

# **EUCAST in 2012**

**Update May 2012**



**EUCAST**

**EUROPEAN COMMITTEE  
ON ANTIMICROBIAL  
SUSCEPTIBILITY TESTING**

European Society of Clinical Microbiology and Infectious Diseases



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

Contract 2011 - 14

**EUCAST General Committee**  
All European Countries + Countries from outside

**EUCAST Steering Committee**  
BSAC, CA-SFM, CRG, NWGA, SRGA  
And 3 reps from the General Committee



**Subcommittees**  
Antifungals  
Expert Rules  
Anaerobes  
Resistance mechanisms

Experts (ECDC  
Networks, ESCMID  
Study Groups)

# EUCAST Steering Committee from April 2012

- **Rafael Canton (Chairman)**
- Derek Brown (Scientific secretary)
- **Gunnar Kahlmeter (Clinical data coordinator)**
  
- Johan Mouton (The Netherlands)
- Claude James Soussy/Luc Debreuil (France)
- Christian Giske (Sweden)
- Alasdair MacGowan (UK)
- Martin Steinbakk/Arnfinn Sundsfjord (Norway)
- Petra Apfalter (Austria, GC)
- **Luis Martinez Martinez (Spain, GC)**
- **Robert Skov (Denmark, GC)**

## Organization

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## General Committee

The General Committee consists of the Chairman, the Scientific Secretary, the Clinical Data Co-ordinator, a representative from each of the European countries and one representative from each of ISC and FESCI.

The current EUCAST general committee is listed below. Nominations for representatives of countries where no official representative is listed should be sent to the EUCAST Administrative Secretariat.

### Chairman

✉ [Gunnar Kahlmeter](#)

### Scientific Secretary

✉ [Derek Brown](#)

### Clinical data coordinator

✉ [Rafael Canton](#)

### Country Representatives

**Australia** Prof John Turnidge

**Austria** Dr Petra Apfalter

**Belgium** Prof Jan Verhaegen

**Bosnia** Dr Selma Uzunovic-Kamberovic

**Bulgaria** Prof Krassimir Metodiev

**Croatia** Dr Arjana Tambic-Andrasevic

**Czech Republic** Dr Helena Zemlickova

**Denmark** Dr Robert Skov

**Estonia** Dr Marina Ivanova

# EUCAST subcommittees

- ~~Expert rules and interpretive reading~~
  - Major revision (v 2.0) available 2011
  - Supplement in CMI during 2011
- Antifungal susceptibility testing
  - Breakpoints and RDs for *Candida* and *Aspergillus*
- ~~Anaerobe susceptibility testing~~
  - Currently dormant
- Methods for detection of resistance mechanisms of clinical and/or epidemiological importance (Febr 2012).
  - Evaluate and recommend methodology
  - Work closely with EARS-NET (ECDC)

## Expert rules in antimicrobial susceptibility testing Version 2.0, 2011

Roland Leclercq (Laboratoire de Microbiologie, CHU Côte de Nacre, Caen Cedex, 14033, France), Rafael Cartón (Servicio de Microbiología, Hospital Universitario Ramón y Cajal, Carretera de Colmenar Km 9.1, 28034-Madrid, Spain), Christian Giske (Department of Clinical Microbiology, L2.02, Karolinska University Hospital, Solna, SE-17176 Stockholm, Sweden), Peter Heisig (Department of Pharmacy Biology & Microbiology, Institute of Pharmacy, University of Hamburg, Bundesstrasse 45, D-20146 Hamburg, Germany), Patrice Nordmann (Service de Bactériologie-Virologie, Hôpital de Bicêtre, 78 rue du Général Leclerc, 94275 Le Kremlin-Bicêtre Cedex, France), Gian Maria Rossolini (Dip. di Biologia Molecolare, Sezione di Microbiologia, Policlinico Le Scotte, 53100 Siena, Italy), Trevor Winstanley (Department of Microbiology, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK)

