

Société belge d'infectiologie et de microbiologie clinique

Belgische vereniging voor infectiologie en klinische microbiologie

30th Symposium : What will change in your daily practice with the new
Elwijt, 26-05-2008 EUCAST breakpoints for antibiotic susceptibility testing

INTRODUCTION OF NEW BREAKPOINTS IN THE LABS: CHALLENGES AND SOLUTIONS

Pierrette Melin, CHU of Liege

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



- **Introduction**
- **Implementation of new interpretative criteria for AST**
- **AST methods and switch to different interpretative criteria**
- **AST and role of SBIMC-BVIKM**
- **AST in Belgium**
- **Level of preparation for a switch to EUCAST breakpoints**
- **Summary**

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**

Achievement of harmonization of antimicrobial breakpoints in Europe and in Belgium ?

Implementation of the EUCAST breakpoints To be successful

- **National antimicrobial susceptibility committees**
 - BSAC, CA-SFM, CRG, DIN, NWGA, SRGA, Poland, Italy
 - None in Belgium
 - Role of the SBIMC-BVIKM
- **Manufacturers of AST devices**
- **Microbiologists**

Switch to EUCAST breakpoints : painful ?

- **Multitude of documents**
 - To be amended
 - To be distributed
 - To be implemented by
 - Authorities, manufacturers and laboratories
- **To be modified by manufacturers of AST devices**
 - Media, dilutions, algorithms, package inserts, interpretative criteria in software of automated systems, expert rules

Switch to EUCAST breakpoints : painful ?

- **To be modified in/by laboratories**
 - Update of automated systems (sometimes expensive?)
 - Laboratory manuals and SOPs
 - Laboratory computer systems
- **To update education of clinicians, of students, and laboratory personnel**
- **Rates of antimicrobial resistance in surveillance programs affected**

AST methods & systems

Reference norms

- **MIC determinations**
 - Broth dilution
 - Agar dilution
 - Automated systems
 - Vitek 2, Phoenix, etc
 - Etest (Abbiotisk), MIC Evaluator (Oxoid)
- **Disk (or tablet) diffusion**
- **ATB expression** (breakpoints panels)

Interpretative criteria for categorization SIR

MIC and diameters

CLSI (formely NCCLS) + other European sets of breakpoints

Switch to EUCAST breakpoints: Limiting factors

For MIC determination

- **Adaptation of automated systems**
 - **Composition of panels and concentrations of antimicrobial agent per well.**
 - Validation, manufacturing, stock and distribution
 - **Update of software (interpretative criteria)**
 - Each system ready for the target date
 - **Update of expert software (expert rules)**
 - Each system ready for the target date

Switch to EUCAST breakpoints: Limiting factors

For ATB expression

- **Composition of panels and concentrations of antimicrobial agent per well to be adapted.**
 - Validation, manufacturing, stock and distribution

For Disk (tablet) Diffusion

- **Availability of interpretative criteria**
 - **« Currently » no EUCAST breakpoints !!**
 - Breakpoints to be defined by EUCAST in collaboration with laboratories from different countries

