IDENTIFYING RESISTANCE™

International Newsletter
n° 8 • January 2009

BIOMÉRIEUX

Since 2001, with the help of many respected experts we have published the International Identifying Resistance Newsletter to ensure our readers receive the latest news on bacterial resistance as well as offering practical solutions to ever increasing resistance detection issues.

From this edition onward, we will be combining the experience and know-how of bioMérieux with the knowledge gained through the acquisition of AB BIODISK to provide essential information and solutions regarding this complex topic of bacterial resistance.

In this issue with Tim Walsh, we examine the escalation of antimicrobial resistance mechanisms, the rapidly changing epidemiology of resistance in different parts of the world, treatment constraints due to resistance combined with a limited antibiotic development pipeline, and ultimately the clinical threat posed to patients. Although *P. aeruginosa*, *A. baumanii*, *S. maltophilia* and *Burkholderia* spp. are significant nosocomial pathogens associated with life threatening infections, treatment of high-risk immunocompromised patients is still largely guided only by S-I-R results. The importance of on-scale MIC testing to help target individual therapy in these highly variable and non-standardized patients is increasingly apparent.

Gunnar Kahlmeter, Chairman of EUCAST, helps us gain an insight into the important work the EUCAST committee is doing to harmonize European breakpoints which are so essential in MIC testing.

We hope you enjoy this issue.

Dr. Marie-Françoise Gros
Executive Director, Medical Affairs & Communications
bioMérieux

State-of-the-Art

The Gram-negative Threat
Patients at Risk?

Tim Walsh, PhD.,
Professor of Medical Microbiology,
Antibiotic Resistance School of Medicine,
Department of Medical Microbiology,
Cardiff University, UK.

Background

Whilst MRSA continue to capture journalistic headlines, there is an increasing awareness and foreboding amongst the medical fraternity **that antibiotic resistance in Gram-negative aerobic bacteria has equaled, if not surpassed that of Gram-positive aerobic bacteria**. This notion is now supported by indisputable and compelling epidemiologic evidence. So **why has resistance occurred so quickly in Gram-negative bacteria?** Although our understanding may still be lacking, we can speculate the following:

a) complexity of bacterial genetics,
b) rapid increase in human travel,
c) overuse and "misuse" of antibiotics,
d) lack of targeted therapy in high-risk patient groups.

These factors and other circumstances, yet to be identified, may have contributed to the present situation, which is worrying, if not threatening.

The Gram-negative Threat
Patients at Risk?

FIG 1: MDR *P. aeruginosa* - susceptible to colistin only

Drug development programs have regrettably "evaded" the multi-drug resistant (MDR) Gram-negative non-fermenters (GNNF) such as *Pseudomonas aeruginosa* (Figure 1), *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*. Indeed, **most new antibiotics are directed at solely Gram-positive bacteria**, and in particular MRSA. Consequently, **a clinical void has emerged** with potentially devastating repercussions, especially for high risk patient populations. **This situation has revived the need for old drugs** such as colistin and also highlights the necessity to optimise the selection and dosing of current antibiotics. **The need for accurate resistance detection and quantitative susceptibility testing (MIC) to target individual patient therapy is self-evident, more than ever.**

Epidemiology of Resistance - Tip of the IceBerg?

Although the epidemiology of Gram-negative resistance varies from country to country, higher resistance rates are generally found in Southern and Central Europe, the Middle East and Africa, South America and Asia Pacific. The sporadic data now emerging from India, China and North Africa suggest alarmingly high rates of resistance in these regions. **Until defined surveillances are systematically conducted using accurate MIC testing methods, the true level of resistance in many parts of the world will not be fully known.**

Paul *et al.* [1] recently correlated antibiotic consumption with levels of resistance and showed that resistance increased in *Acinetobacter* spp. when blood stream infections were treated with a particular drug, and that the increase would often be preceded by a lag phase of a few months – depending on the antibiotic. There is little doubt that **once resistance is established, the use of an antibiotic merely selects for proliferation of the resistant phenotypes.** However, the spontaneous event whereby an individual bacterium becomes resistant to an antibiotic is fortuitous and not necessarily dependent on the presence of the drug. The exception to spontaneous mutations is resistance selected by quinolones and fluoroquinolones, compounds that can alter the DNA topology of the bacterium and render the cell genome more receptive to new DNA, and/or to promote gene movement [2].