Comments and suggestions for additions to the next version of this document should be sent to the EUCAST Scientific Secretary (see <http://www.eucast.org> for contact details)



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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. 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

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QUICK NAVIGATION

### EUCAST News

17 Jan 2012

**Posaconazole vs. Aspergillus breakpoints and RD**

12 Jan 2012

**Amphotericin and itraconazole aspergillus breakpoints and RDs**

31 Dec 2011

**EUCAST AFST Subcommittee distributes for consultation.**

24 Dec 2011

**EUCAST Breakpoint Tables v 2.0**

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## EUCAST News

Here you can find the latest news and updates from EUCAST.

17 Jan 2012

### **Posaconazole vs. Aspergillus breakpoints and RD**

The new posaconazole breakpoints and rationale document for aspergillus [\[...\]](#)

12 Jan 2012

### **Amphotericin and itraconazole aspergillus breakpoints and RDs**

Amphotericin and itraconazole vs. aspergillus breakpoints and rationale [\[...\]](#)

31 Dec 2011

### **EUCAST AFST Subcommittee distributes for consultation.**

Consultation on Definitive Document EDef 7.2. [\[...\]](#)

[EUCAST Chairman report](#)

## RSS

-  [RSS 2.0](#)
-  [RDF](#)
-  [ATOM 0.3](#)

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# EUCAST and the harmonisation process

## Harmonised 2002 - 2009

- Aminoglycosides ✓
- Carbapenems & aztreonam ✓
- Cephalosporins iv ✓
- Cephalosporins oral ✓
- Fluoroquinolones ✓
- Glycopeptides ✓
- Macrolides and lincosamines ✓
- Miscellaneous antimicrobials ✓
- Penicillins ✓
- Tetracyclines ✓
- **Antifungal drugs**
  - Breakpoints for *Candida* and *Aspergillus*

## Topical agents:

Retapamulin (ECOFF)  
Mupirocin (LLR/HLR)  
Fidaxomicin (ECOFF)

# EUCAST

- breakpoints for new drugs with EMA

- Daptomycin ✓
- Tigecycline ✓
- Doripenem ✓
- Telavancin ✓
- Glycopeptides (one ongoing)
- Cephalosporins (activity against MRSA - ongoing)
- Anti-MTB (one - two agents - ongoing)
  
- Glycopeptide (withdrawn)
- Fluoroquinolone (withdrawn)
- Diaminopyrimidine (withdrawn)
  
- Extensions of indications (currently none)

EMA = European Medicines Agency



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## 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](#)

[Amoxicillin v 1.0](#)

[Benzylpenicillin v 1.0](#)

[Cefotaxime v 1.0](#)

[Ceftazidime v 1.0](#)

[Cefuroxime iv v 1.0](#)

[Ciprofloxacin v 1.9](#)

[Colistin v 1.0](#) EUCAST Chairman report

[Daptomycin v 1.0](#)

**Jan 2011: 39 RDs**

**Jan 2012: 45 RDs**

# EUCAST breakpoints March 2012

## % Laboratories

 >50%

 10-50%

 <10%

 No information 2012



Countries not on the map:

 Australia

 Iceland

 Israel



**Gennaio  
2012**



**EUCAST**



**CLSI**

**86 lab.** ●  
**98,8 %**



# EUCAST

EUROPEAN COMMITTEE  
ON ANTIMICROBIAL  
SUSCEPTIBILITY TESTING

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## ***Stenotrophomonas maltophilia***

### **The organism**

*Stenotrophomonas maltophilia* is a ubiquitous environmental organism. In patients it is most often associated with colonization, but is an occasional cause of infection, particularly in immunocompromised patients and patients with cystic fibrosis.