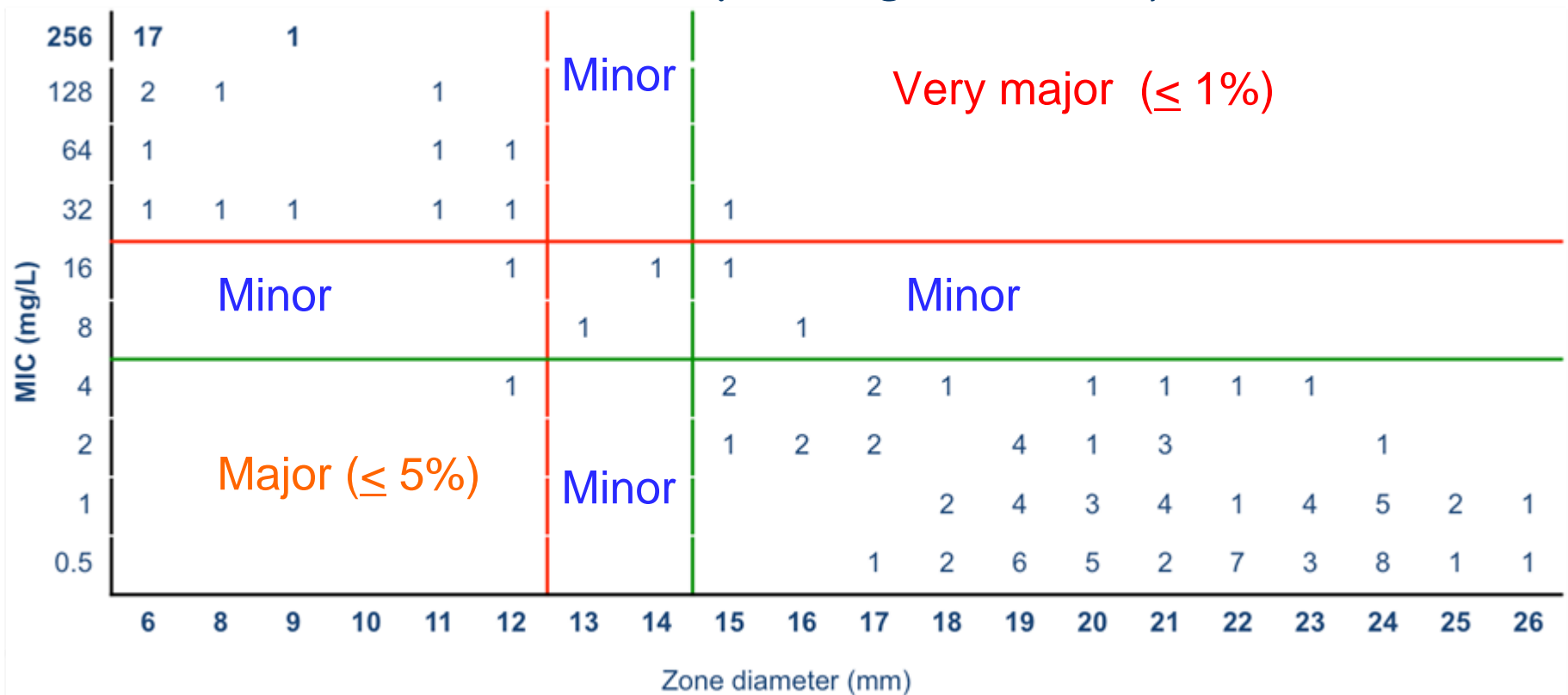
Switch to EUCAST breakpoints: Limiting factors

To define breakpoints for disk diffusion

- To construct scattergrams of zone diameters vs MICs of closely related species by species
- To fit regression lines
 - Different methods
 - None is perfect, no consensus
- Medium- and inoculum size-dependant
 - Different SOPs // Commitees
 - Harmonization ??
 - Inoculum 0.5 McF, MH agar ? Or ?

Switch to EUCAST breakpoints: Limiting factors

To define breakpoints for disk diffusion (/charge of an atb in define operating conditions)



« Scattergram of MICs versus zone diameters

Initiative of the SBIMC-BVKM

- **Implementation of the EUCAST antimicrobial breakpoints**
 - **To achieve success: Key role of the national antimicrobial susceptibility committees**

To be successful in Belgium

To smooth over the switch

To convince and help all labs to switch to EUCAST breakpoints

Initiative of the SBMIC-BVIKM to fulfill some missions entrusted to antimicrobial susceptibility committees

The « EUCAST working group »

- Initiative supported by ISP-WIV
- Coordinator
 - Johan van Eldere (KUL)
- First meeting of an invited panel in September 2007

Appointment of two working parties

① Microbiological aspects

② Clinical aspects

- Links between groups, SBIMC-BVIKM, EUCAST and others
- Invitation to participate in one of these groups sent to all members (October 2007)

