reuniones al año</p>	<p>Comité (12) con voto con representantes profesionales y de la industria, 12 observadores (profesionales, industria, FDA, CDC, EUCAST)</p> <p>2 reuniones al año</p>
<p><b>General committee</b>, representantes de todos los países europeos (y algunos no europeos), FESCI y ISC</p> <p>Una reunión abierta al año</p>	<p>Miembros por subscripción</p>
<p>Industria: papel consultivo</p>	<p>Industria: parte de las decisiones</p>

# Relación con las autoridades reguladoras

EUCAST	CLSI
<p>EUCAST establece los puntos de corte (<i>breakpoints</i>) para la <i>European Medicines Agency</i> (EMA)</p> <p>Procedimiento estándar de actuación (SOP) específico con la EMA</p> <p>Asesora al ECDC (contrato) y a la EFSA</p>	<p>FDA (<i>United States Food and Drug Administration</i>) establece los puntos de corte específicos en EEUU</p> <p>CLSI solo define los puntos de corte para un nuevo antibiótico a requerimiento de la compañía</p>
<p>Traslado de los puntos de corte de EUCAST en el “resumen de las características de producto” de la EMA (SmPCs)</p>	<p>Puntos de corte de la FDA en el “resumen de las características de producto” en EEUU</p>

# Puntos de corte de nuevos antimicrobianos

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EUCAST	CLSI
Puntos de corte en paralelo al proceso de autorización en la EMA	Si la compañía solicita puntos de corte al CLSI no puede ser diferentes de los de la FDA hasta 2 años después
Presentación cerrada (propuesta) de la compañía farmacéutica al <i>Steering Committee (SC)</i> *	Presentation abierta de la compañía farmacéutica al CLSI
Discusión cerrada en el SC y consulta con comités nacionales de puntos de corte durante el proceso de autorización con la EMA	Discusión tras la presentación
Decisión por <b>consenso</b> de los puntos de corte	Decisión por <b>votación</b> del comité del CLSI tras la discusión

\*SOP 1.1- Setting breakpoints for new agents. 2013

# Revisión de los puntos de corte

EUCAST	CLSI
<p>Proceso continuo de revisión de puntos de corte*:</p> <ul style="list-style-type: none"><li>- armonización de puntos de corte utilizados en Europa (proceso finalizado)</li><li>- revisión de los puntos de corte armonizados (en proceso)</li></ul>	<p>Escasos cambios en los puntos de corte desde su definición inicial (ej.)</p> <ul style="list-style-type: none"><li>- cefalosporinas y carbapenemes en Enterobacteriaceae</li><li>- piperacilina-tazobactam y <i>Pseudomonas aeruginosa</i></li><li>- vancomicina y <i>Staphylococcus aureus</i></li></ul> <p>Ausencia de cambios en los puntos de corte de la FDA</p>

\*SOP 2.1 – Harmonization of breakpoints for existing antimicrobial agents. 2013

SOP 3.0 – Review and revision of antimicrobial breakpoints. 2013

Organization

EUCAST News

Clinical breakpoints

Expert rules

Setting breakpoints

MIC distributions

Zone diameter distributions

Antimicrobial susceptibility testing

Antifungal susceptibility testing (AFST)

Frequently Asked Questions (FAQ)

Meetings

EUCAST Presentations

Documents

Rationale Documents

**Standard Operation Procedures**

Discussion documents

Publications in journals

Technical notes

## The European Committee on Antimicrobial Susceptibility Testing

### Standard Operation Procedures

 [EUCAST SOP 1.1 Setting breakpoints for new agents \(2013-06-09\)](#)  
( previous version)

 [EUCAST SOP 2.1 Harmonising breakpoints for new agents \(2013-08-14\)](#)  
( previous version)

 [EUCAST SOP 3.0 Review and revisions of breakpoints \(2013-01-03\)](#)

 [EUCAST SOP 4.1 EUCAST Committees and subcommittees \(2013-08-14\)](#)  
( previous version)

 [EUCAST SOP 5.0 Interactions with NACs \(2013-01-03\)](#)

 [EUCAST SOP 6.0 Organisation and maintenance of EUCAST websites \(2013-05-02\)](#)

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Standard Operating Procedure

Setting breakpoints for new antimicrobial agents

EUCAST SOP 1.1

1 June 2013

Standard Operating Procedure

Harmonization of breakpoints for existing antimicrobial agents

EUCAST SOP 2.1

20 July 2013

Standard Operating Procedure

Review and revision of antimicrobial breakpoints

EUCAST SOP 3.0

3 January 2013



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# Proceso de definición de puntos de corte clínicos

1. Dosis (autorización de comercialización de EMA)
2. Microorganismos diana
3. Valores CMI y distribuciones para cada microorganismo diana
  - puntos de corte que no dividan distribuciones de poblaciones salvajes
  - determinación de **ECOFFs** para cada especie
4. Mecanismos de resistencia en microorganismos diana
5. Indicaciones clínicas
6. Farmacocinética (C<sub>max</sub>, AUC, T<sub>1/2</sub>, unión a proteínas, V<sub>d</sub>, ...)
7. Farmacodinamia y parámetros Pk/Pd: C<sub>max</sub>/MIC, AUC/MIC, T<sub>>MIC</sub>
8. Respuesta clínica en relación a valores de CMI



**Puntos de corte clínicos (S, I, R)**

# ¿Por qué puntos de corte de EUCAST?

- Puntos de corte para **dosis máximas y mínimas** en **Europa**
- Basados en indicaciones aprobadas por la **EMA** en función de los ensayos clínicos, PK/PD y distribuciones de CMI
- Aceptados por las **agencias europeas (EMA, ECDC, EFSA)** y recogidos en los **SmPC** europeos
- Utilizados en los **estudios epidemiológicos** en **Europa** (ECDC, EARS-net) y justificados en **documentos de libre acceso** (*rational documents*)
- Independientes de intereses comerciales y aceptados por las compañías
- **Revisiones periódicas** (con cada nuevo antibiótico de una clase, promovido por la EMA, la industria farmacéutica o por EUCAST)
- En el **dominio público** y de **libre acceso** sin coste económico



# Financiación

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EUCAST	CLSI
<p>Contrato con el ECDC</p> <p>ESCMID (<i>European Society of Clinical Microbiology and Infectious Diseases</i>)</p> <p>Comites Nacionales de Puntos de Corte - Comités Nacionales del Antibiograma (NAC)</p>	<p>Suscripciones de los miembros</p> <p>Venta de los documentos</p> <p>Ayuda gubernamental para la distribución de los documentos a países en vías de desarrollo</p>

# Documentos y recursos

EUCAST	CLSI
Documento anual de puntos de corte (enero)	Documento anual de puntos de corte (enero)
“Rationale documents” (RDs) publicados sistemáticamente	“Rationale documents” (RDs) no publicados sistemáticamente
Guías metodológicas, datos de calibración de los métodos (difusión con disco), recomendaciones, ...	Guías metodológicas
Reglas de experto con explicaciones y soporte bibliográfico	Some expert rules included in breakpoint tables
Documentos libres ( <a href="http://www.eucast.org">www.eucast.org</a> )	Documentos de pago y acceso restringido a la pagina web ( <a href="http://www.clsi.org">www.clsi.org</a> )

Organization

**EUCAST News**

Clinical breakpoints

Expert rules

Setting breakpoints

MIC distributions

Zone diameter distributions

Antimicrobial susceptibility testing

Antifungal susceptibility testing (AFST)

Frequently Asked Questions (FAQ)

Meetings

EUCAST Presentations

Documents

Information for industry

Links

Website changes



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**EUCAST News**



03 Oct 2012

**Ceftaroline breakpoints released**

12 Aug 2012

**Anidulafungin RD updated - error in dosing corrected**

03 Aug 2012

**Consultation until 14 Sept 2012 on Campylobacter breakpoints**

03 Aug 2012

**Consultation until 14 Sept 2012 on P.multocida breakpoints**

30 Jun 2012

**QC-tables - updated version June 29, 2012**

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## The European Committee on Antimicrobial Susceptibility Testing - EUCAST

EUCAST is a standing committee jointly organized by ESCMID, ECDC and European national breakpoint committees. It is responsible for the technical aspects of phenotypic and genotypic susceptibility testing and functions as the breakpoint setting body in Europe. EUCAST does not deal with antibiotic policies. It is supported by a network of national microbiology, pharmaceutical and device manufacturers. EUCAST is responsible for the development of legal susceptibility testing and on methods for detection of resistance mechanisms of clinical and/or epidemiological importance.