### **Antimicrobial resistance**

Intrinsic antimicrobial resistance of this organism is a major problem, particularly to aminoglycosides and carbapenems. Multiple efflux pumps and modifications to outer membrane proteins confer variable resistance to a wide range of agents. Chromosomal genes for beta-lactamases affect all beta-lactams including carbapenems. Aminoglycoside acetyl transferase and SmQnr genes (conferring reduced susceptibility to fluoroquinolones) are almost always present (3). In addition, acquired genes may be present conferring resistance to a wide range of agents, including trimethoprim-sulfamethoxazole (co-trimoxazole) (17). Moreover, the formation of biofilms reduces antimicrobial effectiveness.

## **Why do EUCAST have no systemic breakpoints for Enterobacteriaceae with oral cephalosporins?**

There have been multiple questions from clinicians, particularly those working in orthopaedics, who have “successfully used oral cephalosporins for prophylaxis and to treat Enterobacteriaceae infections for many years”. They ask what has changed and why these agents are now considered inappropriate.

In EUCAST rationale documents it is stated that Enterobacteriaceae are inappropriate targets in sites other than uncomplicated urinary tract infection, but there is no further explanation. In early EUCAST discussions oral cephalosporins were originally considered inappropriate for treatment of infections in other sites than the urinary tract infection for several reasons:

1. Comparison of free drug pharmacokinetics with MICs alone indicates that inadequate concentrations are achieved for most agents and are borderline at best (see table).
2. The relevant pharmacodynamic relationship indicative of activity of cephalosporins is  $T > MIC$  and the target  $\%fT > MIC$  is 40-50%. Approximate calculations based on common dosages indicate that activity is inadequate for all agents (see table). It should be emphasized that the figures in the table are based on pharmacokinetic parameter values for the mean of the population. Monte Carlo simulations would show that the  $\%fT > MIC$  values are even less than those in the table for half the population treated.

## **Direct antimicrobial susceptibility testing**

In direct antimicrobial susceptibility testing the specimen (commonly urines) is used as the source of the inoculum. Tests where positive blood cultures are used as the source of the inoculum are also included as direct tests, although they do not use the specimen directly.

The advantage of direct testing is that results may be available earlier than when the organism is isolated in pure culture before testing and this may have direct patient benefit in terms of early appropriate chemotherapy. There may be additional benefits from the ability to narrow the spectrum of therapy at an early stage.

The main disadvantage is that the inoculum cannot be effectively controlled. Also there may be mixed cultures and there may be pH variations or substances in the specimens that affect results (e.g. antimicrobial agents in urine, antimicrobial absorption materials in blood cultures). These problems may result in less reliable results than with pure cultures. EUCAST does not recommend primary susceptibility testing and any laboratory using this approach must take responsibility for ensuring that results are reliable. The following should be noted:

1. There are currently no validated methods for processing specimens to ensure that the correct inoculum is achieved.
2. Tests should be repeated on pure cultures as needed and the correlation of direct and secondary tests should be monitored so that the reliability of direct tests can be assessed.
3. In disk diffusion tests, if the inoculum is visibly light, do not report susceptible results as zone diameters may be increased leading to resistant isolates appearing susceptible.



# EUCAST breakpoint decisions 2011/12

- *Moraxella catarrhalis* breakpoints for all relevant agents.
- *C.difficile* breakpoints for metronidazole (2/2 mg/L) and vancomycin (2/2 mg/L).
- *H.pylori* breakpoints (based on ECOFFs) for several agents.
- *L. monocytogenes* breakpoints for several agents.
- Fosfomycin breakpoints **removed** from *Pseudomonas*.
- Nitrofurantoin breakpoints **removed** from *E. fecium*.
- Vancomycin breakpoints for Coag neg staphs **increased** from 2/2 to 4/4 mg/L.
- Trimethoprim breakpoints 2/2 mg/L included for *S. agalactiae* in UTI.
- Amoxicillin & amox/clav breakpoints in *H. influenzae* **increased** to 2/2 mg/L.
- Chloramphenicol breakpoint in *H. influenzae* **increased** to 2/2 mg/L.
- Rifampicin breakpoint in *H. influenzae* **increased** to 1/1 mg/L.
- Ceftibuten – **removed** "uncomplicated" in the caveat "uncomplicated UTI".
- Replace "IE" with "dash" for ceftibuten for *S. pneumoniae*.
- *Stenotrophomonas maltophilia* – guidance document.
- Oral cephalosporins – no systemic breakpoints for Enterobacteriaceae (position document on website).