Microbiology working group

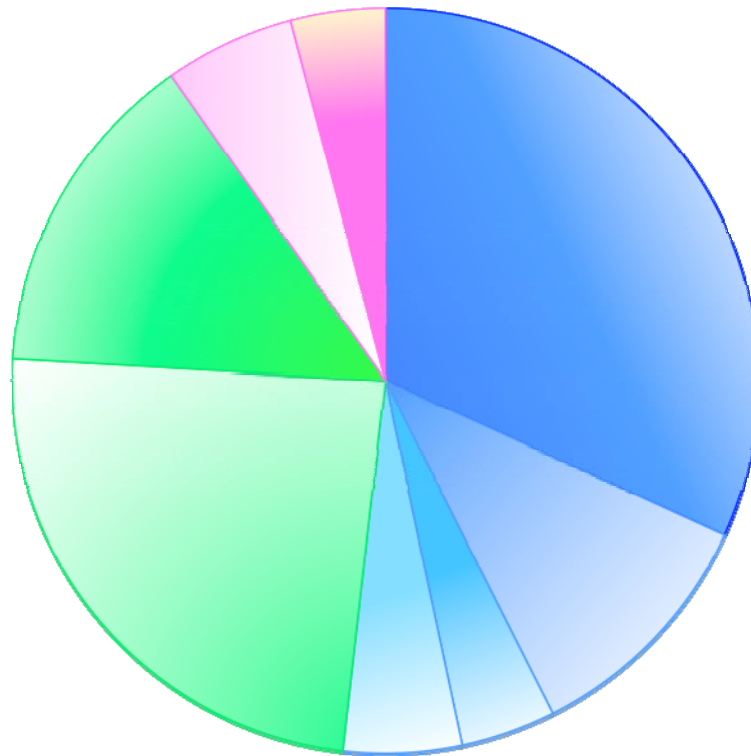
- **Coordinators**
 - Pierrette Melin (Ulg) & Jan Verhaegen (KUL), Belgian representative at the EUCAST general committee
- **+/- 20 members**
- **First decisions**
 - **Convincing arguments pro-switching to EUCAST**
 - **Switch made in ALL labs at the SAME TIME**
 - **The best date: a 1st of January (2009 or 2010)**

Microbiology working group

- **Tasks**
 - **To liaise with AST devices manufacturers**
 - Safeguarding of deadlines:
 - update of systems, available stocks of updated items, update of kit inserts, update of expert systems, etc
 - **To monitor the switch to EUCAST breakpoints**
 - Preparation of technical documents, validation
 - **To prepare information and communication strategy towards microbiology labs**
 - Symposia, LOK's GLEM's, slide-sets, Information on SBIMC-BVIKM website, papers in journals, EQC of IPH, etc