Subcommittees on expert rules for antimicrobial susceptibility testing and antimicrobial susceptibility testing of anaerobes have completed their tasks and have been disbanded.

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.

**Información nueva**

# EUCAST breakpoints, 2013



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EUCAST News

Clinical breakpoints

Information on breakpoint tables

Expert rules

Setting breakpoints

MIC distributions

7

The European Committee on  
Antimicrobial Susceptibility Testing – EUCAST

**European Committee on Antimicrobial Susceptibility Testing**  
Breakpoint tables for interpretation of MICs and zone diameters

Version 3.1, valid from 2013-02-11

[Clinical breakpoints - fungi \(v 6.1\)](#) - pdf file for printing (2013-03-11)

[Clinical breakpoints - fungi \(v 6.1\)](#) - excel file for screen (2013-03-11)

Errata in v 6.0 (March 1 - 11, 2013) were corrected in v 6.1

Information for industry

Links

→ [Previous versions of breakpoint tables.](#)

[definitions of clinical breakpoints and epidemiological cut off values](#)

[procedure for harmonizing and defining breakpoints](#)

[Website changes](#)

# EUCAST breakpoints, 2013

## Enterococcus spp.

EUCAST Clinical Breakpoint Table v. 3.1, valid from 2013-02-11

In endocarditis, refer to national or international endocarditis guidelines for breakpoints for

Disk diffusion (EUCAST standardised disk diffusion method)  
 Medium: Mueller-Hinton agar  
 Inoculum: McFarland 0.5  
 Incubation: Air, 35±1°C, 18±2h (for glycopeptides 24 h)  
 Reading: Read zone edges as the point showing no growth viewed from the back of the plate against a dark background illuminated with reflected light (except for glycopeptides, see below).  
 Quality control: *Enterococcus faecalis* ATCC 29212

Acceso a los  
rational  
documments

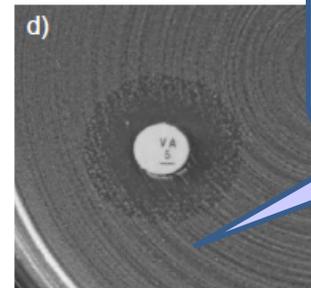
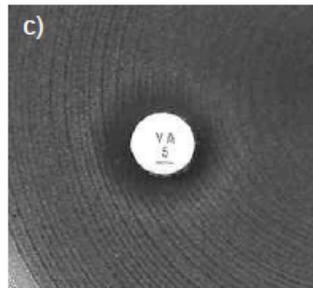
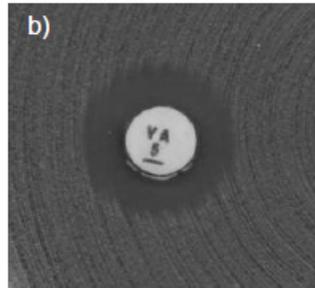
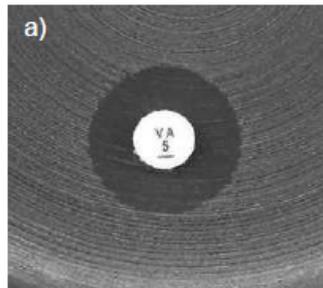
Cambios  
anuales  
destacados

Notas  
técnicas de  
métodos

Acceso al  
programa de  
distribuciones

Guías  
técnicas  
visuales

Antibiotic	S ≤		S ≥		R <	Notes
	µg	mm	µg	mm	µg	
Chloramphenicol	-	-	-	-	-	
Colistin	-	-	-	-	-	
Daptomycin	1E	1E	-	-	-	
Fosfomycin iv	-	-	-	-	-	
Fosfomycin oral	-	-	-	-	-	
Fusidic acid	-	-	-	-	-	
Linezolid	4	4	-	-	-	
Metronidazole	-	-	-	-	-	
Mupirocin	-	-	-	-	-	
Nitrofurantoin (uncomplicated UTI only)	64 <sup>1</sup>	64 <sup>1</sup>	15 <sup>A</sup>	15 <sup>A</sup>	-	1/A. Nitrofurantoin breakpoints apply to <i>E. faecalis</i> only.
Rifampicin	-	-	-	-	-	
Spectinomycin	-	-	-	-	-	
Trimethoprim (uncomplicated UTI only) <sup>2</sup>	0.02	1	5	50	21	2. The activity of trimethoprim is uncertain against enterococci, hence the wild type population is categorised as intermediate.
Trimethoprim-sulfamethoxazole <sup>3</sup>	0.03	1	1.25-23.75	50	21	3. Trimethoprim-sulfamethoxazole in the ratio 1:19. Breakpoints for



Examples of inhibition zones for *Enterococcus spp.* with vancomycin.

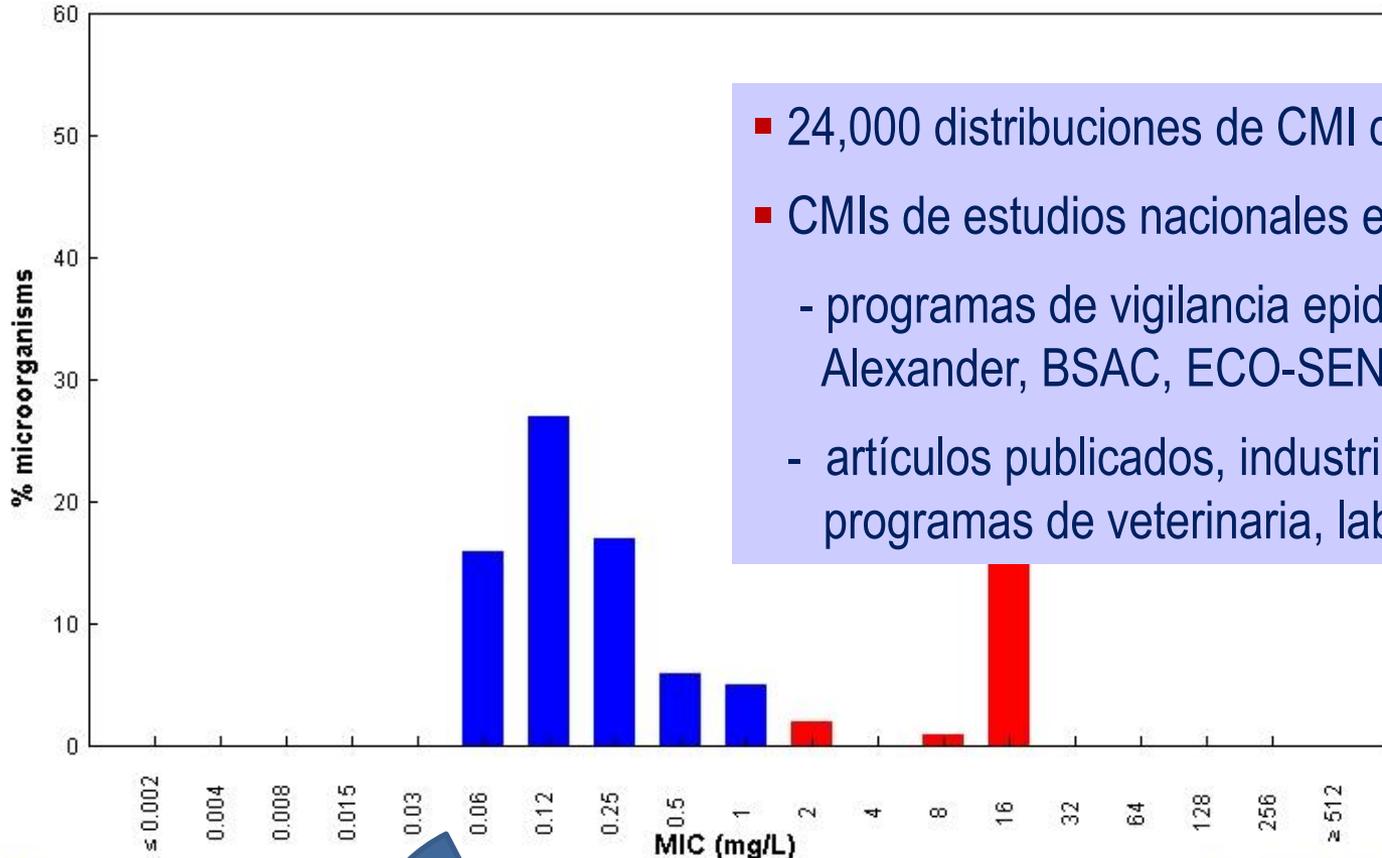
a) Sharp zone edge and zone diameter ≥ 12 mm. Report susceptible.

