The implementation of the EUCAST standard in BD Phoenix™ and BD EpiCenter™ Systems

BD

Helping all people live healthy lives

The goals of this booklet are to:

1- Introduce EUCAST*

- what EUCAST has achieved so far,
- the approach/methodology that was used by EUCAST,
- what is the future of EUCAST,

2 - Present the BD initiatives, with details on

- what BD has done so far to prepare implementation of the EUCAST standard in the BD Phoenix™/ BD EpiCenter™ system,
- ongoing BD projects with regards to EUCAST.

* The first section of this booklet reproduces information from the EUCAST website, with kind permission from the EUCAST committee

EUCAST
An Introduction

EUCAST structure, objectives and main concepts

Procedure for setting breakpoints

EUCAST and EMEA

EUCAST and the future

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

EUCAST

European Committee on Antimicrobial Susceptibility Testing
formed in 1997 and restructured in 2002

convened by
European Society for Clinical Microbiology and Infectious Diseases (ESCMID)
National Breakpoint Committees in Europe

and financed by
ESCMID
National Breakpoint Committees in Europe
DG-SANCO of the European Union
(3 year grant from May 2004)
European Centre for Disease Prevention & Control (ECDC)
(1 year interim funding from May 2007 and 3 year grant from Sept 2008)

EUCAST Structure

EUCAST General Committee:

- one representative, from each European country,
- one representative each from ISC and FESCI,
- chairperson, Scientific secretary and Clinical Data Coordinator (appointed by ESCMID),
- meets once a year at ECCMID,
- provides comment on proposal referred by Steering Committee.

EUCAST Steering Committee:

- chairperson, Scientific Secretary and Clinical Data Coordinator (appointed by ESCMID),
- one representative each from the European national breakpoint committees,
- two representatives from the EUCAST General Committee.

EUCAST industry email network:

- manufacturers of pharmaceuticals and susceptibility testing devices,
- steering Committee proposals are referred to the industry network for comments before decision.

EUCAST Steering Committee Membership

• Chairperson	Gunnar Kahlmeter	2008 -11
• Scientific secretary	Derek Brown	2008 -11
• Clinical data coordinator	Rafael Canton	2008 -11
• BSAC (The UK)	Alasdair MacGowan	2008 -11
• CA-SFM (France)	Fred Goldstein/C-J Soussy	2008 -11
• CRG (The Netherlands)	Johan W. Mouton	2008 -11
• DIN (Germany)	Arne Rodloff	2008 -11
• NWGA (Norway)	Martin Steinbakk	2008 -11
• SRGA (Sweden)	Inga Odenholt	2008 -11
• General Committee rep	Antti Hakanen (Finland)	2008 -10
• General Committee rep	Paul Tulkens (ISC)	2008 -10

EUCAST General Committee 2010

Austria	Prof Helmut Mittermayer
Belgium	Prof Jan Verhaegen
Bosnia	Dr Selma Uzunovic-Kamberovic
Bulgaria	Prof KrassimirMetodiev
Croatia	Dr ArjanaTambic-Andrasevic
Czech Republic	Dr PavlaUrbaskova
Denmark	Dr Niels Frimodt-Møller
Estonia	Dr M Ivanova
Finland	Dr Antti Hakanen
France	Prof Luc Dubreuil
Germany	Prof Bernd Wiedemann
Greece	Prof Alkiviadis Vatopoulos
Hungary	Dr ÉvaBán
Iceland	Dr Karl Gustaf Kristinsson
Ireland	Dr Martin Cormican
Italy	Prof Pietro Varaldo
Latvia	Dr Arta Balode
Lithuania	Prof Arvydsa Ambrozaitis
Macedonia	No representative
Netherlands	Prof John Degener
Norway	Dr Martin Steinbakk
Poland	Prof Waleria Hryniewicz
Portugal	Prof Jose Melo Cristino
Romania	No representative
Russia	Dr Olga Stetsiouk
Serbia	Dr LazarRanin
Slovak Republic	Prof. Milan Niks
Slovenia	Dr Jana Kolman
Spain	Dr Francisco Soriano
Sweden	Dr Barbro Olsson-Liljequist
Switzerland	Prof Jaques Bille
Turkey	Dr Deniz Gur
UK	Prof Alasdair Mac Gowan
ISC	Prof Paul Tulkens
FESCI	Dr David Livermore

Email network of industry with interest in antimicrobials

Chairperson: Gunnar Kahlmeter, Sweden
Scientific Secretary: Derek Brown, UK
Clinical data coordinator: Rafael Canton, Spain

EUCAST Subcommittees

EUCAST Subcommittee on Antifungal Susceptibility Testing (EUCAST AFST)

- Develop reference methods for antifungal susceptibility testing.
- Set breakpoints for antifungal drugs.
- Financed through EUCAST.
- EUCAST processes for breakpoint setting, decisions and consultation.

EUCAST Subcommittee on Expert Rules

- To develop/update expert rules for antimicrobial susceptibility testing.

