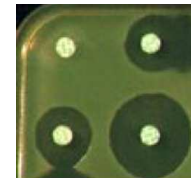
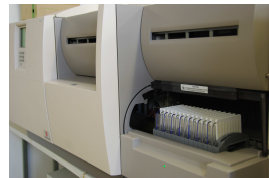


# IMPLEMENTATION OF EUCAST BREAKPOINTS

***BELGIAN /GDL COUNTDOWN  
UNTIL 1ST JANUARY 2010 :  
64 DAYS***

**Pierrette Melin, CHU of Liege**

**Coordinator of the SBIMC-BVIKM/EUCAST microbiology  
working party**



- **Introduction**
- **Vitek systems**
  - **Update of systems**
  - **New AST Cards**
- **From EUCAST**
  - **Last news**
  - **Interpretative criteria for disk diffusion**
- **Implementing EUCAST : Memo of things to do**

## **Introduction**

Vitek Systems  
From EUCAST  
Implementing EUCAST

# **Generation of AST results**

**One of the most important functions of  
microbiology laboratories**

**Directly affect therapy chosen for treatment of  
patients**

**Critical to be confident in AST procedures**

**To provide accurate and reliable results**

## Introduction

Vitek Systems  
From EUCAST  
Implementing EUCAST

# Evolution of antimicrobial breakpoints : a need

- **Evolving therapeutic indications and practices**
- **New resistance mechanisms**
- **Changing dosages**
- **New pharmacokinetic-pharmacodynamic knowledge**
- **Clinical outcome data**
- **MIC distribution for wild-type populations**

**EUCAST interpretative criteria:  
the European answer to implement**

## **Introduction**

Vitek Systems  
From EUCAST  
Implementing EUCAST

# **Evolution of antimicrobial breakpoints : a need**

**Conclusion of the Symposium of the  
SBIMC-BVIKM the 26<sup>th</sup> of May 2008**

**Implementation of EUCAST interpretative  
criteria for AST  
the 1<sup>st</sup> January 2010  
in all Belgian labs**

## Introduction

Vitek Systems  
From EUCAST  
Implementing EUCAST

# Switch to EUCAST interpretative criteria

- **Convincing arguments**
- **Identification of technical limiting factors**
- **Role of SBIMC-BVIKM**
  - **EUCAST working groups**
- **Conditional deadlines**
  - **EUCAST breakpoints for disk diffusion**
    - **!!! Still used routinely in many laboratories !!!**
  - **Diagnostic companies and AST devices**

**Introduction**

Vitek Systems  
From EUCAST  
Implementing EUCAST

# Switch to EUCAST breakpoints : painful ?

## AST Products Manufacturers



**Technologist**



**Infectious disease physician**



**Lab computer Team**



**Pharmacist**

## **Introduction**

Vitek Systems  
From EUCAST  
Implementing EUCAST

# **Switch to EUCAST breakpoints : painful ?**

- **Update of a multitude of documents**
- **Update of automated systems and LIS**
- **Update and development by manufacturers of AST devices**
- **To update education of clinicians, of students, and laboratory personnel**
- **Rates of antimicrobial resistance in surveillance programs affected**
- **Impact for pharmacy**



- **Update of software**
  - **Interpretative criteria**
  - **Expert rules**
  
  - **bioMérieux's task**
  - **AIX / PC computer (Windows version)**
  - **Status: ongoing during last trimester 2009**
  
- **Facultative update of hardware**
  - **PC Windows version**

# New Vitek AST Cards

## EUCAST: new breakpoints

**Need for new ranges of concentrations of antimicrobial agents**

**= new validation and manufacturing**

**= opportunity to revised contents of AST Cards**

### ■ **Guide for new proposals of AST card contents**

- **Basic recommended agents/ group of bacteria**
- **Number of wells /agent**
- **Limited number of wells /card**
- **Agents needed for AES**
- **New expected and clinically useful agents**
- **Identification of less useful agents (*not available in Belgium i.e.*)**