b-d) Fuzzy zone edge or colonies within zone. Report resistant even if the zone diameter ≥ 12 mm.

# EUCAST MIC and zone diameter distributions

## Trimethoprim-sulfamethoxazole / *Enterococcus faecium* EUCAST MIC Distribution - Reference Database 2013-11-17

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



- 24,000 distribuciones de CMI de diferente origen
- CMIs de estudios nacionales e internacionales:
  - programas de vigilancia epidemiológica (SENTRY, Alexander, BSAC, ECO-SENS, MYSTIC, ...)
  - artículos publicados, industria farmacéutica, programas de veterinaria, laboratorios individuales

MIC  
Epidemiological cut-off: WT ≤ 1 mg/L

622 observations  
Clinical breakpoints: S ≤ - mg/L, R > - mg/L

proyecto para la definición internacional de ECOFFs

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**Mupirocin breakpoint consultation -  
deadline for comments 22 March**



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Optimized for Explorer 8 or higher  
You're using Explorer 7

Number of visitors since May 2007: 1380514  
EUCAST version 5.13

## Antimicrobial wild type distributions of microorganisms

- [Search database](#)

### MIC- and Inhibition zone diameter distributions of microorganisms without and with resistance mechanisms

#### MIC distributions

The website gives MIC distributions for individual organisms and antimicrobial agents in tables and histograms. The distributions are based on collated data from an increasing total of more than 20000 MIC distributions from worldwide sources. Unless otherwise specifically stated, the data are representative of results obtained with a variety of MIC methods. Different methods do not give exactly the same results but the results rarely vary by more than one doubling dilution step. In this way the aggregated MIC distributions encompass the variation between different investigators and between different methods.

#### Inhibition zone diameter distributions

The website gives inhibition zone diameter distributions for individual organisms and antimicrobial agents in tables and histograms. The distributions are based on collated data from an increasing number of sources worldwide. The data are representative of results obtained

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.

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[MIC - distributions and QC](#)

[Zone diameter distributions](#)

[EUCAST disk diffusion test](#)

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[EUCAST Presentations](#)

**Documents**

**Rationale Documents**

[Discussion documents](#)

[Publications in journals](#)

[Technical notes](#)

[Posters](#)

[Other Documents](#)

[Relevant external documents](#)

[Reports](#)

[Information for industry](#)

[Links](#)

 [Website changes](#)

## The European Committee on Antimicrobial Susceptibility Testing – EUCAST

[Search](#)

... Rationale Documents 

### Rationale Documents from EUCAST

The following Rationale Documents (see General Information on Rationale Documents) are currently available from EUCAST:

 [General Information on Rationale Documents](#)

 [Amikacin](#) v 1.2

 [Ciprofloxacin](#) v 1.9

 [Colistin](#) v 1.0

 [Daptomycin](#) v 1.0

 [Doripenem](#) v 1.0

 [Doxycycline](#) v 1.0

 [Ertapenem](#) v 1.3

 [Fluconazole](#) v 1.0

 [Gentamicin](#) v 1.2

 [Imipenem](#) v 1.3

 [Levofloxacin](#) v 1.5

 [Linezolid](#) v 1.0

 [Meropenem](#) v 1.5

 [Metronidazole](#) v 1.0

 [Minocycline](#) v 1.0

 [Moxifloxacin](#) v 2.3

 [Mupirocin](#) v 1.0

 [Netilmicin](#) v 1.1

# Expresión de los puntos de corte de EUCAST

---

<b>MIC (mg/L) brpts*</b>	<b>S ≤ 2 R &gt; 2 mg/L</b>
<b>Zone (mm) brpts*</b>	<b>S ≥ 22 R &lt; 22 mm</b>
<b>Insufficient evidence</b> (Literature: "not enough evidence for a breakpoint" or "no indication")	<b>IE</b> Can not be substituted. Can be supplemented with an MIC without interpretation.
<b>Inappropriate drug</b> (Literature: poor drug – don't use!)	<b>—</b> Can be substituted with an automatic "R"

\*when numbers are the same = no intermediate category

# EUCAST: metodos

[Organization](#)

[EUCAST News](#)

[Clinical breakpoints](#)

[Expert rules](#)

[Setting breakpoints](#)

[MIC distributions](#)

[Zone diameter distributions](#)

**Antimicrobial susceptibility testing**

[Media preparation](#)

[MIC determination](#)

**[Disk diffusion methodology](#)**

[Disk diffusion implementation](#)

[Compliance of manufacturers](#)

[Breakpoint tables](#)

[QC Tables](#)

[Calibration and validation](#)

[Guidance documents](#)

[Projects and data submission](#)

[Previous versions of tables](#)

**Antifungal susceptibility testing (AFST)**

**Frequently Asked Questions (FAQ)**

**Meetings**

**EUCAST Presentations**

**Documents**



## EUCAST Disk Diffusion Test Methodology

EUCAST has developed a disk diffusion test based on MH media and calibrated to EUCAST clinical breakpoints. Updates are published regularly.