EUCAST Subcommittee on Anaerobes

Main objectives of EUCAST are:

- To set common European breakpoints for surveillance of antimicrobial resistance
- To harmonise breakpoints for existing and new antimicrobial drugs
- To encourage internal and external national and international quality assessment schemes
- To work with groups outside Europe (e.g. CLSI) to achieve international consensus on susceptibility testing

EUCAST definitions of clinical breakpoints

- EUCAST has re-defined susceptible, intermediate and resistant and defined the terms "wild type" and "non-wild type" microorganism.

- The national breakpoint committees have also agreed on a common format for susceptible. S<x mg/L; I>x, <y mg/L; R>y mg/L

Clinically Susceptible (S)

- a microorganism is defined as susceptible if inhibited in-vitro by a concentration of an antimicrobial agent that is associated with a high likelihood of therapeutic success,
- a microorganism is categorized as susceptible (S) by applying the appropriate breakpoint in a defined phenotypic test system.

Clinically Intermediate (I)

- a microorganism is defined as intermediate by a level of antimicrobial agent activity associated with uncertain therapeutic effect.
  - It implies that an infection due to the isolate may be appropriately treated in body sites where the drugs are physically concentrated or when a high dosage of drug can be used; it also indicates a buffer zone that should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations.
- a microorganism is categorized as intermediate (I) by applying the appropriate breakpoints in a defined phenotypic test system.

Clinically Resistant (R)

- a microorganism is defined as resistant if inhibited in-vitro by a concentration of an antimicrobial agent that is associated with a high likelihood of therapeutic failure.
- a microorganism is categorized as resistant (R) by applying the appropriate breakpoint in a defined phenotypic test system.

EUCAST definitions of epidemiological cut off values

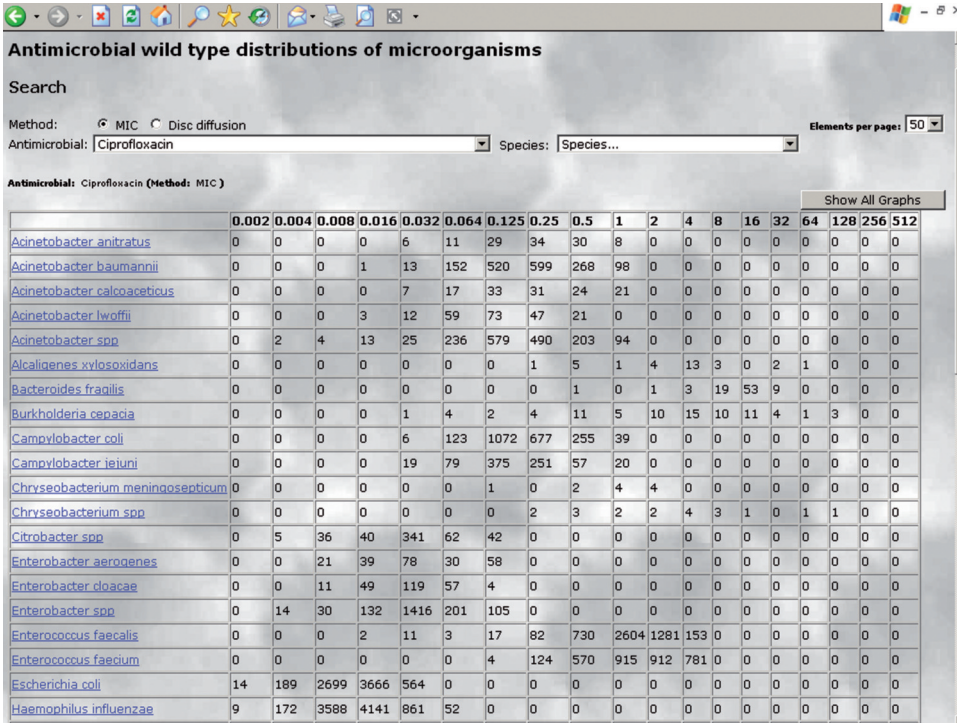
Wild type (WT) :a microorganism is defined as wild type (WT) for a species by the absence of acquired and mutational resistance mechanisms to the drug in question.

Microbiological resistance - non-wild type (NWT): a microorganism is defined as non-wild type (NWT) for a species by the presence of an acquired or mutational resistance mechanism to the drug in question.

The cut-off values (ECOFF) used to categorize an organism as WT or NWT were determined by collecting and analyzing a large amount of MICs data (MIC distributions).

The cut-off values are drug/species-specific.

Antimicrobial wild type distributions of microorganisms



Antimicrobial wild type distributions of microorganisms

Search

Method: MIC Disc diffusion

Antimicrobial: Ciprofloxacin Species: Species...