## EUCAST disk diffusion test

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[Implementation guide](#)

[Breakpoint tables](#)

[Disk diffusion methodology](#)

[QC Tables](#)

**[Calibration and validation](#)**

[Projects and data submission](#)

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# Development and validation of EUCAST Disk Diffusion breakpoints

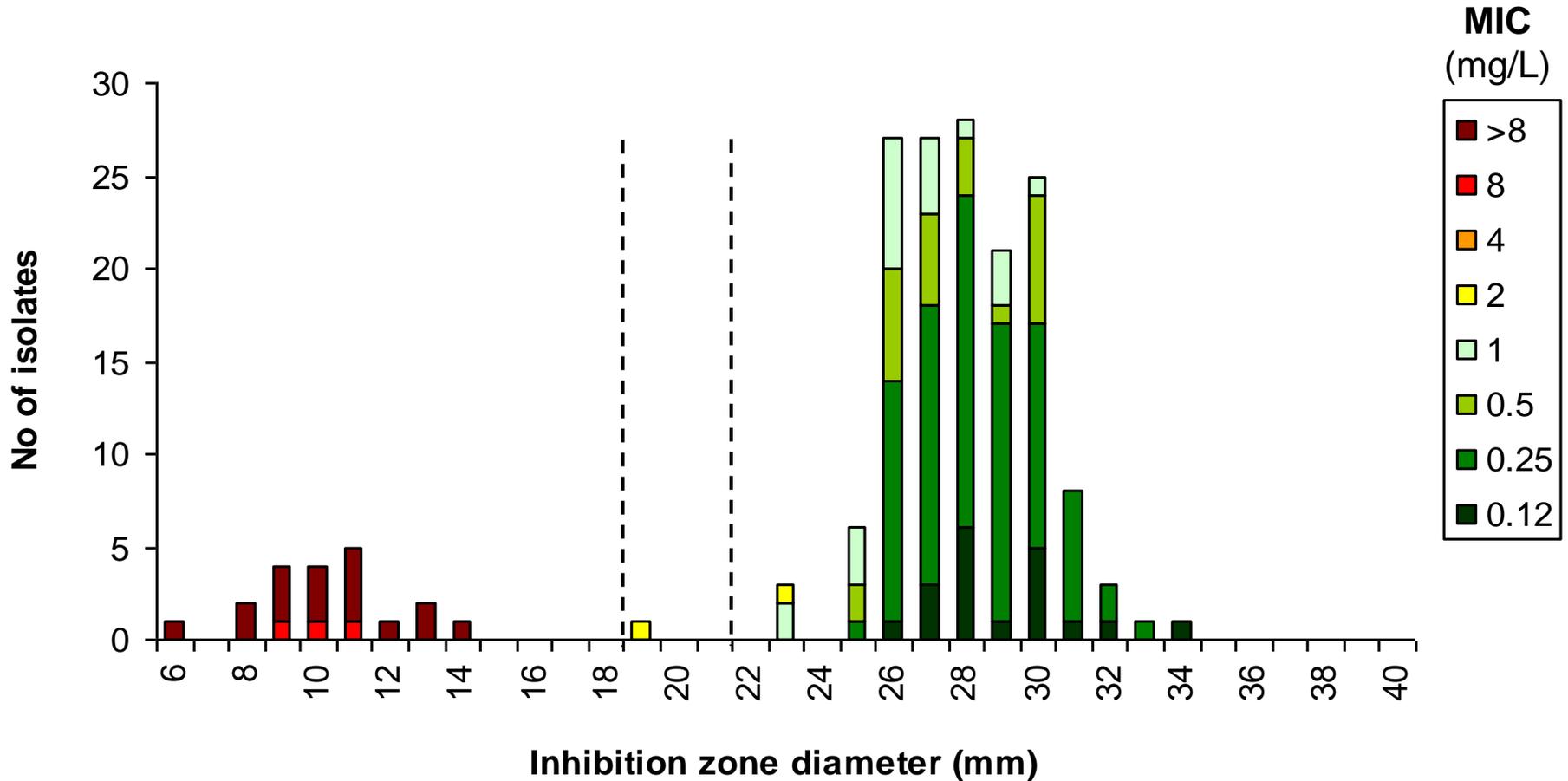
The EUCAST Disk Diffusion test was developed by EUCAST during 2009 - 2011 under the auspices of ESCMID and with the help of many laboratories. The help of these laboratories is gratefully acknowledged.