 [EUCAST Disk Diffusion - Manual](#) (v 2.1, 7 Feb\* 2012)

 [EUCAST Disk Diffusion - Slide Show](#) (2.1, 7 Feb\* 2012)

 [EUCAST Disk Diffusion - Reading Guide](#) (v. 2.0, 2 May 2012)

\*minor corrections (typo) compared to v 2.0 from 26 Jan, 2012

 [EUCAST Blättchendiffusionstest - Handbuch](#) (v 2.1, 7 Feb\*, 2012)



 [EUCAST Blättchendiffusionstest - Diashow](#) (v 2.1, 7 Feb\*, 2012)

 [EUCAST Blättchendiffusionstest - Ablesehilfe](#) (v 2.0, 5 Jun, 2012)

\*minor corrections (typo) compared to v 2.0 from 26 Jan, 2012

 [Descripción del método de disco](#) (v 1.1)

 [EUCAST: método de difusión con discos para el estudio de la sensibilidad a los antimicrobianos](#) (v 1.1 Jun 3, 2010)

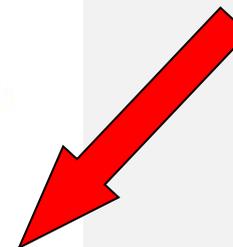
 [EUCAST: método de difusión con discos - Guía de lectura](#) (v 1.0 June 27, 2010)

 [Méthode de diffusion en gélose EUCAST](#) (v 2.1, 2012)



 [Diaporama sur la méthode de diffusion EUCAST sur la toile de l'EUCAST](#) (v 2.1, 2012)

 [Guide de lecture](#) (v 2.0, 2012)



# Método estandarizados de difusión con disco

	CLSI	EUCAST	BSAC/ SRGA	CA-SFM
Medium for non-fastidious	MH	MH	ISA	MH
Medium for <i>Haemophilus</i>	HTM	MH-F*	ISA-F	HTM
Medium for Streptococci	Sheep blood	MH-F*	ISA-F	Sheep blood
Inoculum	McF 0.5 "Just confluent"	McF 0.5 "Just confluent"	"Semi-confluent"	"Semi-confluent"

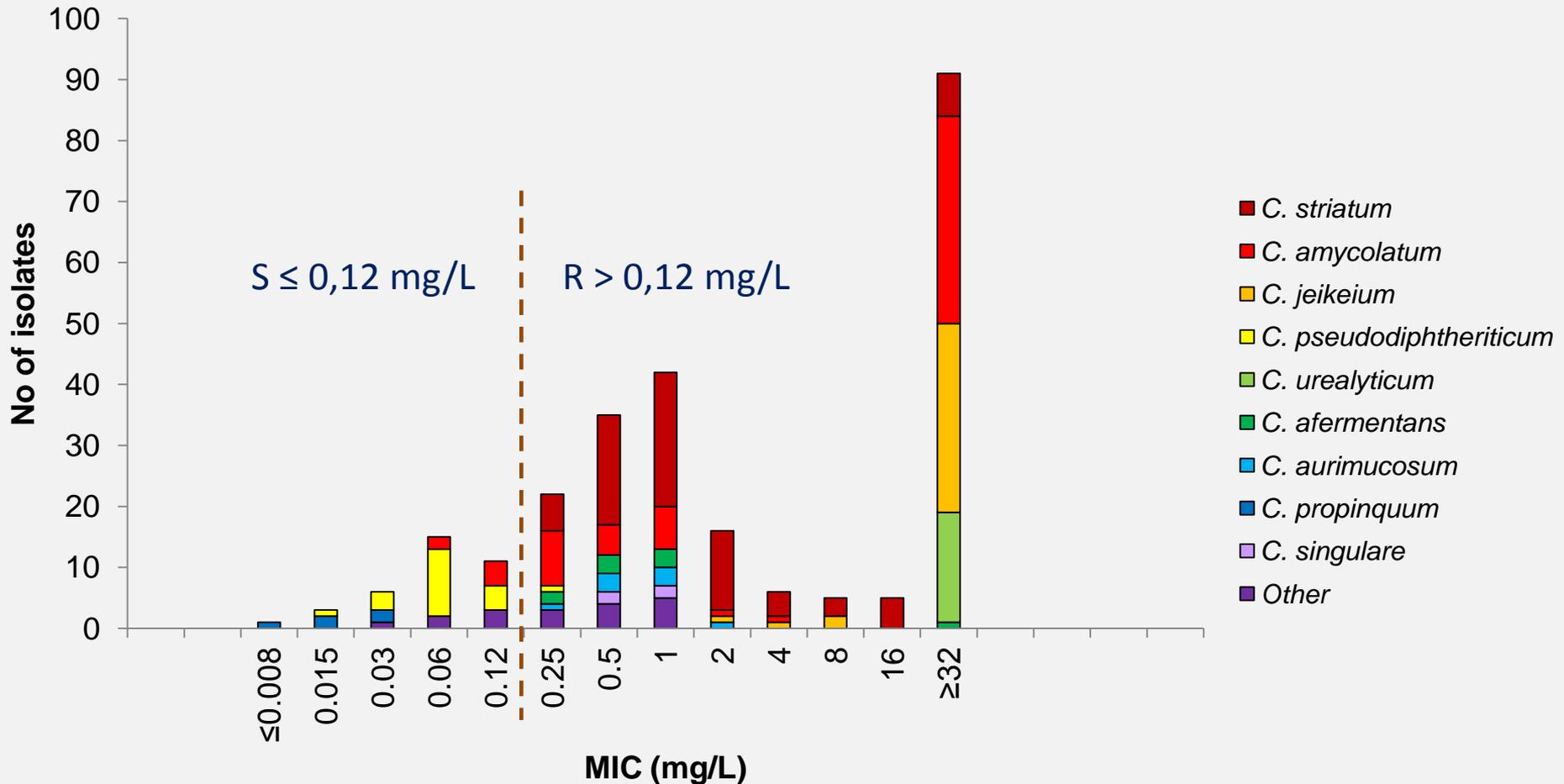
\*MH-F: Mueller-Hinton agar + 5% defibrinated horse blood and 20 mg/L  $\beta$ -NAD



información de calibración frente a CMI-ISO en [www.eucast.org](http://www.eucast.org)

# Corynebacterium spp. breakpoints

## Benzylpenicillin MIC vs. species Corynebacterium spp., 258 clinical isolates



E. Matuschek/G. Kahlmeter (Växjö, Sweden, EUCAST Lab),  
R. Jones (JMI Lab, US) Santander, Spain (L. Martinez-Martinez)

# EUCAST breakpoints, 2013: Guías técnicas



## Antimicrobial susceptibility testing of *B. cepacia* complex

- It is not currently possible to establish MIC breakpoints for BCC organisms:
  - No evidence to describe a relationship between MIC and outcome
  - BCC is frequently part of a mixed infection
  - The MIC distributions are wide and include the PK/PD breakpoint.
  - The ECOFFs cannot be used to define the WT population, “S” or “R”
- Susceptibility testing methodology is problematic:
  - Reproducible MIC results with ISO-BMD method and MH-broth
  - MICs with gradient strips are less reproducible than BMD
  - Correlations of ISO BMD-MICs and disk diffusion zones are poor

### Recommendations :

While the ISO-BMD method may give reproducible MICs (gradient-MIC and disk diffusion methods are not reproducible), it is currently not possible to recommend susceptibility testing of BCC organisms to guide patient therapy

# EUCAST: adecuación de métodos comerciales

- Organization
- EUCAST News
- Clinical breakpoints
- Expert rules
- Setting breakpoints
- MIC distributions
- Zone diameter distributions
- Antimicrobial susceptibility testing**
  - Media preparation
  - MIC determination
  - Disk diffusion methodology
  - Disk diffusion implementation
  - Compliance of manufacturers**
  - Breakpoint tables
  - QC Tables
  - Calibration and validation
  - Guidance documents
  - Projects and data submission
  - Previous versions of tables

Compliance of manufacturers with EUCAST guidelines, 9 September 2013

## Phoenix/EpiCenter automated system (BD)

EUCAST terminology implemented	In computer database	S ≤	Yes
		R >	No (R ≥)
		-	Yes
		IE	Yes
EUCAST terminology implemented	In reports	S ≤	Yes
		R >	Yes (≥ converted to R >)
		-	Yes (MICs reported for agents with no EUCAST breakpoints)
		IE	Yes (MICs reported for agents with no EUCAST breakpoints)
EUCAST Expert Rules implemented	All rules incorporated. There are additional rules but EUCAST rules have priority.		
EUCAST organism groups with no test in the system	<i>H. influenzae</i> <i>M. catarrhalis</i>	<i>N. meningitidis</i> <i>N. gonorrhoeae</i>	Gram-negative anaerobes Gram-positive anaerobes
Agents in EUCAST tables but not available in the system	Ampicillin-sulbactam with fixed 4 mg/l sulbactam		
Agents available but EUCAST breakpoints not implemented in the system	Rifampicin ( <i>Staphylococcus</i> spp. cannot be reported susceptible) Trimethoprim ( <i>Enterococcus</i> spp. cannot be reported susceptible) Cotrimoxazole ( <i>Enterococcus</i> spp. cannot be reported susceptible)		

# EUCAST breakpoint tables v3.1, 2013

## ■ Puntos de corte PK/PD en tablas independientes

### PK/PD (Non-species related) breakpoints

EUCAST Clinical Breakpoint Table v. 3.1, valid from 2013-02-11

These breakpoints should not be used when there are species specific breakpoints, such as values, Note or "-" in the tables.