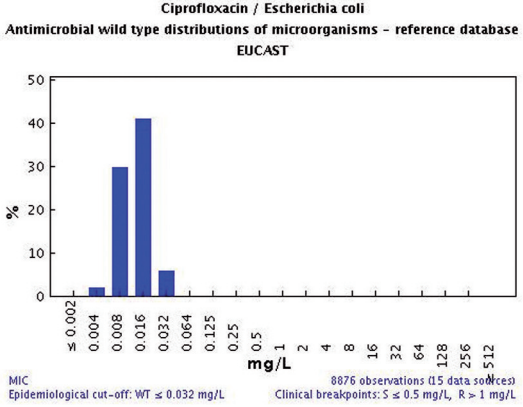
Elements per page: 50

Antimicrobial: Ciprofloxacin **(Method:** MIC **)**

Show All Graphs

	0.002	0.004	0.008	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	16	32	64	128	256	512
Acinetobacter anitratus	0	0	0	0	6	11	29	34	30	8	0	0	0	0	0	0	0	0	0
Acinetobacter baumannii	0	0	0	1	13	152	520	599	268	98	0	0	0	0	0	0	0	0	0
Acinetobacter calcoaceticus	0	0	0	0	7	17	33	31	24	21	0	0	0	0	0	0	0	0	0
Acinetobacter lwoffii	0	0	0	3	12	59	73	47	21	0	0	0	0	0	0	0	0	0	0
Acinetobacter spp	0	2	4	13	25	236	579	490	203	94	0	0	0	0	0	0	0	0	0
Alcaligenes xylosoxidans	0	0	0	0	0	0	0	1	5	1	4	13	3	0	2	1	0	0	0
Bacteroides fragilis	0	0	0	0	0	0	0	0	1	0	1	3	19	53	9	0	0	0	0
Burkholderia cepacia	0	0	0	0	1	4	2	4	11	5	10	15	10	11	4	1	3	0	0
Campylobacter coli	0	0	0	0	6	123	1072	677	255	39	0	0	0	0	0	0	0	0	0
Campylobacter jejuni	0	0	0	0	19	79	375	251	57	20	0	0	0	0	0	0	0	0	0
Chryseobacterium meningosepticum	0	0	0	0	0	0	1	0	2	4	4	0	0	0	0	0	0	0	0
Chryseobacterium spp	0	0	0	0	0	0	0	2	3	2	2	4	3	1	0	1	1	0	0
Citrobacter spp	0	5	36	40	341	62	42	0	0	0	0	0	0	0	0	0	0	0	0
Enterobacter aerogenes	0	0	21	39	78	30	58	0	0	0	0	0	0	0	0	0	0	0	0
Enterobacter cloacae	0	0	11	49	119	57	4	0	0	0	0	0	0	0	0	0	0	0	0
Enterobacter spp	0	14	30	132	1416	201	105	0	0	0	0	0	0	0	0	0	0	0	0
Enterococcus faecalis	0	0	0	2	11	3	17	82	730	2604	1281	153	0	0	0	0	0	0	0
Enterococcus faecium	0	0	0	0	0	0	4	124	570	915	912	781	0	0	0	0	0	0	0
Escherichia coli	14	189	2699	3666	564	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Haemophilus influenzae	9	172	3588	4141	861	52	0	0	0	0	0	0	0	0	0	0	0	0	0

The above table is available on the EUCAST website.
Click on any species to obtain a graph like the one displayed below for ciprofloxacin/*E.coli*



Use of EUCAST wild type distributions

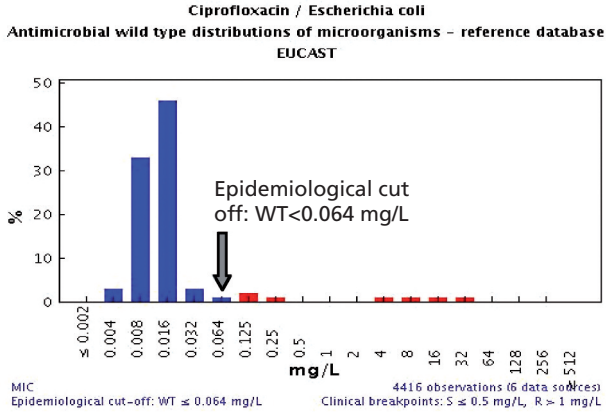
Wild Type MIC distributions can serve as:

- reference material for epidemiological cut-off values for antimicrobial resistance surveillance,
- reference material for (national) committees involved in decisions on clinical breakpoints,
- reference MIC ranges of wild type organisms for a wide spectrum of species and antimicrobials,
- an international reference for "calibration" of antimicrobial susceptibility testing methods.

EUCAST procedure for setting breakpoints

1. Data on dosing, formulations, clinical indications and target organisms are reviewed and differences which might influence breakpoints are highlighted.

2. Multiple MIC-distributions are collected, the wild type MIC distribution is defined and tentative epidemiological cut-off values determined (WT <X mg/L).