# New Vitek AST-GN Cards

## ■ New “N045”

- Ampicillin
- Amoxicillin/clav.acid
- **Cefoxitin**
- Cefuroxime
- Ceftazidime
- Cefotaxime
- Cefepime
- ESBL confirm
- Temocillin
- Piperacilline/tazobactam
- **Imipenem**
- Meropenem
- Ciprofloxacin
- Norfloxacin
- Amikacin
- Gentamicin
- Nitrofurantoin
- **Tobramycin**
- **Tigecycline**
- Trimethoprim /sulfa
- **Fosfomycin-??**

# New Vitek AST-GN Cards

## ■ New “N046”

- Ampicillin
- Amoxicillin/clav.acid
- **Cefazolin**
- **Cefoxitin**
- Cefuroxime
- Ceftazidime
- Cefotaxime
- Cefepime
- **Aztreonam**
- ESBL confirm
- Temocillin
- Piperacilline/tazobactam
- Meropenem
- Nalidixic acid
- Ciprofloxacin
- Levofloxacin
- Norfloxacin
- Amikacin
- Gentamicin
- Nitrofurantoin
- **Tobramycin**
- **Tigecycline**
- Trimethoprim /sulfa

# New Vitek AST-GN Cards

## ■ New “N022”

- Ceftazidime
- Cefepime
- ~~Cefpirome~~
- Aztreonam
- Piperacilline
- Piperacilline/tazobactam
- Ticarcillin
- Ticarcillin/clav.acid
- Doripenem
- Imipenem
- Meropenem
- Ciprofloxacin
- Levofloxacin
- ~~Pefloxacin~~
- Amikacin
- Gentamicin
- ~~Isepamicin~~
- Netilmicin
- Tobramycin
- Trimethoprim /sulfa
- Colistin

# New Vitek AST-GP Cards

## ■ New “P549”

- Benzylpenicillin
- Cefoxitin screen
- Oxacillin
- Erythromycin
- Clindamycin
- Inducible clindamycin R
- ~~Ciprofloxacin~~
- Moxifloxacin
- Levofloxacin
- ~~Norfloxacin~~
- Teicoplanin
- Vancomycin
- Gentamicin
- Kanamycin
- Tobramycin
- Nitrofurantoin
- Linezolid
- ~~Fosfomycine~~
- Fusidic acid
- Minocycline
- ~~Tetracycline~~
- Tigecycline
- Trimethoprim /sulfa
- Mupirocin
- ~~Quinupristine/dalfo-~~
- Rifampicin

# **EUCAST Disk Testing**

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

- **Documents address**
  - **Preparation of agar plates**
  - **Testing conditions**
    - **Inoculum preparation/standardization**
    - **Incubation time**
    - **Incubation T°**
  - **Interpretation of results**
  - **QC procedures**

# EUCAST Disk Testing

**For end november – starting December 2009,  
EUCAST own criteria  
to match its clinical breakpoints**

**Development and validation of EUCAST disk  
testing criteria**

- **for non-fastidious organisms**
  - **Possibility to use CLSI regression analysis**
    - **For some drug/bug combinations**
- **for *S.pneumoniae*, *H.influenzae* and other fastidious organisms**
  - **New medium, everything to be done from beginning**



# EUCAST Disk Testing

**European disk test derived from the Kirby-Bauer method (1966), based on two media:**

- **Mueller Hinton agar for non-fastidious organisms including enterococci**
- **MH + 5% Horse blood + 20 mg/L  $\beta$ -NAD (MH-F) for *S.pneumoniae*, *Haemophilus spp* and other fastidious organisms (+ana)**

# EUCAST Disk Testing

**Inoculum < overnight colonies in saline to a suspension of Mc Farland 0.5 for all organisms**

- **Mueller Hinton agar**
  - 18h +/- 2 h within 15 minutes from application of disks
  - In air
- **MH + 5% Horse blood + 20 mg/L  $\beta$ -NAD (MH-F)**
  - 18h +/- 2 h within 15 minutes from application of disks
  - 4-6 % CO<sub>2</sub> in air
- **Commercially prepared plates or home made**

# EUCAST Disk Testing

- **Reading**
  - **Even and confluent lawn of growth**
  - **Zone diameter**
    - **Zone edges read as point showing no obvious growth (unaided – naked eye)**
- **Recommended strains for internal QC (tables available)**
  - ***E.coli* ATCC 25922**
  - ***P.aeruginosa* ATCC 27853**
  - ***S.aureus* ATCC 29213 (*β-lactamase producing strain-weak*)**
  - ***E.faecalis* ATCC 29212**
  - ***H.influenzae* NCTC 8468 (*susceptible to β-lactam antibiotics* )**
  - ***S.pneumoniae* ATCC 49619**