Penicillins	MIC breakpoint (mg/L)		PK/PD (Non-species related) breakpoints are based on the following dosages (See section 8 in Rationale Documents)
	S ≤	R >	
Benzylpenicillin	0.25	2	
Ampicillin	2	8	
Ampicillin-sulbactam	2	8	
Amoxicillin	2	8	
Amoxicillin-clavulanate	2	8	
Piperacillin	4	16	
Piperacillin-tazobactam	4	16	
Ticarcillin	8	16	
Ticarcillin-clavulanate	8	16	
Phenoxyethylpenicillin	IE	IE	
Oxacillin	IE	IE	
Cloxacillin	IE	IE	
Dicloxacillin	IE	IE	
Flucloxacillin	IE	IE	
Mecillinam	IE	IE	

- Sustentados solo en **datos PK/PD**
- Utilizados para definir los **puntos de corte clínicos**
- Pueden modificarse en función de los datos microbiológicos y clínicos
- **Se pueden utilizar cuando no hay puntos de corte para un microorganismo dado**
- No sustituyen a los puntos de corte definidos para un microorganismo, si hay o aparece “-” en la tabla

# EUCAST: novedades en 2014

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## ■ Nuevos puntos de corte y revisión de anteriores

- **Nuevos antibióticos (EMA):** anti-SARM, cephalosporinas, macrolidos glicopeptidos, anti-tuberculostáticos, ...
- **Colistina** (conjuntamente con CLSI, iniciativa TATFAR)
- **Agentes tópicos**
- *S. agalactiae* e isoxazolilpenicilinas
- Benzylpenicilina y estafilococos coagulasa-negativa
- **Puntos de corte en ITU:** quinolonas y enterococo amox/clav y Enterobacteriaceae
- *Corynebacterium* spp.
- *Acinetobacter* spp. & sulbactam
- *Pseudomonas no-aeruginosa*
- *Neisseria gonorrhoeae*
- *Kingella kingae*
- Otros: *Legionella*, *Actinomyces*, *Nocardia*, *Streptomyces*, HACEK, *Aeromonas*, *Vibrio*, *Leuconostoc*, *Lactobacillus*, *Pediococcus*

## ■ Validación de **tiras en gradiente**

## ■ Guías para la detección de **mec. de R** y **reglas de experto**

# Transatlantic Taskforce on Antimicrobial Resistance



Transatlantic Taskforce on  
Antimicrobial Resistance



Recommendations for future collaboration  
between the U.S. and EU

2011

- Antimicrobial resistance is a significant and multifaceted public health problem

- **Purpose of the taskforce**

To identify urgent antimicrobial resistance issues that could be better addressed by intensified cooperation between the US and the EU within the following key areas:

1. Appropriate therapeutic use of antimicrobials in the medical and veterinary communities
2. Prevention of healthcare- and community-associated drug-resistant infections
3. Strategies for improving the pipeline of new antimicrobial drugs

**Definición común  
de puntos de corte**

# Colistin / polymixin B breakpoints

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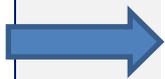
- Initiative to set common EUCAST and CLSI breakpoints
- Memorandum of Understanding (MOU)
  - signed Oct-12, 2012 and effective Nov-1, 2012 – Nov 1, 2013
- Creation of *ad hoc* Working Group
  - 2 co-chairs, 2+2 members representing EUCAST and CLSI
  - absence of members with commercial / industry affiliation
  - colistin and polymixin B breakpoints for
    - Enterobacteriaceae
    - *Pseudomonas aeruginosa*
    - *Acinetobacter* spp.



**MEMORANDUM OF UNDERSTANDING BETWEEN THE CLINICAL AND LABORATORY STANDARDS INSTITUTE (CLSI) AND THE EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING (EUCAST)**

This Memorandum of Understanding (“MOU”), dated this twelve day of October, 2012 (“Effective Date”) is entered into among the following parties: Clinical and Laboratory Standards Institute (“CLSI”) and the European Committee on Antimicrobial Susceptibility Testing (“EUCAST”) (collectively the “Parties). CLSI and EUCAST desire to form a joint Working Group (defined below). This MOU is not a contract and includes no written or implied legal obligations on the part of either CLSI or EUCAST.

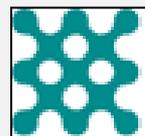
**2013**



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EUROPEAN COMMITTEE  
ON ANTIMICROBIAL  
SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

[www.eucast.org](http://www.eucast.org)



**ESCMID**  
EUROPEAN SOCIETY  
OF CLINICAL MICROBIOLOGY  
AND INFECTIOUS DISEASES

EUROPEAN SOCIETY  
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**National Breakpoint Committees**  
F, N, NL, S, UK