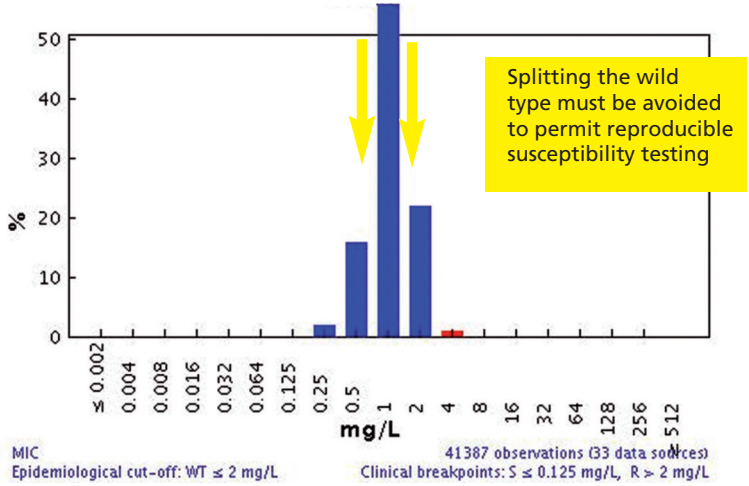
3. Existing national clinical breakpoints are compared.

4. Using available Pk/Pd data, Monte Carlo simulations are performed and a Pk/Pd breakpoint calculated based on conventional dosing regimens.

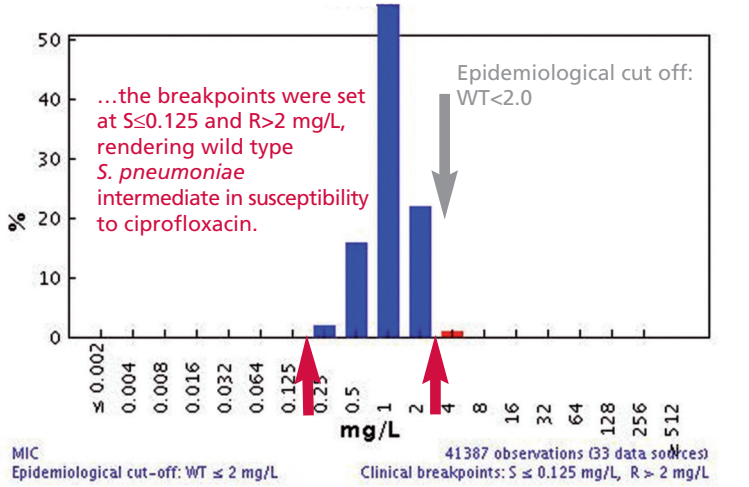
5. Clinical data relating outcome to MIC-values, wild type and resistance mechanisms are assessed in relation to the tentative breakpoint.

6. Tentative breakpoints are checked against target species wild type MIC distributions to avoid splitting the wild type to obtain tentative breakpoints.

Ciprofloxacin / Streptococcus pneumoniae
Antimicrobial wild type distributions of microorganisms - reference database EUCAST



Ciprofloxacin / Streptococcus pneumoniae
Antimicrobial wild type distributions of microorganisms - reference database EUCAST



EUCAST procedure for setting breakpoints

7. Tentative breakpoints proposed by the EUCAST Steering Committee are referred to the national breakpoint committees for comments. When Steering Committee and national committees agree, the tentative breakpoints are subjected to the EUCAST consultation process.

8. Consultation process on tentative breakpoints:
   - EUCAST General Committee
   - Expert groups (eg Neisseria, anaerobes)
   - Pharmaceutical industry, AST device manufacturers
   - Others via EUCAST website.

9. Rationale document prepared and published on website.

EUCAST breakpoint tables available at http://www.eucast.org

Enterobacteriaceae

EUCAST Clinical Breakpoint Table v. 1.0 2009-12-22

Penicillins[1]	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes Numbers for comments on MIC breakpoints Letters for comments on disk diffusion
	S ≤	R>		S ≥	R<	
						1. For aminopenicillin breakpoints, the resistant breakpoint of >8 mg/L ensures that all isolates with resistance mechanisms are reported resistant. The wide range of dosages and intravenous versus oral administration significantly affect therapeutic efficacy. The unspecified susceptible breakpoint enables the user to categorise wild type *Escherichia coli* and *Proteus mirabilis* as either susceptible or intermediate to the aminopenicillins depending on dosing, route of administration and whether the infection is systemic or affects the urinary tract only.
Benzylpenicillin	-	-		-	-	
Ampicillin	Note[1]	8	**10**	Note[A]	14	**A.** Clinical MIC breakpoints allow laboratories to decide on the basis of national dosing practices whether Enterobacteriaceae without resistance mechanisms to aminopenicillins should be categorized as S or I. To categorize wild type Enterobacteriaceae as S use disk diffusion breakpoints of 12/12 mm; to categorize as I use 50/12 mm.
Ampicillin-sulbactam[2]	Note[1]	8	**10-10**	IP	IP	**2.** For susceptibility testing purposes, the concentration of sulbactam is fixed at 4 mg/L.
Amoxicillin	Note[1]	8	**-**	Note[B]	Note[B]	**B.** Susceptibility inferred from ampicillin.
Amoxicillin-clavulanate[3]	Note[1]	8	**20-10**	Note[A]	12	**3.** For susceptibility testing purposes, the concentration of clavulanate is fixed at 2 mg/L.
Piperacillin	8	16	**30**	18	15	
Piperacillin-tazobactam[4]	8	16	**30-6**	18	15	**4.** For susceptibility testing purposes, the concentration of tazobactam is fixed at 4 mg/L.
Ticarcillin	8	16	**75**	23	22	
Ticarcillin-clavulanate[3]	8	16	**75-10**	23	22	
Phenoxymethylpenicillin	-	-		-	-	
Mecillinam (uncomplicated UTI only)	8	8	**10**	15	15	