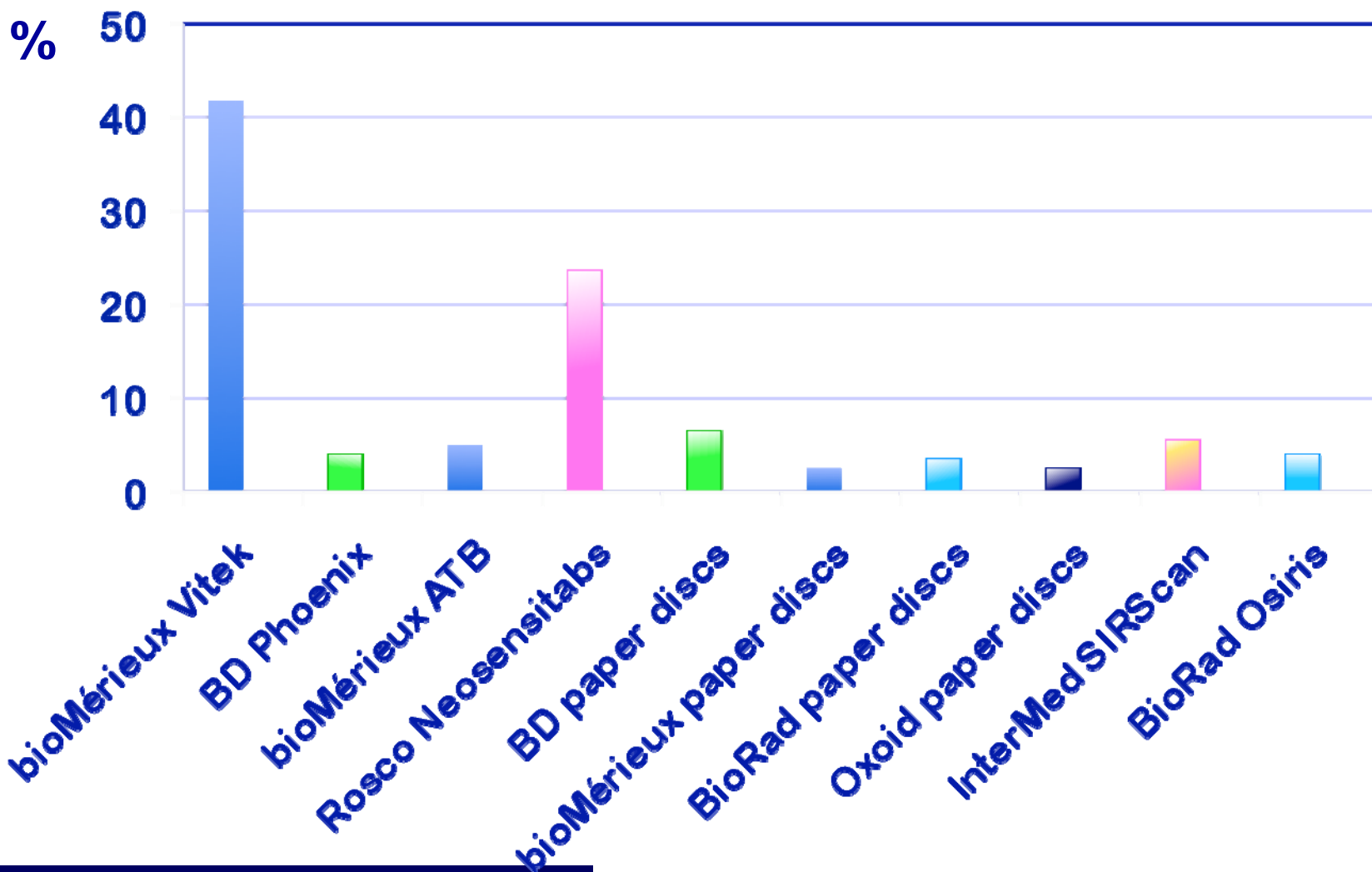
Inventory of AST methods & systems in Belgian laboratories

Distribution of AST methods in Belgian laboratories (EQC 01.2008)



- Vitek2
 - Vitek2 Compact
 - Phoenix
 - ATB Expression
 - Neosensitabs
 - Paper disks
 - SIRScan
 - Osiris
- + Etests (Abbiotest)

Distribution of Diagnostics firms in Belgium



Diagnostic manufacturers: Inventory of the levels of preparation

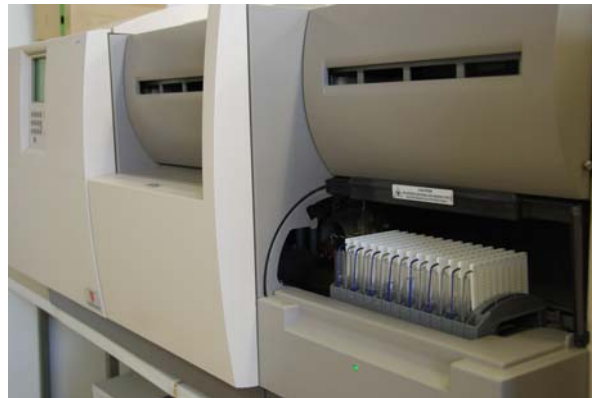
- **What needs to be done to comply with EUCAST breakpoints, wild type distributions, and expert rules**
- **Belgium will not be the first to switch**
 - **What has been already analysed, performed and validated?**
- **Progress status**
- **Remaining deadlines**
- **Contact person**

bioMérieux

Level of preparation



Vitek 2 & Vitek 2 Compact



MiniApi - ATB expression

Paper Discs (< BD)



Vitek 2 & Vitek 2 Compact

- **EUCAST implementation team (2006)**
 - **R&D, global marketing, ...**
 - **To assess what needs to be done to update**
 - **Instrument software (Vitek 2 and Vitek 2 Compact)**
 - **AST cards**
 - **Antimicrobial expert systems and software fonctionnality**