**Contract 2011-14**

**NACs = National  
Antimicrobial Susceptibility  
Testing Committees**

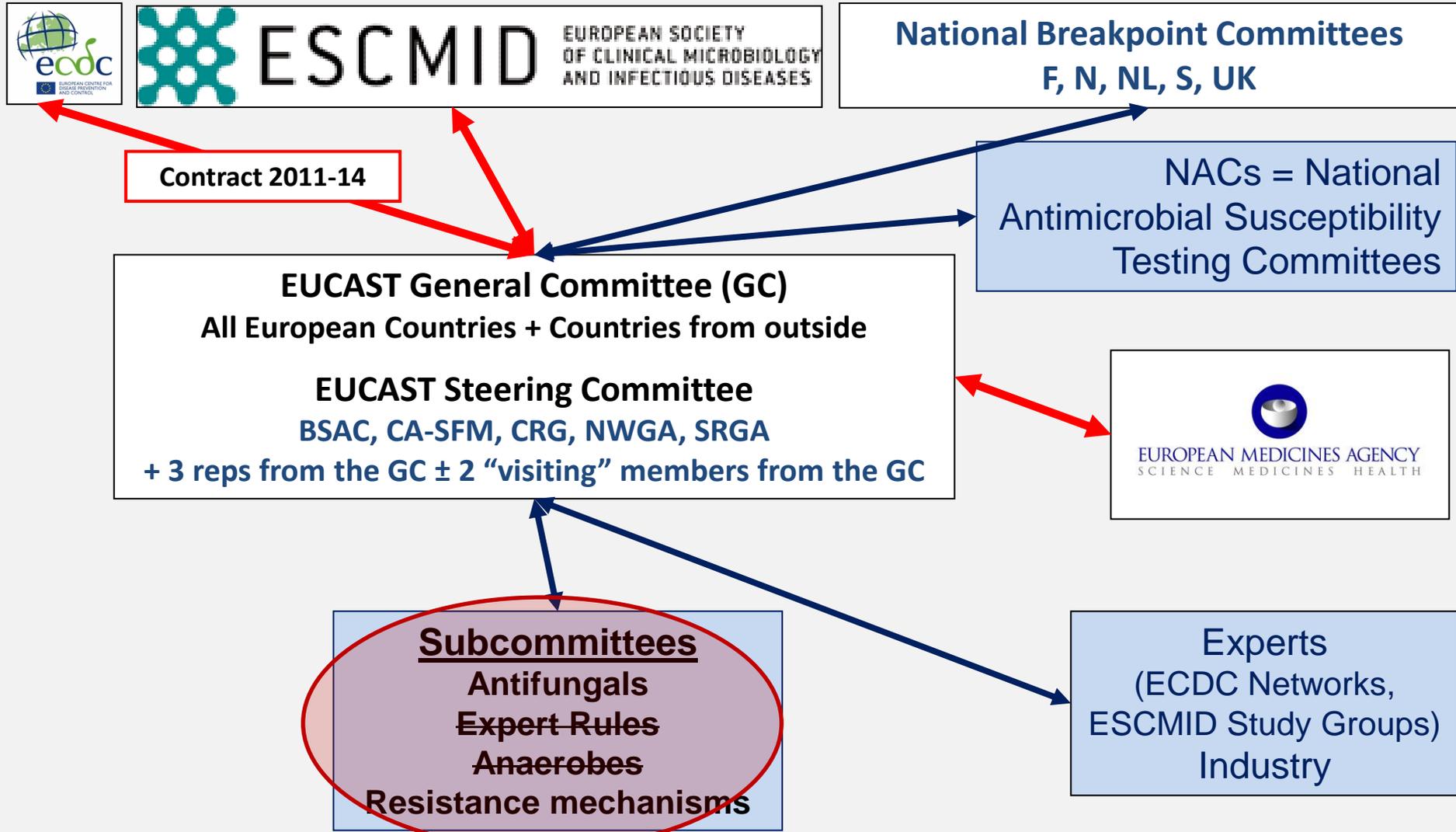
**EUCAST General Committee (GC)**  
All European Countries + Countries from outside

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



**Subcommittees**  
Antifungals  
Expert Rules  
Anaerobes  
Resistance mechanisms

**Experts**  
(ECDC Networks,  
ESCMID Study Groups)  
Industry





# EUCAST

EUROPEAN COMMITTEE  
ON ANTIMICROBIAL  
SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

Home Contact

Organization

EUCAST News

Clinical breakpoints

**Expert rules**

Setting breakpoints

MIC distributions

Zone diameter distributions

Antimicrobial susceptibility testing

Antifungal susceptibility testing (AFST)

Frequently Asked Questions (FAQ)

Meetings

EUCAST Presentations

Documents

Information for industry

Links

## The European Committee on Antimicrobial Susceptibility Testing – EUCAST

### Expert rules

EUCAST expert rules are a tabulated collection of expert knowledge on intrinsic resistances, exceptional resistance phenotypes and interpretive rules that may be applied to antimicrobial susceptibility testing in order to reduce errors and make appropriate recommendations for reporting particular resistances.

**EUCAST Expert rules** (version 2.0 available from 29 Oct, 2011)

Archive:

**EUCAST Expert rules** (version 1.0 valid until 29 Oct, 2011)

[Recommend page](#)



REVIEW

10.1111/j.1469-0691.2011.03703.x

## EUCAST expert rules in antimicrobial susceptibility testing

**R. Leclercq<sup>1,2</sup>, R. Cantón<sup>2,3,4</sup>, D. F. J. Brown<sup>4</sup>, C. G. Giske<sup>2,4,5</sup>, P. Heisig<sup>2,6</sup>, A. P. MacGowan<sup>4,7</sup>, J. W. Mouton<sup>4,8</sup>, P. Nordmann<sup>2,9</sup>, A. C. Rodloff<sup>4,10</sup>, G. M. Rossolini<sup>2,11</sup>, C.-J. Soussy<sup>4,12</sup>, M. Steinbakk<sup>4,13</sup>, T. G. Winstanley<sup>2,14</sup> and G. Kahlmeter<sup>4,15</sup>**

1) *Laboratoire de Microbiologie, CHU Côte de Nacre, Caen, France*, 2) *EUCAST Subcommittee on Expert Rules*, 3) *Servicio de Microbiología and CIBER en Epidemiología y Salud Pública (CIBERESP), Hospital Universitario Ramón y Cajal, Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain*, 4) *EUCAST Steering Committee*, 5) *Clinical Microbiology, MTC-Karolinska Institutet, Karolinska University Hospital, Solna, Sweden*, 6) *Department of Pharmacy, Biology & Microbiology, University of Hamburg, Hamburg, Germany*, 7) *Department of Medical Microbiology, Southmead Hospital, Bristol, UK*, 8) *Department of Medical Microbiology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands*, 9) *Service de Bactériologie-Virologie, Hôpital de Bicêtre, Le Kremlin-Bicêtre, France*, 10) *Institut für Medizinische Mikrobiologie der Universität Leipzig, Leipzig, Germany*, 11) *Dipartimento di Biotecnologie, Sezione di Microbiologia, Siena, Italy*, 12) *Hôpital Henri Mondor, Service de Bactériologie, Creteil, France*, 13) *Department of Bacteriology and Immunology, Division of Infectious Disease Control, Norwegian Institute of Public Health, Oslo, Norway*, 14) *Department of Microbiology, Royal Hallamshire Hospital, Sheffield, UK* and 15) *Clinical Microbiology, Central Hospital, Växjö, Sweden*

*Clin Microbiol Infect*, 2013; 19:141-60.

- EUCAST created a subcommittee in 2012 to establish guidelines for the **detection of resistance mechanisms of clinical and/or epidemiological importance**

The screenshot shows the EUCAST website interface. On the left is a navigation menu with the following items: EUCAST statutes, Steering Committee, General Committee, **Subcommittees** (highlighted), Resistance Mechanisms, EUCAST AFST, and National AST Committees (NAC). Below the menu are links for EUCAST News, Clinical breakpoints, Expert rules, Setting breakpoints, MIC distributions, and Zone diameter distributions. The main content area has a header "The European Committee on Antimicrobial Susceptibility Testing – EUCAST". Below the header is a search bar with "search term" and a "Search" button, and a dropdown menu for "Subcommittees". The main heading is "Subcommittees". The text below reads: "EUCAST subcommittees are set up to deal with specific issues or areas requiring particular expertise. Consultations and decisions on subcommittee proposals are made through the EUCAST Steering Committee." Below this is a list of subcommittees, with the first one highlighted: "The EUCAST subcommittee on the detection of resistance mechanisms of clinical and/or epidemiological importance". Other subcommittees listed include "EUCAST Subcommittee on Antifungal Susceptibility Testing". At the bottom of the main content area is a "Recommend page" link with an envelope icon.



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

Version 1.0  
July 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).