Cephalosporins[1]	MIC breakpoint (mg/L)		Disk content (µg)	Zone diameter breakpoint (mm)		Notes Numbers for comments on MIC breakpoints Letters for comments on disk diffusion
	S ≤	R>		S ≥	R<	
						1. The cephalosporin breakpoints for Enterobacteriaceae will detect resistance mediated by most ESBLs and other clinically important beta-lactamases in Enterobacteriaceae. However, some ESBL-producing strains may appear susceptible or intermediate with these breakpoints. For epidemiological or infection control purposes laboratories may want to use a test which specifically screens for the presence of ESBLs.
Cefaclor	-	-		-	-	
Cefadroxil (uncomplicated UTI only)	16	16	**30**	12	12	
Cefalexin (uncomplicated UTI only)	16	16	**30**	IP	IP	
Cefazolin	-	-		-	-	
Cefepime	1	8	**30**	24	18	
Cefixime (uncomplicated UTI only)	1	1	**5**	17	17	
Cefotaxime	1	2	**5**	21	18	
Cefoxitin (screen)	NA	NA		NA	NA	
Cefpodoxime (uncomplicated UTI only)	1	1	**10**	21	21	
Ceftazidime	1	8	**10**	20	15	
Ceftibuten (uncomplicated UTI only)	1	1	**30**	21	21	
Ceftriaxone	1	2	**30**	23	20	
Cefuroxime	8[2]	8	**30**	18	18	**2.** The S/I breakpoint has been increased from 4 to 8 mg/L to avoid splitting the wild type MIC distributions of relevant Enterobacteriacae. The breakpoint relates to a dosage of 1.5 g x 3 and to *E. coli* and *Klebsiella* spp only.
Cefuroxime axetil (uncomplicated UTI only)	8	8	**30**	18	18	

EUCAST agreed breakpoints

- **Penicillins** benzylpenicillin, ampicillin, ampicillin-sulbactam, amoxicillin, amoxicillin-clavulanate, piperacillin, piperacillin-tazobactam, ticarcillin, ticarcillin-clavulanate, phenoxymethylpenicillin, mecillinam, oxacillin, cloxacillin, dicloxacillin, flucloxacillin
- **Monobactams** aztreonam
- **Cephalosporins** cefazolin, cefepime, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, cefaclor, cefadroxil, cefalexin, cefixime, cefpodoxime, ceftibuten
- **Carbapenems** doripenem, ertapenem, imipenem, meropenem
- **Fluoroquinolones** ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin
- **Aminoglycosides** amikacin, gentamicin, netilmicin, tobramycin
- **Glycopeptides** vancomycin, teicoplanin
- **Macrolides** azithromycin, clarithromycin, erythromycin, roxithromycin, telithromycin, clindamycin, quinupristin-dalfoproistin
- **Tetracyclines** doxycycline, minocycline, tetracycline, tigecycline
- **Miscellaneous** chloramphenicol, colistin, daptomycin, fosfomycin, fusidicacid, linezolid, metronidazole, nitrofurantoin, rifampicin, spectinomycin, trimethoprim, trimethoprim-sulfamethoxazole

How to implement EUCAST breakpoints

- The national breakpoint committees have committed theselves to implementing EUCAST breakpoints –which means that any one using any of the European national systems will gradually adhere to the EUCAST breakpoint system.

- Breakpoints as presented in EUCAST tables can be directly applied to MIC distributions (local and national surveillance, EARSS, etc)

- Systems for automated susceptibility testing can be set up with EUCAST MIC breakpoints (currently being implemented).

- Through an agreement between EMEA, EUCAST and the pharmaceutical companies, new antimicrobials will be given breakpoints through EUCAST as part of the registration process. The SPC for these drugs will contain only EUCAST breakpoints.

- A disk diffusion method based on the Kirby-Bauer procedure but with zone diameter breakpoints calibrated to EUCAST MIC breakpoints has been developed.

EUCAST & EMEA

- Co-ordinated process between the Pharmaceutical Companies, EMEA (European Medicine Agency) and EUCAST.

- When a Company applies for registration of a new agent in Europe:
  - EMEA decides on indications
  - **EUCAST decides on breakpoints.**

- EUCAST breakpoints for new drugs are included **as the only breakpoints in the SPC** (Summary of Product Characteristics).