Level of preparation

- **Agreement data using EUCAST breakpoints for**
 - Aminoglycosides, fluoroquinolones, cephalosporins, monobactams & carbapenems, glycylicyclines, oxazolidinones, glycopeptides and lipopeptides :
 - Overall performance was very good
 - Few couples of drug/bacteria need further analysis
 - Tigecyclines/*Enterobacter/Serratia*
 - Meropenem/*Acinetobacter*
 - Etc
 - For macrolides, penicillins and miscellaneous (*recently launched by EUCAST*) and for EUCAST experts rules (*recently finalized*)
 - Agreement and impact on Vitek and AES to be analyzed

Complete EUCAST implementation on VT2

Goal is in mid-2009

■ EUCAST implementation team

■ Composition of new AST-Cards

- European cards: ready
- Belgian cards: to be decided
- If antimicrobial agents without EUCAST criteria still on new cards, maintenance of CLSI criteria

■ Software

■ Update ready for implementation in customers' systems \geq May 2009

- Feasible (easiest) with equipment associated to PC Systems rather than AIX Systems (eg, CC4)
- Transition proposal: Patch CLSI/EUCAST
- In 2009, replacement of AIX systems by PC systems

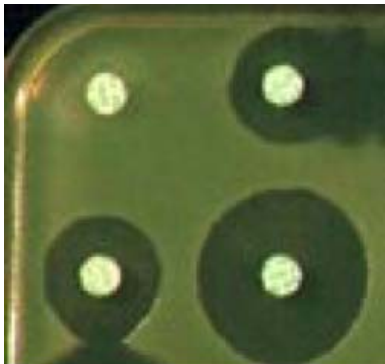
ATB Expression, mini API

- **ATB EUCAST project (2007)**
 - Initialization of update
 - New development to be compliant with EUCAST
 - To implement new ATB EUCAST strips in all European countries
 - **Verification of performances in progress**
 - Complete verification
 - ATB strip MIC production
 - Different strips manufactured and checked
 - Performances: analysis in progress

Becton Dickinson Level of preparation



Phoenix



Paper discs

Becton Dickinson

Level of preparation

- **Contact and discussion with EUCAST Committee**

Phoenix

- **Validation and verification of new AST-panels to comply with EUCAST criteria**
 - Antimicrobial agents and range of concentrations
- **Users' meeting already held**
 - Belgian proposal for new EUCAST panels
 - Between decision, manufacturing and distribution:
+/- 6 months

No defined deadline to be fully prepared for the switch
Should be ready by end of 2008

Becton Dickinson

Level of preparation

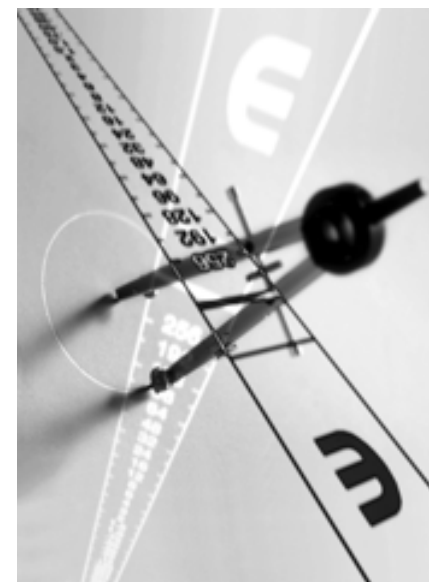
Paper disks

- **Currently, the validation of disks:**
 - For a define charge and a specific procedure
 - Expected ranges of inhibition zone diameters for reference strains
- **Waiting for EUCAST breakpoints for disk diffusion method to progress with the validation process**