Clinical Areas of Concern

Patients most at risk for severe and life threatening infections caused by MDR Gram-negative bacteria are those with compromised immune systems e.g. bone marrow transplants, immunologic disorders and patients in intensive care units (ICUs). These patients often have **central venous catheters** and are subjected to invasive procedures that provide access to endogenous and exogenous flora. Moreover, the colonising and/or invasive nosocomial Gram-negative bacteria in the ICU often comprise a MDR phenotype making prudent antibiotic management a necessity. ICU case studies reported by Mohr *et al.* [3] have shown that empiric regimens are often inappropriate and inadequate, and that **on-scale MIC results used in pharmacodynamic/pharmacokinetic (PD/PK) models can help target the drug choice, dose and dosing regimen to help optimise clinical outcome** (Table 1).

Table 1: Key findings from an ICU Case Study (Mohr *et al* 2004)

PARAMETER	ICU patients (N)	ICU patients (%)
Empiric therapy		
- did not achieve PD goals:	16/19	84
- inappropriate (isolate non-susceptible)	8/16	50
- inadequate (isolate at the S breakpoint)	6/8	75
Targeted therapy		
- achieved PD goals:	18/19	95
- monotherapy given	8/19	42
- combination therapy given	11/19	58
Clinical cure	17/19	89

PD – pharmacodynamic targets

Many national ICU resistance surveys show a steady increase in resistance levels to many classes of antibiotics. The study by Rhomberg *et al.* and Makedou *et al.* [4, 5] showed moderate increases in resistance rates in ICUs in North America whereas resistance levels were alarmingly high in countries such as Greece. Currently, epidemiologic data is limited from the emerging economic superpowers – **China and India, where resistance may potentially be a "sleeping giant"**. Given the expected explosion in trade and human travel to and from these countries in the next decade, well defined surveillances are needed to provide an important bench-mark of resistance, not least, ICU resistance. Countless studies have reported how travelers have returned home from abroad with infections caused by MDR GNNF bacteria not representative of their country of origin.

New Antibiotics?

The salutary article by Rice [6] reviews the current status of drug development with respect to new anti-GNNF antibiotics, and one is left with the overwhelming impression that all is not well! The new antibiotic arsenal for Gram-positive pathogens that now consists of dalfopristin/quinupristin, linezolid, daptomycin and tigecycline, may soon include dalbavancin, televancin, ceftobiprole and pleuromutilin. Of these, only tigecycline has activity against MDR *Acinetobacter* spp., and none are active against *Pseudomonas* spp.

The early antibiotic pipeline is looking equally lamentable [7] – few of the newer derivatives of fluoroquinolones (e.g. garenoxacin), carbapenems (e.g. doripenem, faropenem), and trimethoprim (e.g. iclaprim), exhibit significant anti-GNNF activity, and none appear to offer significant advantages over parent compounds. Accordingly, **attention is now directed towards novel entities such as antimicrobial peptides**. Whilst the Lipinski criteria [8] still dictates traditional antibiotic development, the article by Projan [9] "small molecules for small minds" offers a refreshing mode of thinking.

The question now being asked is "How did we get here?". The rapid emergence, escalation and spread of ESBL, metallo-ß-lactamase (MBL), serine carbapenemases (*Klebsiella pneumoniae* carbapenemase – KPC) and plasmid mediated AmpC seems to have caught us by surprise; some have even speculated that ß-lactam antibiotics may soon become redundant [10]. A similar argument could be made for fluoroquinolones. Regardless of structure or size, a new anti-GNNF compound must either circumnavigate the Gram-negative outer-membrane or simply blast through it - **it is this formidable hydrophobic barrier that is the downfall of many experimental compounds**.

Old Antibiotics Revisited

The emergence of MDR paralleled with a lack of novel molecules with anti-GNNF activity, has resulted in the renaissance of colistin [11]; more a case of *fait accompli* rather than a preferred clinical choice. Colistin still exhibits excellent activity against most GNNF bacteria, although sporadic reports of resistance and hetero-resistance among *P. aeruginosa* and *A. baumannii* are becoming increasingly prevalent. Thus, **colistin monotherapy is not advisable for critical infections**, especially in immunocompromised patients.

GNNF studies have shown cases of synergy between colistin and drugs such as rifampicin, fosfomycin and minocycline. These observations point to the potential of using directed combination therapy for managing infections caused by MDR *P. aeruginosa* and *Acinetobacter* spp., when all else fails.