- The cooperation between EUCAST and EMEA will be continued and extended

EUCAST : latest news

- EUCAST has developed a European disk test with zone diameters which correlate to EUCAST clinical breakpoints. This was published in December 2009

BD initiatives

Update of past, present and future activities to include the EUCAST standard in the BD Phoenix™ and the BD EpiCenter™ system

BD initiatives

What does it take to be EUCAST ready ?

Drugs		Manufacturers should have all required drugs validated and available, in the correct formulation (eg : amox/clav).
Breakpoints		BP should be implemented in new panel designs and should be validated with trials.
Rules		Expert system should be updated with new rules and checked for conflicts or interpretation issues.
Wild Type - ECOFF		Lower concentrations and broader MIC ranges are needed to cover ECOFF. The system should include enough wells to handle this.

EUCAST and BD

2005

- Interest of BD in EUCAST dates back to 2005
- Contacts were established by the European ID/AST team with the Chairman of EUCAST (Gunnar Kahlmeter) and other Steering Committee members.

2006

- Active discussions engaged with BD in US to obtain necessary commitment and resources and develop a EUCAST standard (once available).

2007-2008

Prof. Kahlmeter agrees to evaluate BD Phoenix™ using EUCAST breakpoints:

- Specific panels designed and manufactured
- Evaluation started in January '08
- First data presented during ECCMID Apr'08
- Final results presented at customer event in Sweden (Sept '08)

2009-2010

- Two posters were presented at ECCMID 2009, Helsinki:

- EUCAST breakpoints in automated susceptibility testing of Gram-positive bacteria - BD Phoenix™ validated
  R. Smyth, S. Bengtsson, G. Kahlmeter, G. Babini, E. Montrucchio (Växjö, SE; Buccinasco, IT)
- EUCAST breakpoints in automated susceptibility testing of Gram-negative bacteria - BD Phoenix™ validated
  R. Smyth, S. Bengtsson, G. Kahlmeter, G. Babini, E. Montrucchio (Växjö, SE; Buccinasco, IT)

- Two evaluations were carried out in Italy (Prof. Rossolini, University of Siena) and Spain (Prof. Canton, Hospital Ramon y Cajal, Madrid).
  The results of these studies will be presented at ECCMID 2010, Vienna, posters: Abstract no. 1680, Abstract no 2590.
- The integration of EUCAST expert rules in the existing BD Xpert system was evaluated by Professor R. Leclerc (Caen University Hospital, France)

Evaluation of the BD Phoenix™ for antimicrobial susceptibility testing using EUCAST breakpoints

Gunnar Kahlmeter, Robert Smyth and Stina Bengtsson
Clinical Microbiology, Växjö, Sweden

In collaboration with BD with special thanks to
Gioia Babini, Scientific Affairs Manager ID/AST Europe and
Enrico Montrucchio, European Application and Scientific Manager

- The first evaluation of EUCAST breakpoints in an automated system.
- EUCAST breakpoints were customized by BD for Phoenix and panels containing relevant antibiotics and covering EUCAST breakpoints were specifically manufactured for this study.
- The work was performed in 2007/2008 in the Department of Clinical Microbiology, Växjö, Sweden.
- Two sets of microorganisms were used for the evaluation:

- **Set I:** 358 stored clinical isolates with various resistance mechanisms tested simultaneously with Phoenix (BD) and SRGA disk diffusion methodology, both with EUCAST breakpoints (Phoenix MIC breakpoints and SRGA zone diameter breakpoints calibrated to EUCAST breakpoints).

- **Set 2:** 139 consecutive clinical isolates of agreed species, tested as above.

- Discrepancies between PHX and DISK test results were resolved with MIC-determination against EUCAST clinical breakpoints, using Etest.

Clinical Isolates Tested

Species	No.	Characteristics
Staph.aureus (MSSA)	64	PCG, ERY, CLI, FUSA, FUSB, CIP/MOX, GEN
Staph.aureus (MRSA)	30	Various spa-types
Staph.lugdunensis	9	ERY, CLI, TET
Coagulase negative staphs	31	Various R´s
Streptococcus pneumoniae	43	PCG MICs 0.125 – 0.5; PCG, AMO-I, CTX-I, CLI, ERY
Streptococcus pyogenes	49	ERY, TEL, CLI, TET, LEV
Enterococcus faecalis	10	WT, vanA, vanB; GENTAMICIN LLR & HLR;
Enterococcus faecium	15	WT, vanA, vanB; AMP, IMI, NIT.
Pseudomonas aeruginosa	36	CIP, IMI, MER, GEN, PTZ
Enterobacteriaceae ESBL	30	**CTX-M types** (1, 9, 14, 15).
Escherichia coli		64CTX-I, CXM, CIP, TRI, TSU, GEN, PTZ-I
Enterobacter aerogenes	10	AMC, CPM-I, CXM
Enterobacter cloacae	12	AMC, AZT, CTX, CFZ, CXM, CIP, PTZ, TRI, TSU
Klebsiella pneumoniae	44	AMC, AZT, CTX, CFZ, CXM, CPM, CIP, GEN, TOB, TRI, TSU
Klebsiella oxytoca	12	AMC, AZT, CPM, CTX, CXM, GEN, TOB-I, PTZ, TRI, TSU
Proteus mirabilis	22	TRI, TSU
Morganella morganii	12	AMC, AZT, CTX, CFZ-I, CXM, CIP, TRI, TSU