For each of the species listed below projects are either ongoing or have been concluded. The material for each of these is now being summarized and will be made available during the second half of 2011 ([📄 Example 1](#)). All MIC and zone diameter data are entered in the EUCAST MIC- and Zone diameter distribution program ([🔗 Example 2](#)).

- [📄 Enterobacteriaceae](#)
- [📄 Pseudomonas aeruginosa](#)
- Salmonella spp.
- Acinetobacter spp.
- [📄 Staphylococcus aureus](#) (updated 2011-12-12)
- [📄 Staphylococcus, coagulase-negative](#)
- [📄 Streptococcus pyogenes \(group A\)](#)
- [📄 Streptococcus pneumoniae](#)
- [📄 Enterococcus spp.](#)
- [📄 Viridans Group Streptococci](#)
- [📄 Haemophilus influenzae](#) - general breakpoints
- [📄 Haemophilus influenzae](#) - **screening for betalactam resistance**
- [📄 Moraxella catarrhalis](#) (update 2011-12-12)
- Pasteurella multocida
- [📄 Listeria monocytogenes](#)
- Corynebacterium spp.
- Campylobacter spp.

# Tetracycline 30 µg vs. MIC

## *S. aureus*, 172 clinical isolates



Breakpoints		ECOFF
MIC	S ≤ 1, R > 2 mg/L	WT ≤ 1 mg/L
Zone diameter	S ≥ 22, R < 19 mm	

# EUCAST ongoing projects

- Breakpoints for new agents (with EMA)
  - Anti-mrsa cep, glycopeptide, anti-mycobacterials (?)
- Breakpoints and/or disk diffusion methodology
  - *Campylobacter* (CB/DD)
  - *Corynebacterium* spp (CB/DD)
  - *Pasteurella multocida* (CB/DD)
  - *Yersinia enterocolitica* (CB/DD)
  - Anaerobic bacteria (DD )
  - *Neisseria gonorrhoeae* (DD)
  - Validation project on Streptococci and *S. pneumoniae* (validation)
  - Screening for beta-lactam resistance in Viridans group streptococci (validation)
  - Screening for FQ resistance in *Salmonella* (DD)
  - *Pseudomonas non-aeruginosa* (CB/DD)
  - *Actinomyces* & *Nocardia* (CB)
  - *Burkholderia* (CB)
  - *Staphylococcus pseudintermedius* (methicillin resistance, DD)
- Breakpoints for topicals - based on ECOFFs for clinically relevant agents and species.