Testing Methods

GNNF bacteria have an impressive array of intrinsic resistance mechanisms that they can activate to mediate small incremental rises in "resistance", whilst maintaining biological fitness. Such mechanisms include outer-membrane porin mutations, efflux pump activation, topoisomerase mutations and ß-lactam degradation by different ß-lactamases. These sometimes subtle yet clinically significant resistances can be induced and/or amplified *in vivo* under different circumstances.

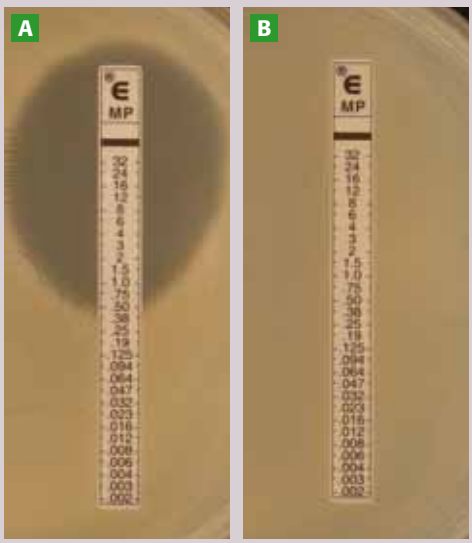
Testing methods such as disk diffusion may have inherent limitations for the detection of these subtle resistances. GNNF organisms are slower growing compared to *Enterobacteriaceae* and therefore the critical time at which enough cell mass is formed to enable resistance to be detected may be prolonged. This characteristic can challenge the performance of the disk diffusion method (i.e. unstable gradient) where larger zones may simply reflect slower growth.

The formulation of susceptibility test media can also influence the detection of certain resistance mechanisms. A typical example is the importance of using Mueller Hinton media for carbapenem testing since it has physiologic levels of zinc ions, a co-factor necessary for the activity of MBL enzymes that mediate resistance [12]. The use of isotonic media such as Iso-Sensitest, which has low inherent levels of zinc, can give false susceptible results for carbapenems despite the presence of the MBL phenotype (Figure 2).

FIG 2: *S. maltophilia* - (MBL+) -
A: Iso-Sensitest - false negative
B: Mueller Hinton - correct positive

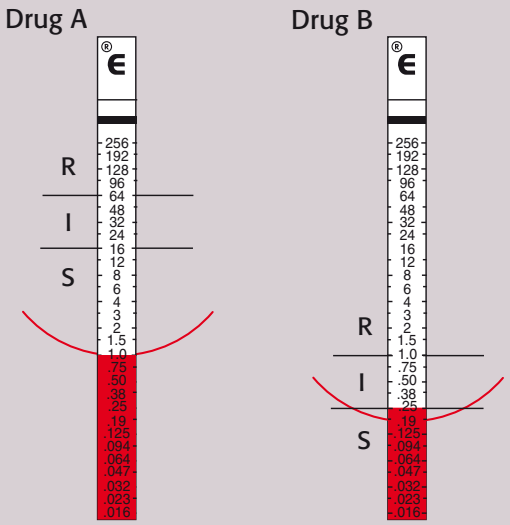
Iso-Sensitest may also be unsuitable for testing of other "cation sensitive" antibiotics against an important pathogen such as *P. aeruginosa* as recently demonstrated by Giske *et al* (Figure 3) [13].

FIG 3: False meropenem susceptibility for MBL+ *P. aeruginosa*;
A: Iso-Sensitest - false susceptibility
B: Mueller Hinton - correct MIC (growth along entire strip)



Given the critical status of high risk patients that may be infected with GNNF bacteria, the "window of safety" between the MIC value and the susceptible (S) breakpoint becomes pivotal. The quotient between the S cut-off and the MIC value (Figure 4) can help guide the selection of the antibiotic, dose and dosing regimen relative to expected drug levels (PK) and thus the PD targets necessary to improve the probability of treatment outcomes.