Summary of CA Results

Organism group	CA @1st test(n)	CA @1st test(%)	Final CA(n)*	Final CA(%)*	total test
MRSA	354	98,3	358	99,4	360
MSSA	760	99,0	765	99,6	768
CNS	295	98,3	295	98,3	300
S. lugdunensis	90	100,0	90	100,0	90
S. pneumoniae	256	99,2	258	100,0	258
GAS	244	99,6	244	99,6	245
E. faecalis	116	100,0	116	100,0	116
E. faecium	76	100,0	76	100,0	76
total Gram-positive (a)	2191	99,0	2202	99,5	2213
P.aeruginosa	305	94,1	314	96,9	324
ESBL(b)	443	92,3	463	96,5	480
E coli	937	97,6	952	99,2	960
K. Pneumoniae	652	98,8	660	100,0	660
K. Oxytoca	176	97,8	180	100,0	180
P. mirabilis	321	97,3	328	99,4	330
M. morganii	176	97,8	179	99,4	180
E. cloacae	172	95,6	177	98,3	180
E. aerogenes	147	98,0	149	99,3	150
Total Gram-negative	3329	96,7	3402	98,8	3444
Overall	5520	97,6	5604	99,1	5657

* Final CA calculated after discrepancies were resolved either after re-test or by Etests.

Evaluation of the BD Phoenix™ for antimicrobial susceptibility testing using EUCAST breakpoints

Conclusions:

- EUCAST breakpoints (including tentative penicillin breakpoints) were introduced in Phoenix by the manufacturer.

- EUCAST breakpoints in Phoenix were evaluated by comparing SIR-categorisation by Phoenix and SRGA disk testing with MIC-determination to resolve discrepancies.

- Sixteen bacterial species with many resistance mechanisms were tested against 5 – 15 antimicrobials in 498 clinical isolates.

- Only few problems were identified during the evaluation:
  - the Phoenix inability to detect inducible clindamycin resistance,
  - a cefepime potency problem in the Pseudomonas panel.

BD initiatives

- **April 2008:** EUCAST releases most of the missing breakpoints and first version of EUCAST expert rules.

- **May 2008:** R&D team in US starts to develop a full EUCAST standard for BD Phoenix™ and BD EpiCenter™.

- **June 2008:** first set of EUCAST panels designed and agreed for the "first" EUCAST/Phoenix users (in Wales, U.K. and the Netherlands): panels available since Nov '08.

- **April 2009 - today:**

- Release of BD Phoenix™ full EUCAST standard (breakpoints, rules and Expert system).

- Panel design program : discussions with individual countries were carried out to understand the timeline of EUCAST implementation at national level. BD is now rolling out EUCAST-compliant panels across Europe in line with these national timelines.

Why is EUCAST an opportunity?

- EUCAST is a unique opportunity to harmonize and standardize the way of interpreting and reporting susceptibility testing results.

- EUCAST BP's and ECOFF settings are opening a new era in surveillance of emerging resistances:

- "Reference material for epidemiological cut-off values for antimicrobial resistance surveillance "

- Accurate determination of real MICs to track emerging resistances !!!!

- This will have a tremendous positive effect on international surveillance: finally there will be a chance to compare "apples with apples"!!!

Impact of different BPs on EARSS

Susceptibility results for E. coli isolates in United Kingdom (UK), Italy (IT), France (FR) and Germany (DE)

Antibiotic	Number			Total	Percentage		
	S	I	R	N	S	I	R
United Kingdom (UK) 3rd gen. ceph.	1651	5	172	1828	90.3	0.3	9.4
Italy (IT) 3rd gen. ceph.	830	6	107	943	88.0	0.6	11.43
France (FR) 3rd gen. ceph.	7253	122	195	7840	96.0	1.6	2.5
Germany (DE) 3rd gen. ceph.	893	6	75	974	91.7	0.6	7.7

3rd gen. ceph. = Cefotaxime or Ceftazidime or Ceftriaxone or Ceftizoxime

BPs in 2007 for ceftazidime:

UK(BSAC):	S < 1	I=2-8	R> 16
IT (CLSI) :	S < 8	I=16	R> 32
FR (CASFM):	S < 4	I=8-16	R> 32
DE: ??? DIN or CLSI?			
DIN:	S < 4	I=8-16	R> 32

Data adapted from 2007 EARSS database

BD is committed to continuously provide its customers with up-to-date solutions.