# Topical agents - Draft for consultation

Organisms	ECOFF (mg/L)										
	Gentamicin <sup>1</sup>	Ciprofloxacin <sup>1</sup>	Levofloxacin <sup>1</sup>	Ofloxacin <sup>1</sup>	Chloramphenicol <sup>1</sup>	Colistin <sup>1</sup> (for Polymyxin B)	Fusidic acid <sup>1</sup>	Neomycin <sup>2</sup> (framycetin)	Bacitracin <sup>2</sup>	Mupirocin <sup>2</sup>	Retapamulin <sup>2</sup>
Enterobacteriaceae	2	0.12	0.25	0.5	16	2	-	8?	-	-	-
<i>Acinetobacter</i> spp.	4	1	0.5	1	-	2	-	ND	-	-	-
<i>Pseudomonas aeruginosa</i>	8	0.5	2	2	-	4	-	ND	-	-	-
<i>Staphylococcus aureus</i>	0.5-2	1	0.5-1	1	8-16	-	0.5	1	ND	1 <sup>3</sup>	0.5
<i>Streptococcus pneumoniae</i>	-	2	2	4	8	-	1	ND	ND	-	-
$\beta$ -haemolytic streptococci	-	2	1-2	4	8	-	0.5	ND	ND	0.5	0.12
<i>Haemophilus influenzae</i>	4	0.06	0.06	0.06	1	-	ND	ND	-	-	-
<i>Moraxella</i> spp.	0.25	0.12	0.12	0.25	2	-	ND	ND	-	-	-
<i>Neisseria gonorrhoeae</i>	32?		0.016	0.06	8?	-	ND	ND	ND	-	-
<i>Neisseria meningitidis</i>	ND	0.016	0.03	ND	2	-	ND	ND	ND	-	-

- = inappropriate combination.

ND = No ECOFF defined on EUCAST MIC distribution website.

? = Estimates where there are few data and no ECOFF defined on the MIC distribution website, or where there are differences among species in the group.

<sup>1</sup>Agents also available for systemic use.

<sup>2</sup>Agents available for topical use only.

<sup>3</sup>Breakpoints for nasal decontamination  $S \leq 2$ ,  $R > 256$  mg/L.

# Compliance of manufacturers

see [www.eucast.org](http://www.eucast.org) for comprehensive review

- Almost all manufacturers of disks can now provide all “EUCAST strength disks”:
  - Abtek
  - BD
  - Bio-Rad
  - I2A
  - Liofilchem
  - Mast group
  - Thermo Fisher Scientific (Oxoid)
  - Rosco (tablets)

Each manufacturer is responsible for the quality of their products used for AST.

EUCAST will not be able to provide comprehensive QC on all disks from all manufacturers but will, on initiative from EUCAST, users or manufacturers provide important information on products used for AST on the website.

# Compliance of manufacturers

see [www.eucast.org](http://www.eucast.org) for comprehensive review

- Manufacturers with commercial MH-F plates:
  - Thermo Fisher Scientific (Oxoid)
  - bioMérieux
  - Bio-Rad
  - Liofilchem
- Manufacturers not yet ready to supply MH-F plates:
  - BD

Each manufacturer is responsible for the quality of their products used for AST.

EUCAST will not be able to provide comprehensive QC on all disks from all manufacturers but will, on initiative from EUCAST, users or manufacturers provide important information on products used for AST on the website.

# Automated devices

- None of the automated devices is yet fully compliant with EUCAST breakpoints and/or terminology.
- This is now the major obstacle for the implementation of EUCAST breakpoints in many countries. Vitek2 is the most commonly used device, which may be one reason for why most complaints are on this device.

**Countries are encouraged to form  
National AST Committees (NAC).**

**NAC**

# NAC

- **Antimicrobial susceptibility testing**

- Strategy at national level
- Implementation of breakpoints and methods
- Education (national workshops, websites)
- Liaison and consultation with EUCAST (chairman or scientific secretary GC representative)
- Liaison with groups involved in AMR-surveillance (ECDC, EARSS, ....).
- QA

- **Antimicrobial Policies**

- **Antimicrobial Resistance Surveillance**

- **Antimicrobial Consumption and Policies**

# National AST Committee (NAC) March 2012

Yes

In the process of forming a NAC

No

No information 2012



Countries not on the map:

Australia

Iceland

Israel