FIG 4: Breakpoint (BP)/MIC Quotient (BMQ) to guide therapy



The strategy of optimising the PD indices would also help minimise resistance selection, especially in the immune compromised patient. Clearly, the MIC is a crucial denominator for targeting antimicrobial therapy for high risk patients. Numerous studies on ICU patients with serious Gram negative infections have repeatedly shown that inadequate therapy has resulted in unacceptably high levels of mortality in excess of 50% [14], thus warranting a different approach than the over-simplistic standard S-I-R results for guiding therapy selection. We cannot choose the medical nor personal details of the ICU patient, their co-morbidities, the type of pathogen or how resistant or virulent it may be. ICU patients are among the most non-standardised of patient groups and **the only realistic intervention is to help optimise treatment outcome by ensuring that the antibiotic and dosage regimen selected may be expected to give drug levels well in excess of 5 to 10 times the MIC** [3].

Patients at risk

The first clinical case of a South American MBL positive *P. aeruginosa* (susceptible to colistin only) was reported in the SENTRY study in 1997 [15]. The patient, a four year old girl presenting with leukaemia, sadly succumbed to the infection. Zavascki *et al.* [16] has recently reported that MBL positive *Pseudomonas* spp. strains from this same region account for up to 77% of imipenem resistance observed – a number that would have been close to zero 10 years ago. If this is an example of what is to come, media reports heralding the "end of the antibiotic era by 2015", appear to be becoming increasingly realistic – at least for GNNF. Thus, surely it is incumbent upon us to maximise the use of these time-limited and precious lifesaving commodities, and more than ever, **promote the rational use of antibiotics through good practice laboratory medicine** – sentiments first proposed by Ericsson and Sherris over 40 years ago [17].

BMQ (Breakpoint MIC Quotient) is "calculated by dividing the MIC breakpoint with the MIC value for a particular pathogen. This is particularly useful for agents with pharmacodynamics characterized by concentration dependent killing. Assuming important parameters such as toxicity have been accounted for in the selection of breakpoints, the lower the MIC and the higher the MBQ, the more efficacious an agent is expected to be. Equally, the lower the MIC and the higher the MBQ, dosages can be adjusted without compromising on the PD indices goal e.g. for neonatal infections. So, in the simplest of formats, the MIC value relative to the susceptible breakpoint may become a very practical tool to target and fine-tune antimicrobial therapy"

Richard B. Thomson, Jr., Ph.D. Evanston Northwestern Healthcare, Professor of Pathology, Northwestern University Feinberg School of Medicine Chicago, Illinois, USA.

References

- 1. Paul M, Weinberger M, Siegman-Igra Y, Lazarovitch T, Ostfeld I, Boldur I, Shula, H, Carmeli Y, Rubinovitch B, Pitlik S. *Acinetobacter baumannii*: emergence and spread in Israeli hospitals 1997- 2002. J Hosp Infect. 2005.
- 2. Beaber JW, Hochhut B, Waldor, MK. SOS response promotes horizontal dissemination of antibiotic resistance genes. Nature. 2004.
- 3. Mohr JF, Wanger A, Rex JH. Pharmacokinetic/pharmacodynamic modeling can help guide targeted antimicrobial therapy for nosocomial gram-negative infections in critically ill patients. Diagn Microbiol Infect Dis. 2004.
- 4. Rhomberg PR, Fritsche TR, Sader HS and Jones RN. Contemporary activity of meropenem and comparator broad-spectrum agents: MYSTIC program report from the United States component (2005). Diagn Microbiol Infect Dis. 2007.
- 5. Makedou KG, Tsiakiri EP, Bisikilis AG, Chatzidimitriou M, Hlavantzis AA, Ntoutsou K and Alexiou-Daniel S. Changes in antibiotic resistance of the most common Gram-negative bacteria isolated in intensive care units. J Hosp Infect. 2005.
- 6. Rice L. Challenges in identifying new antimicrobial agents effective for treating infections with Acinetobacter and *Pseudomonas aeruginosa*. Clin Infect Dis. 2006.
- 7. Projan SJ and Shales DM. Antibacterial drug discovery: is it all downhill from here? Clin Microb Infect. 2004.
- 8. Lipinski, CA, Lombardo F, Dominy BW and Fenney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv Drug Deliv Rev. 2001.
- 9. Projan SJ. Small molecules for small minds? The case for biologic pharmaceuticals. Expert Opinion on Biol Ther. 2004.
- 10. Thomspon K. and Bonomo R. The threat of antibiotic resistance in Gram-negative pathogenic bacteria: ß-lactams in peril! Current Opinions in Microbiol. 2005.
- 11. Li J, Nation RL, Turnidge JD, Milne RW, Coulthard K, Rayner CR, Paterson DL. Colistin: the re-emerging antibiotic for multi-drug resistant Gram-negative bacterial infections. Lancet Infect Dis. 2006.
- 12. Walsh TR. The Emergence and implications of Metallo-ß Lactamases in Gram-Negative Bacteria. Clin Microb Infect. 2005.
- 13. Giske1 C G, Karlsson I, Karlsson Å, Johnson Å, Yusof A. Influence of Medium on Susceptibility Testing of Cation-Affected Antibiotics in *Pseudomonas aeruginosa*, Acinetobacter species and *Stenotrophomonas maltophilia* ICAAC 2007, D1588.
- 14. Cosgrove S. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. Clin Infect Dis. 2006.
- 15. Toleman MA, Simm AM, Murphy TA, Gales AC, Biedenbach DJ, Jones RN, Walsh TR. Molecular characterization of SPM-1, a novel metallo-beta-lactamase isolated in Latin America: report from the SENTRY antimicrobial surveillance programme. J Antimicrob Chemother. 2002.
- 16. Zavascki AP, Gasperato PB, Martins AF, Gonclaves AL and Barth AL. Outbreak of carbapenem-resistant *Pseudomonas aeruginosa* producing SPM-1 metallo-ß-lactamases in a teaching hospital in Southern Brazil. J Antimicrob Chemother. 2005.
- 17. Ericsson HM and Sherris JC. Antibiotic Sensitivity Testing - Report of an international collaborative study. 1971 Acta Path et Microbiol Scand. Suppl 271.