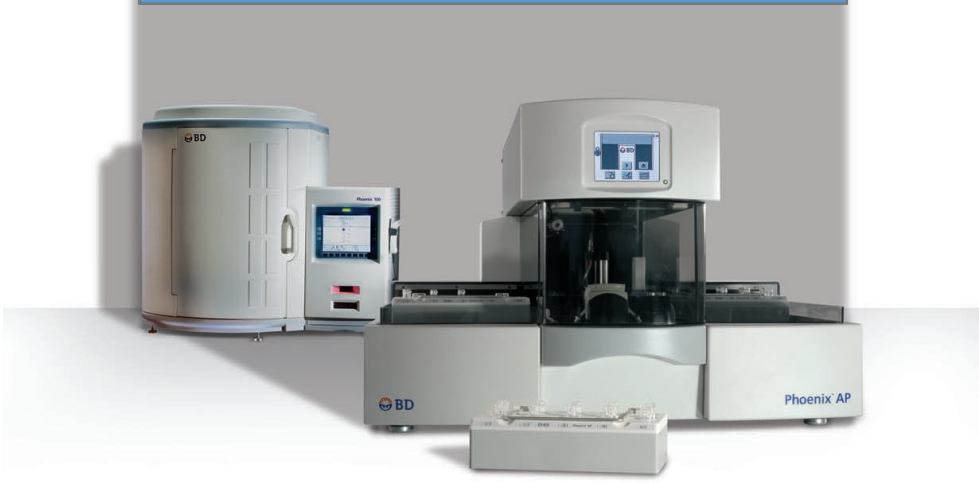
EUCAST is a reality in the Nordic countries, UK, France, Belgium and Germany.

We believe EUCAST will soon be adopted as The European Gold Standard.

BD Phoenix™ – BD EpiCenter™ system is EUCAST ready.

Win with the First Complete Offer

New BD Phoenix™ EUCAST compliant panels



BD

Helping all people
live healthy lives

BD Phoenix™ EUCAST compliant panels

BD is committed to continuously providing its customers with up to date solutions.
EUCAST is already a reality in the Nordic countries, UK and France, and we believe that EUCAST will soon be adopted as THE European Gold Standard.

We are proud to announce the availability of the first BD Phoenix™ EUCAST compliant panel set.

Phoenix Gram negative
Cat. No: 448103
Format: NMIC/ID-76

Phoenix Gram Negative		
code	**Antimicrobic**	**(µg/mL)**
AN	Amikacin	4 - 16
AXC	Amoxicillin/Clavulanate	2/2 - 8/2
AM	Ampicillin	2 - 8
ATM	Aztreonam	1 - 16
CZ	Cefazolin	1 - 4
CTX	Cefotaxime	0.5 - 4
CAZ	Ceftazidime	0.5 - 8
CXM	Cefuroxime	1 - 8
CN	Cephalexin	2 - 16
CIP	Ciprofloxacin	0.125 - 1
CL	Colistin	1 - 4
ETP	Ertapenem	0.25 - 1
ESR	ESBL	yes
FF	Fosfomycin	16 - 64
GM	Gentamicin	1 - 4
IPM	Imipenem	1 - 8
MEM	Meropenem	1 - 8
FM	Nitrofurantoin	16 - 64
TZP	Piperacillin/Tazobactam	4/4 - 16/4
NN	Tobramycin	1 - 4
TMP	Trimethoprim	1 - 4
SXT	Trimethoprim/ Sulfamethoxazole	1/19 - 4/76

Phoenix Gram positive
Cat. No: 448089
Format: PMIC/ID-67

Phoenix Gram Positive		
code	**Antimicrobic**	**(µg/mL)**
AXC	Amoxicillin/Clav.	2/2 - 8/2
AM	Ampicillin	2 - 8
NCF	Beta-lactamase	yes
FOX	Cefoxitin	2 - 8
CIP	Ciprofloxacin	0.5 - 2
CC	Clindamycin	0.25 - 1
DAP	Daptomycin	1 - 4
E	Erythromycin	0.25 - 2
FA	Fusidic Acid	0.5 - 8
GM	Gentamicin	1 - 4
GMS	Gentamicin-Synergy	500
LZD	Linezolid	0.5 - 4
MXF	Moxifloxacin	0.125 - 1
MUP	Mupirocin	1 - 4
MUH	Mupirocin - High Level	256
FM	Nitrofurantoin	16 - 64
OX	Oxacillin	0.25 - 2
P	Penicillin	0.0625 - 0.25
RA	Rifampin	0.25 - 1
TEC	Teicoplanin	1 - 8
TE	Tetracycline	0.5 - 2
NN	Tobramycin	1 - 4
TMP	Trimethoprim	1 - 4
SXT	Trimethoprim/ Sulfamethoxazole	1 /19 - 4/76
VA	Vancomycin	0.5 - 8

Notes

BD European Marketing Team
Feb. 2010

BD Diagnostics
Tullastrasse 8-12
D-69126 Heidelberg
Germany
Tel. +49-6221 305 0

www.bd.com