## Contents

### Chapter

1. Introduction
2. Carbapenemase-producing Enterobacteriaceae
3. Extended-spectrum  $\beta$ -lactamase-producing Enterobacteriaceae
4. Acquired AmpC  $\beta$ -lactamase-producing Enterobacteriaceae
5. Methicillin resistant *Staphylococcus aureus*
6. Glycopeptide non-susceptible *Staphylococcus aureus*
7. Vancomycin resistant enterococci
8. Penicillin non-susceptible *Streptococcus pneumoniae*

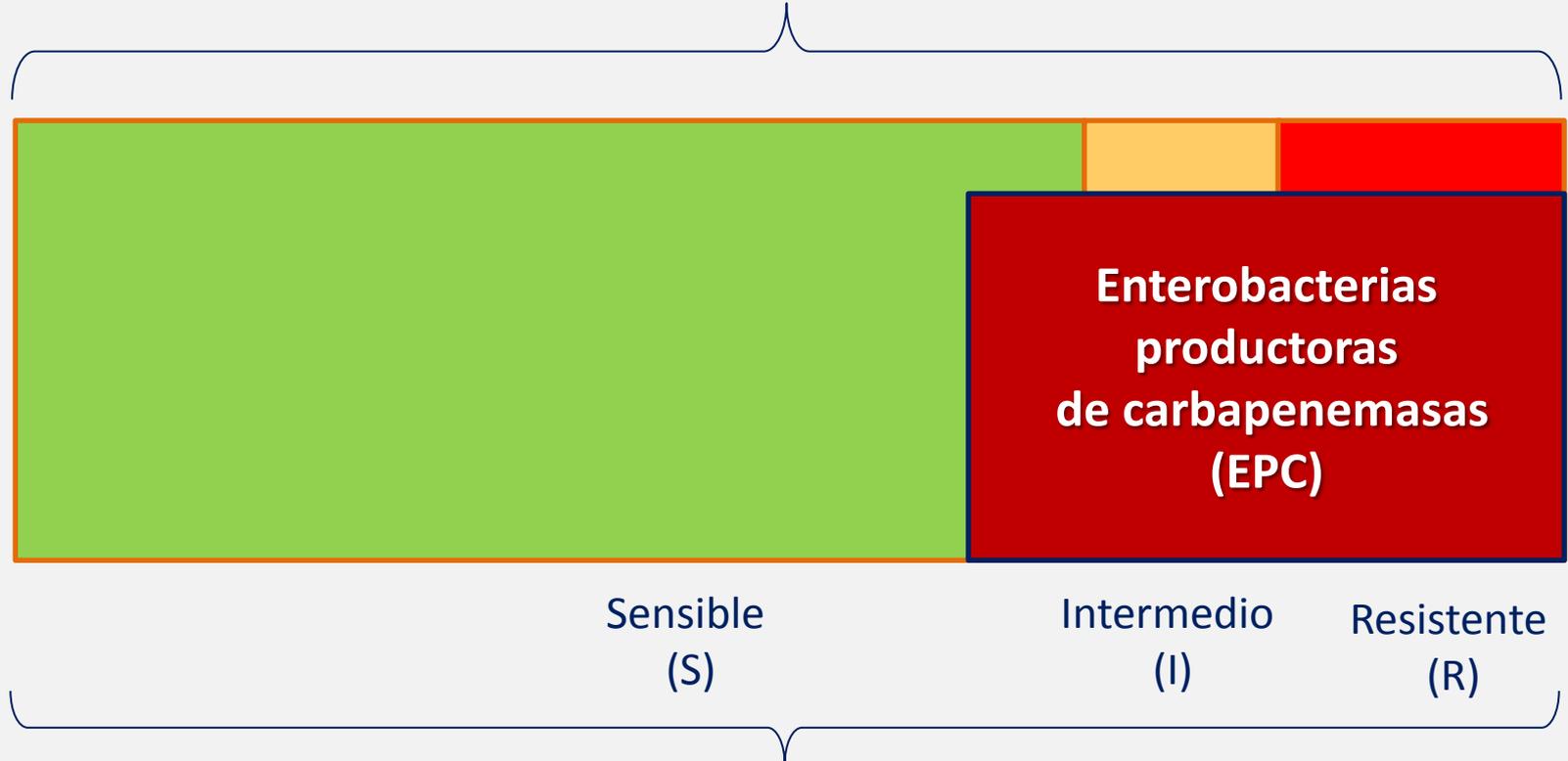
## 2. Carbapenemase-producing Enterobacteriaceae

Importance of detection of resistance mechanism	
Required for antimicrobial susceptibility categorization	No
Infection control	Yes
Public health	Yes

# Enterobacterias productoras de carbapenemasas

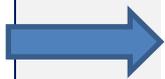
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Enterobacterias



Respuesta clínica a los carbapenems

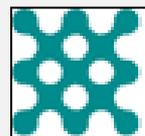
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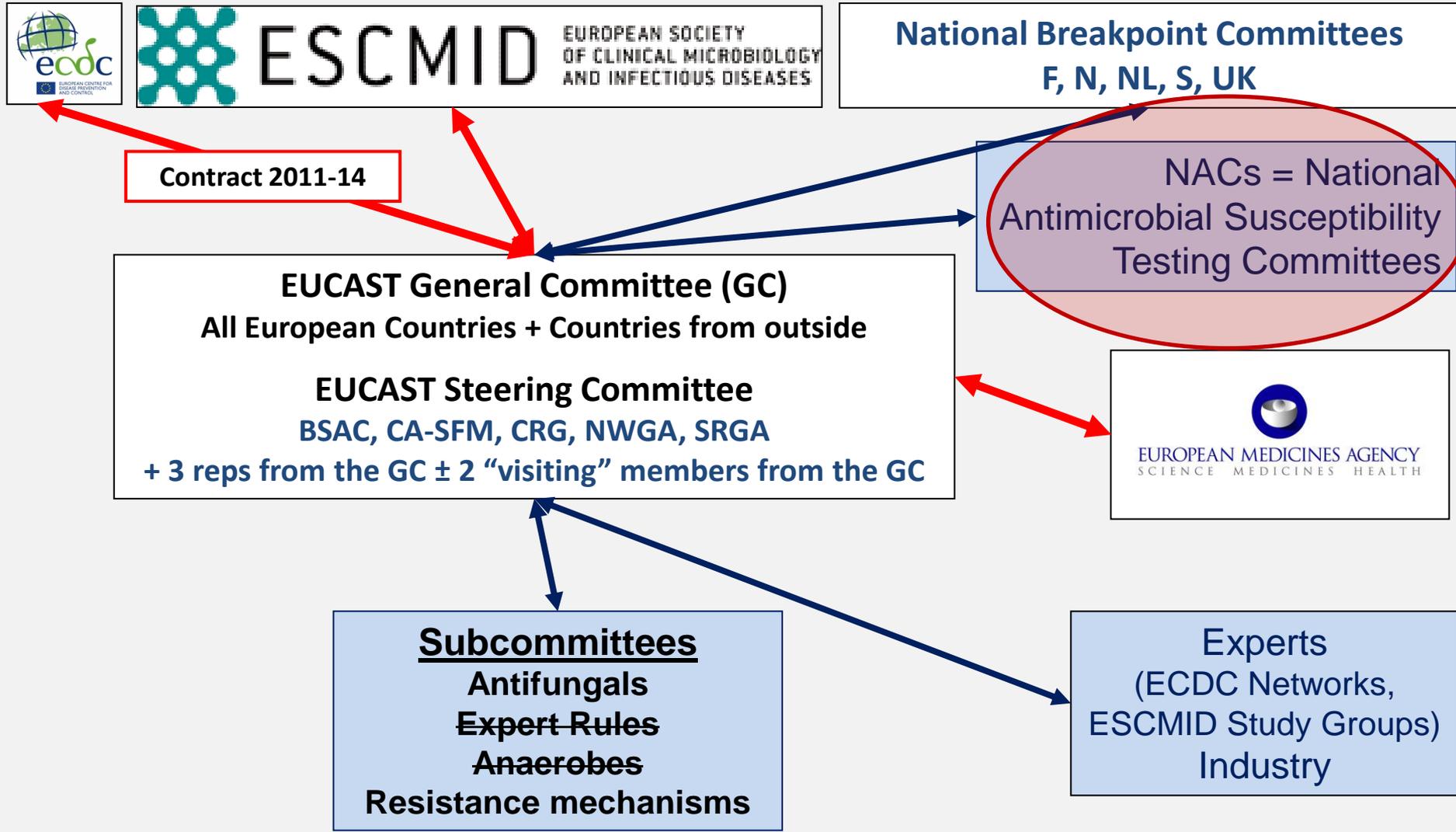
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**Subcommittees**  
Antifungals  
Expert Rules  
Anaerobes  
Resistance mechanisms