EUCAST - the European Committee on Antimicrobial Susceptibility Testing

Gunnar Kahlmeter, MD, Ph.D
Head of the Department of Clinical Microbiology, Centrallasarettet Växjö, Sweden and Chairman of the EUCAST Committee

What is EUCAST's mission?

- To **harmonise** and regularly **review** European breakpoints for phenotypic susceptibility testing of bacteria and fungi.
- To **act** as a European breakpoint committee for setting breakpoints for new agents as part of the regulatory approval process through EMEA.
- To **standardise** European susceptibility testing methods for bacteria and fungi.
- To **liaise** with European authorities involved in issues related to new antimicrobials, resistance development and surveillance, disease prevention, food and feed safety and clinical microbiology and infectious diseases throughout Europe.

How is EUCAST organised?

EUCAST was instituted by ESCMID. It is now the joint responsibility of ECDC, ESCMID and the national breakpoint committees of six European countries (France, Germany, United Kingdom, Norway, Sweden and The Netherlands). **All European countries** (not only EU countries) **have one representative on the EUCAST General Committee** which in turn has two representatives on the EUCAST Steering Committee. The Steering committee otherwise consists of a representative from each of the 6 national breakpoint committees and a chairman, a scientific secretary, and a clinical data coordinator. The latter three are appointed by ESCMID. The Steering Committee meets 4 – 5 times per year, the General Committee meets once a year.

Who finances EUCAST?

ESCMID and the National breakpoint Committees have financed EUCAST to varying degrees since it was formed in 1996. For four years, DG "Sanco" of EU and ECDC financed 60% of EUCAST's activity. Since 15th September 2008, **ECDC takes major responsibility for EUCAST**. ESCMID and national breakpoint committees in Europe will continue to be the professional driving force behind EUCAST and ESCMID will continue to support EUCAST financially.

What is "harmonisation of European breakpoints" and "when will it be finished"?

Historically, national breakpoint committees have published six different sets of breakpoints used in the countries where these respective breakpoint committees reside. Laboratories in European countries without national committees often subscribe to CLSI breakpoints and CLSI AST methodology. When a national strategy was lacking, laboratories chose the only system that was perceived as having some international standing. Thus, with the six national systems and the CLSI system, there were seven sets of breakpoints in Europe. With the gradual harmonisation of European breakpoints this is now reduced to two systems - European breakpoints used in France, Germany, Norway, Sweden, The Netherlands and The United Kingdom and US breakpoints still used in many or most other European countries.

What is the relationship between EUCAST and EMEA?

An SOP drawn up by EMEA, EUCAST and the Pharmaceutical Industry regulates the role of EUCAST for setting breakpoints as part of the regulatory process for the approval of new drugs through EMEA. In collaboration with EMEA, breakpoints for daptomycin, tigecycline and doripenem have been determined and several other antibiotics are currently being addressed. **EUCAST breakpoints are now the only breakpoints in the Summary of Product Characteristics (SPC)**.