No deadline as long as no EUCAST breakpoints for disk diffusion method

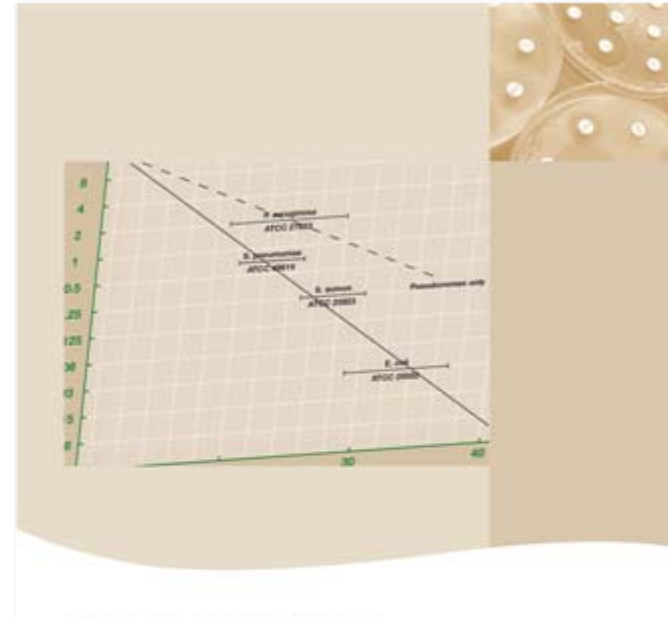
Etests

- **Determination of MICs**



- **To update product packages inserts with EUCAST interpretative criteria**

ROSCO – International Medical Level of preparation



Regression Lines
CLSI potency
Neo-Sensitabs®

Rosco Diagnostica A/S
2008

For presentation purpose only

ROSCO
DIAGNOSTICA

ROSCO – International Medical Level of preparation

Neosensitabs

- **Collaboration with EUCAST Committee (since 2006)**
- **Availability of regression lines for different procedures**
 - **Muller Hinton; Iso-Sensitest**
 - **Inoculum 0.5 Mc Farland or inoculum for semi-confluent growth**
 - **Validated for most antimicrobial agents**
 - **Could be validated for recent released breakpoints : penicillins, macrolides and miscellaneous within a trimester.**
- **To update NeoSensitabs users guide**
 - **Online version, easy to update**

Could be ready before end 2008

ROSCO – International Medical Level of preparation

SIRScan (i2A)

- **Rosco Sensitabs**
- **Antimicrobial Expert Systems**
 - **For French users/ CA-SFM**
 - **Already updated with available EUCAST breakpoints and expert rules**
 - **For complete update**
 - **Before end-2008**

Could be ready before end-2008 .

Paper disks

- **No official action to implement EUCAST breakpoints**
- **No regression lines available**
- **To adapt charges of disk when published:**
 - **No problem**
 - **Waiting for EUCAST breakpoints for disk diffusion method to go on with a validation process**

MIC Evaluators

- **To update product packages inserts with EUCAST interpretative criteria**

Paper disks

- **No regression lines available**
- **Waiting for EUCAST breakpoints for disk diffusion method to go on with a validation process**

OSIRIS

No deadline as long as no EUCAST breakpoints for disk diffusion method.



Summary of Actions and Expected Deadlines

	≤ 2007	2008 Semester I	2008 Semester II	2009 Semester I	2009 Semester II	2010
Vitek 2 bM	WG Since 2006	New panels validation	Validation ongoing	Update of all systems	Ready	
Phoenix BD		New panels validation	Ready			
Paper disk BD	/	/	?	?	?	?
Paper disk BR	/	/	?	?	?	?
Paper disk Ox	/	/	?	?	?	?
NeoSensitabs tablets	WG since 2006	Validation 0.5McF/MH	Ready			
SIR Scan		Partial update CA-SFM				
Osiris BR			?	?	?	?
ATB expression	WG Since 2007	New panels validation	Ready			
Etest & MIC evaluator	Ready // EUCAST breakpoints availability					

No deadline for 18 % of currently used method

Summary

Summary

- **Arguments for switching to EUCAST interpretative criteria**
- **Technical limiting factors**
- **Expected role of antimicrobial testing committees & role of SBIMC-BVIKM**
- **Different kinds of updates**
 - **Diagnostic Companies and AST devices**
 - **Automated systems : ready by end-2008 to mid-2009**
 - **ATB expression : ready by end-2008 or mid-2009**
 - **Neosensitabs diffusion : ready by end-2008**
 - **Disk diffusion : No deadline as long as no EUCAST breakpoints criteria for this method**

Summary

- **SBIMC-BVIKM microbiology working group**
 - **Tasks to continue or to initiate**
 - **Contact with diagnostic firms to assure respect of deadlines**
 - **To set a communication strategy towards all microbiology labs**
 - **To liaise Belgium with EUCAST Committee**
 - **And perhaps to collaborate with EUCAST for the establishment of the expected EUCAST criteria for disk diffusion method**