# EUCAST Disk Testing

- **Disk concentrations**
  - Most are the same as for CLSI, except:

<u>Agent</u>	<u>EUCAST</u>	<u>CLSI</u>	<u>.</u>
Benzympenicillin	1U	10 U	
Ampicillin BGN	10 µg	10 µg	
Ampicillin S.pn.	2 µg	10 µg	
Cefotaxime	5 µg	30 µg	
Ceftazidime	10 µg	30 µg	
Ppiperacilline/tazob.		30/6 µg	100/10 µg
Vancomycin	5 µg	30 µg	
Linezolid	10 µg	30 µg	
Nitrofurantoin	100 µg	300 µg	

# Lab check-list for Preparing implementation of EUCAST

## From today to end of December

- **To update a multitude of documents**
  - List of reagents
  - SOP for Disk diffusion testing
  - Practical bench documents with interpretative criteria
  - Statistical analysis of R profile
  - QC documents and SOP
- **To update AST automated systems**
  - Software/ Hardware
  - Done, ongoing or to schedule
- **To update LIS if necessary**
- **To educate Lab team**

# Lab check-list for preparing implementation of EUCAST

- **From today**
  - **Choice of a manufacturer/provider accordingly to AQ procedures for**
    - **Disks**
    - **MH and MH-F Agars**
- **December**
  - **To prepare and renew stock of new disks and new AST panels manufactured according to EUCAST concentrations**
- **From today and January**
  - **To discontinue purchase and to discard unused obsolete disks and AST-panel**

# Lab check-list for preparing implementation of EUCAST

- **November – December as soon as disks, MH-F and new panels available**
  - **To perform QC procedures according to QA program**
    - Verification
    - Validation
- **Verification of new panels: evaluation of AST**
  - **Using organisms similar to those commonly isolated and representing local R phenotypes**
    - i.e. MRSA, Clindamycin inducible R SA and CNS, VRE, ...
    - i.e. ESBL-*enterobacteriaceae*, AmpC *enterobacteriaceae*, MDR *P.aeruginosa* and *Acinetobacter* sp
    - At least 30 isolates /antibiotic-panel/card

# Lab check-list for preparing implementation of EUCAST

- **Verification of new panels: Precision (reproducibility)**
  - **i.e. 5 isolates in triplicate for 3-5 days**
    - **Isolates with R phenotypes well known as QC strains**
    - **MIC  $\pm$  twofold dilution agreement**
    - **Categorical agreement**
    - **Acceptable: should be >95%**
    - **If necessary, use a reference method to arbitrate discrepancies**



# Lab check-list for preparing implementation of EUCAST

- **To prepare QC validation**
  - **Cf. QC tables**
    - **Zone diameter QC limits**
      - **Single drug/single organism combination**
  - **For commercial AST systems**
    - **For all QC procedures, to follow manufacturer's recommendations**

# Lab check-list for preparing implementation of EUCAST

- **For new disk testing and for new QC Strains**
  - on MH and MH-F agars
- **For Etests testing**
  - on MH-F agar
- **Batch or lot QC**
  - To test with appropriate QC strains
    - Zone diameters within expected ranges or not: accepted or rejected
- **Frequency of QC testing**
  - Daily / Weekly testing
  - Classical algorithm

# SBIMC-BVIKM check-list for preparing implementation of EUCAST

- **5<sup>th</sup> November**
  - **Meeting with all AST device manufacturers**
    - **Aim of the meeting, to see**
      - how far they are in their preparations
      - how the labs they are working with are responding
      - what difficulties they are encountering
      - what help could possibly the working group give them
- **Summary presented at SBIMC-BVIKM symposium the 12th of November**

# IMPLEMENTATION OF EUCAST BREAKPOINTS

***BELGIAN /GDL COUNTDOWN  
UNTIL 1ST JANUARY 2010 :  
64 DAYS***

**A short time but it should be enough !  
All the limiting factors are fading one by one**