What is the relationship between EUCAST, CLSI and FDA?

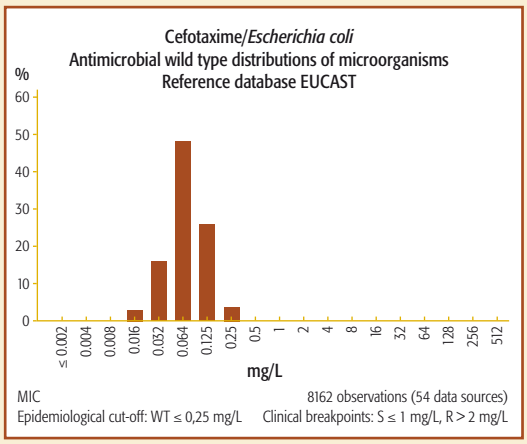
There is **no formal relationship** between EUCAST, CLSI and/or FDA. However, members of the EUCAST steering committee have participated in most of the CLSI meetings (two per year) over the last **8 years** and on several occasions there have been informal discussions on specific breakpoints between the two committees.
EUCAST will on request interact with any national regulatory agency. There are **more than 30 agencies in Europe**.

Who can take the initiative to review and revise breakpoints?

Breakpoints need to be reviewed at regular intervals. The use of drugs evolves, new indications are granted, doses change and new resistance mechanisms sometimes render old breakpoints obsolete. **The EMEA, national medical product agencies, the pharmaceutical company or EUCAST can initiate a process of review**. This may or may not result in a revision of breakpoints. EUCAST will typically review an entire class of antibiotics rather than just a single drug.

What about EUCAST wild type MIC distributions?

These are available on the EUCAST website (**www.eucast.org**). There are more than **17000 MIC** distributions submitted from all over the world, not only from the EU. The distributions include MICs from national and international surveillance programs such as the BSAC resistance surveillance program, the NORM surveillance program, SENTRY, EARSS, MYSTIC and others, as well as MIC distributions from published articles, the pharmaceutical industry, veterinary programs and individual laboratories. Below is a typical graph from the website. It shows the part of the distribution (based on 8162 MIC values aggregated from 54 different sources) that EUCAST considers to represent the "*E. coli* wild type cefotaxime MIC distribution". An *E. coli* isolate with an MIC inside this distribution is by definition devoid of a phenotypically detectable resistance mechanism to cefotaxime. On the basis of the MIC distribution, EUCAST has determined the epidemiological cut-off value for cefotaxime in *E. coli* (ECOFF 0.25 mg/L). An isolate with a MIC above the ECOFF is considered to harbour a cefotaxime resistance mechanism. It may or may not be clinically relevant. The EUCAST clinical breakpoints (S ≤1 mg/L, R >2 mg/L) are also shown on the graph.



Source: http://217.70.33.99/Eucast2/SearchController/regShow.jsp?Id=3217

ECOFFs can be used for sensitive and early detection of resistance development and to compare resistance development between countries with different clinical breakpoints and between different eras (particularly as clinical breakpoints more and more often need revision), between human and veterinary medicine and between different branches of veterinary medicine. They can also be used to **alert a clinician** to the fact that, although the patient isolate is categorised as susceptible by the clinical breakpoint, it has **acquired some resistance mechanism** which may or may not be of importance in a patient with special conditions, or that, although the isolate is categorised as resistant to the antibiotic in question, it does not harbour any phenotypically detectable resistance mechanisms (e.g. *Enterococcus* spp and gentamicin).

When is the non-species related breakpoint applicable?

EUCAST breakpoint tables have different breakpoints for different species -*Enterobacteriaceae*, *Pseudomonas* spp., staphylococci, etc have separate columns. A last column is titled "Non-species related breakpoints". These are based mainly on PK/PD aspects of the drug and **serve as guidelines for setting species-related breakpoints and for guiding therapy of infections caused by species not addressed in the table or its footnotes**.

What systems are available for disk diffusion susceptibility testing with EUCAST breakpoints?

There are currently **three systems available** for disk diffusion AST with EUCAST clinical breakpoints: CA-SFM (France) using Mueller-Hinton medium and an inoculum that yields semi-confluent growth, and the BSAC (UK) and SRGA (Sweden) systems using Iso-sensitest medium and semi-confluent growth. EUCAST will during 2008/09 develop an European disk diffusion method based on MH medium and an inoculum corresponding to a 0.5 McFarland standard.