**Experts**  
(ECDC Networks,  
ESCMID Study Groups)  
Industry





### Standard Operating Procedure

#### Interaction of EUCAST Steering Committee with the network of national antimicrobial susceptibility testing committees

EUCAST SOP 5.0

3 January 2013

## Recommended members:

- Individual experts
- Representatives of:
  - clinical laboratories professional organisations/ societies in clinical microbiology and infectious diseases
  - government and public health authorities
  - quality assurance agencies
  - veterinary and food agencies

## Remit

- To promote high standards in AST
- To facilitate implementation of EUCAST breakpoints and methods
- To provide education on EUCAST criteria
- To liaise and consult with EUCAST
- To liaise with national and international groups and public health agencies involved in antimicrobial resistance surveillance in Europe and more widely, as appropriate



# Implementation of EUCAST breakpoints, January 2013

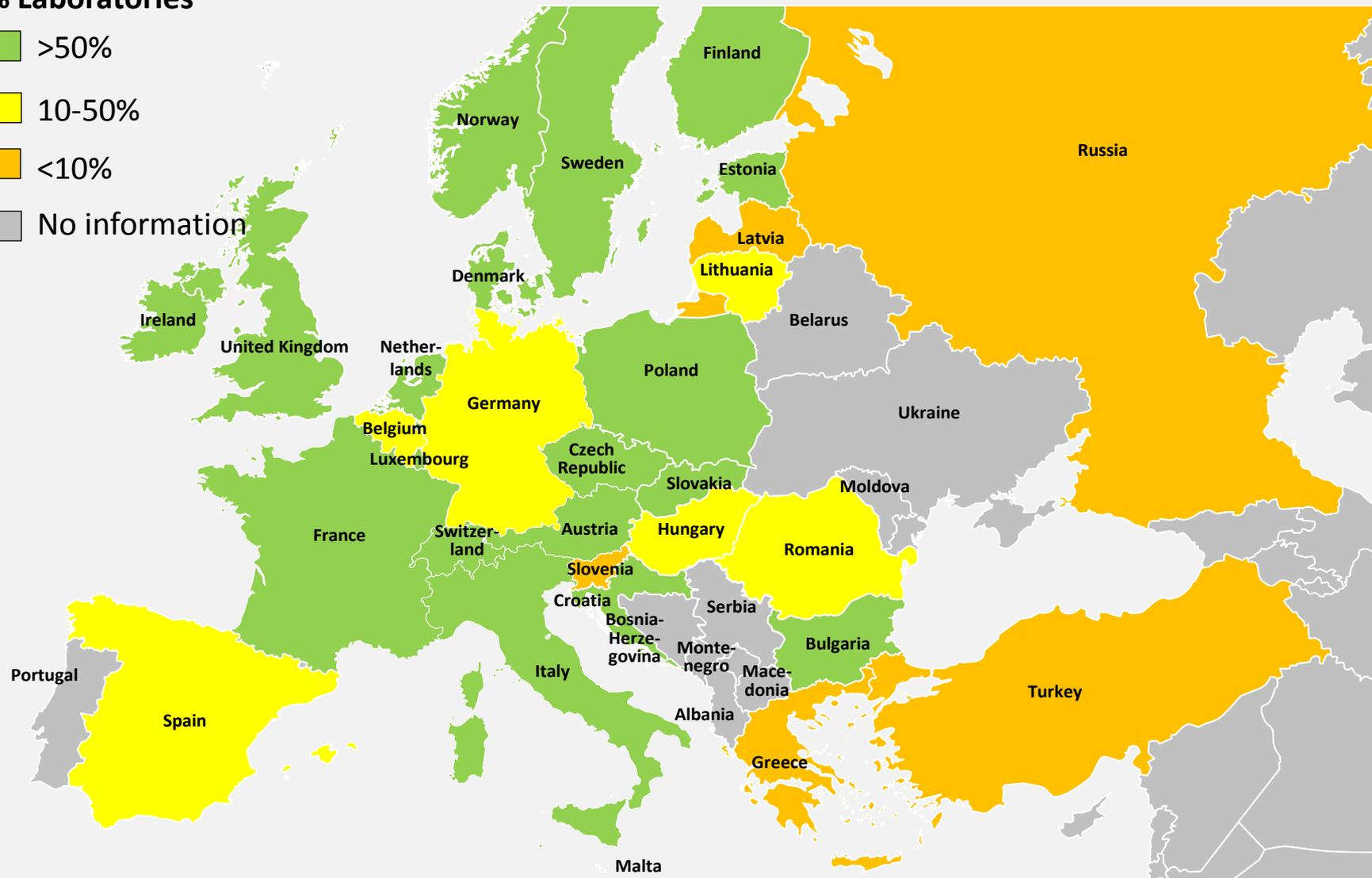
## % Laboratories

 >50%

 10-50%

 <10%

 No information



Countries not on this map:

 Australia

 Iceland

 Israel

# ¿EUCAST-NAC fuera de Europa?



¿Por qué no?

# EUCAST

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- **Comité del Antibiograma en Europa** (*European Committee on Antimicrobial susceptibility testing*)
- Establece **puntos de corte** para la **EMA**, aparecen en el resumen de las características de producto (SmPC) en la comercialización
- Acuerdo de **colaboración con el ECDC y la EFSA**
- Rápida **adopción** de los **criterios EUCAST en Europa** y sustitución de otros nacionales o no europeos (CLSI) con una labor esencial de los comités nacionales (NACs) en el proceso
- Adopción de criterios EUCAST en sistemas y productos comerciales
- NAC-EUCAST fuera de Europa (Australia, Rusia, EEUU, ...)
- Trabajo continuo de EUCAST para mejorar la utilización de los antimicrobianos en el paciente e indirectamente las resistencias



# Agradecimientos

National A&S Committees (NAC)

[EUCAST News](#)

[Clinical breakpoints](#)

[Expert rules](#)

[Setting breakpoints](#)

[MIC distributions](#)

[Zone diameter distributions](#)

[Antimicrobial susceptibility testing](#)

[Antifungal susceptibility testing \(AFST\)](#)

[Frequently Asked Questions \(FAQ\)](#)

[Meetings](#)

[EUCAST Presentations](#)

[Documents](#)

[Information for Industry](#)

## Steering Committee

The ESCMID-appointed Scientific Secretariat, the European national A&S Committees and the EUCAST general secretariat are submitted for the 2011-2014 steering committee and an email discussion list for manufacturing information.

**Chairman (2012-2014):**  
Rafael Canton

**Scientific Secretary (2011-2014):**  
Derek Brown

**Clinical Data Coordinator (2011-2014):**  
Gunnar Kahlmetz

**BSAC (The United Kingdom) Representative (2011-2014):**  
Gordon Macfarlane



Laboratorio de EUCAST y laboratorios participantes

**Representative (2011-2014):**  
Matti Saikku, Amfinn Sundsfjord

**Representative (2011-2014):**  
Matti Saikku

**Representative (2011-2014):**  
Matti Saikku

**Representative (2011-2014):**  
Matti Saikku

**Representative 3 (Denmark, 2012 -2014):**  
Rober Skov