COMMENT BY BIOMERIEUX

When will EUCAST breakpoints be available on the VITEK® 2, ATB™ and mini API® systems?

bioMérieux is currently working on software updates that will contain the EUCAST breakpoints for VITEK 2, ATB and mini API. These updates will include the EUCAST breakpoints applied to the respective system data (VITEK 2, ATB, mini API). Analysis has already been completed for a number of antimicrobials for VITEK 2, and is ongoing for ATB and mini API. Breakpoint changes should not be considered by the user until notified by bioMérieux that the changes have been validated. The software update containing the entire EUCAST interpretation standard is planned for both the VITEK 2 and VITEK 2 Compact systems mid-summer, 2009. ATB and mini API systems will be updated with new software and new panel configurations to follow the current EUCAST recommendations in the fall of 2009.

How do the EUCAST breakpoints affect Etest®?

Etest, with an extensive MIC range that covers the complete range of EUCAST breakpoints, is already available.

LIST OF ABBREVIATIONS

EUCAST:	European Committee on Antimicrobial Susceptibility Testing
EMEA:	European Medicines Agency
ESCMID:	European Society of Clinical Microbiology and Infectious Diseases
ECDC:	European Centre for Disease Prevention and Control
DG "Sanco":	Directorate General for Health and Consumers
SPC:	Summary Product Characteristics
CLSI:	Clinical and Laboratory Standards Institute
AST:	Antimicrobial Susceptibility Testing
SOP:	Standard Operating Procedure
FDA:	U.S. Food and Drug Administration
BSAC:	British Society for Antimicrobial Chemotherapy
DIN:	Deutsche Industrie Norm
NORM:	Norwegian Surveillance Program for Antimicrobial Resistance
SENTRY:	SENTRY Antimicrobial Surveillance Program
EARSS:	European Antimicrobial Resistance Surveillance System
MYSTIC:	Meropenem Yearly Susceptibility Test Information Collection Surveillance Program
MIC:	Minimum Inhibitory Concentration
Pk/Pd:	Pharmacokinetics/Pharmacodynamics
SRGA:	Swedish Reference Group for Antibiotics

IDENTIFYING RESISTANCE™

INTERNATIONAL NEWSLETTER
Director of publications : Thierry Bernard
Editor : Marie-Françoise Gros

VITEK 2 and Etest: Synergy in Resistance Detection

The recent acquisition of AB BIODISK, and their leading product line, Etest, brings together two of the most innovative susceptibility test methods in the field of microbiology.

VITEK 2 Technology provides same-day, clinically relevant identification and susceptibility test results for the majority of organisms encountered in the routine clinical laboratory. Microbiologists and clinicians have made VITEK 2 the leading automated Identification and Antibiotic Susceptibility Testing instrument in the world today.

Ideally, all ID/AST results should be reported the same day the tests are started. VITEK 2 can do this for a vast majority of organisms. However, there are situations when this is not possible, such as slow growing or nutritionally deficient, fastidious organisms. Etest is therefore a perfect complementary solution that enables laboratories to perform AST testing on these "difficult" organisms in a simple, standardized way. As Etest provides a MIC value critical information is obtained to ensure appropriate treatment decisions can be made.

Etest ensures flexibility when testing new, recently introduced antimicrobial agents and facilitates reporting even when breakpoints change. Currently, laboratories striving for LEAN management* utilize these methods, and these methods alone, to streamline laboratory operations.

The many benefits of the synergy between VITEK 2 and Etest - Quantitative MIC for All Patients, Better Antibiotic Stewardship, Improved Financial Performance for Healthcare Institutions, and Improved Patient Outcomes - are vast. Used together, these two AST methods have the potential to meet all of the routine susceptibility testing requirements of today's clinical microbiology laboratory.

Randy Tuner
Global Marketing Director, ID/AST

* LEAN Management is a combination of techniques that aim at eliminating any non-value added activity and in particular, concentrates on reducing losses within an organization while optimizing quality.

bioMérieux S.A.
69280 Marcy l'Etoile
France
Tel. (33) 04 78 87 20 00
Fax (33) 04 78 87 20 90

www.biomerieux.com
www.biomerieux-diagnostics.com

BIOMÉRIEUX