EUCAST Is Making Progress

EUCAST, the European Committee on Antimicrobial Susceptibility Testing is making progress. Breakpoints for several classes of antibiotics have been harmonised and breakpoints for two new drugs have been determined as part of the EUCAST/EMEA process.

Harmonised breakpoints for existing antimicrobial agents

The harmonisation of European breakpoints for existing antimicrobial agents is a major objective for EUCAST. EUCAST European harmonised breakpoints are now available for aminoglycosides, fluoroquinolones, glycopeptides and linezolid (see www.eucast.org). Harmonised breakpoints for aztreonam, carbapenems and cephalosporins will be available after 16th ECCMID in April 2006. A preliminary table of penicillin breakpoints has just been sent for consultation with the National Breakpoint Committees in Europe. The EUCAST Subcommittee on Antifungal Susceptibility Testing has almost completed European breakpoints for fluconazole.

Breakpoints for new antimicrobial agents

A Standard Operating Procedure (SOP) has been developed by EUCAST, the European Medicines Evaluation Agency (EMEA) and the pharmaceutical industry. Following the procedures in this SOP, EUCAST addressed two new antimicrobials during 2005. Daptomycin was registered by EMEA in late autumn 2005 and the breakpoints are available on the EUCAST website (www.eucast.org). Registration of tigecycline is still in process and breakpoints will be made available as soon as the drug is approved by EMEA.

The EUCAST Subcommittee on Antifungal Susceptibility Testing (EUCAST AFST)

The EUCAST AFST has collected large numbers of MIC-distributions for antifungals and tested them for agreement against Candida spp. in preparation for setting breakpoints on antifungal drugs. The MIC distributions for fluconazole will soon be made available on the EUCAST website. The subcommittee is preparing for EUCAST consultation about the proposed European breakpoint of fluconazole. This consultation will involve the EUCAST General Committee as well as the pharmaceutical and device manufacturing companies.

EUCAST workshop in Rome

On 23 November 2005 a EUCAST workshop took place next to St Peter’s Square in Rome with the participation of the EUCAST Steering Committee, many members of the EUCAST General Committee, delegates from the European Antimicrobial Resistance Surveillance System (EARSS) and 25 representatives of pharmaceutical companies and susceptibility testing device manufacturers. There were wide-ranging discussions, including the views of industry on the process of setting EUCAST breakpoints for bacteria and fungi in Europe and their implementation. Various aspects of problems in antimicrobial susceptibility testing and interpretation were also examined. During the following two days EUCAST and EARSS arranged a joint workshop for EUCAST and EARSS delegates, in which aspects of antimicrobial resistance surveillance of common interest were discussed.

EUCAST at 16th ECCMID in Nice

EUCAST has organised a satellite workshop on antimicrobial susceptibility testing to be held on Saturday, 1 April 2006 10.30–12.30 at the Acropolis Conference Centre in Nice. Attendance will be limited to members of the National Breakpoint Committees, the EUCAST General Committee, members of the EUCAST Subcommittee on Antifungal Susceptibility Testing and members of the pharmaceutical and susceptibility testing device manufacturing industries. The workshop will deal with the need for speciation in antimicrobial susceptibility testing.

On the afternoon of Saturday, 1 April 2006 the annual business meeting of EUCAST will be held. This is an open meeting, during which the current activities of EUCAST will be reviewed. All are welcome to attend.

On the afternoon of Tuesday, 4 April 2006 the EUCAST symposium for ECCMID on The clinical implications of low-level resistance will take place. Please see the ECCMID programme for details.

EUCAST and CLSI

For several years the EUCAST chairman has represented ECCMID at the twice yearly Antimicrobial Susceptibility Testing Subcommittee and working group discussions of the CLSI (formerly NCCLS). I and on several occasions, other EUCAST Steering Committee members have taken an active part in the discussions, including those on new cephalosporin breakpoints for Enterobacteriaceae, vancomycin breakpoints for Staphylococcus aureus, fluoroquinolone breakpoints for staphylococci, breakpoints for Acinetobacter spp. and revised breakpoints for Neisseria meningitidis. The work of the Enterobacteriaceae working group has recently been suspended until FDA and CLSI have sorted out their differing viewpoints on procedures for revising breakpoints. A new working group which has been established to revise the M23 document about the procedure of determining breakpoints by CLSI will complete this task. Unfortunately all other working groups involved in much needed revisions of breakpoints are on hold while the discussions between CLSI and FDA are ongoing and the M23 working group is in session. EUCAST strongly believes that there is a need for an internationally-agreed process for setting and revising breakpoints, perhaps under the auspices of the International Standards Organization. This will be pursued by EUCAST.

EUCAST Technical Notes (ETNs) in CMI

Beginning in 2006 a series of EUCAST Technical Notes will be published in Clinical Microbiology and Infection. The ETNs will summarise the background data, on which decisions are made on breakpoints for individual new agents (e.g. daptomycin and tigecycline) or harmonised breakpoints for groups of agents (e.g. aminoglycosides, fluoroquinolones and glycopeptides). The technical notes are based on the more detailed rationale documents produced by EUCAST for each of the antimicrobial agents subjected to the processes of harmonising or setting breakpoints. The rationale documents will be available on the EUCAST website (see www.eucast.org).

EUCAST wild type MIC distributions on the internet

EUCAST wild type MIC distributions for all organism-antimicrobial agent combinations, for which EUCAST has published new or harmonised breakpoints, are
available on the EUCAST website (see www.eucast.org). The MIC distributions are the combined data from many data sources, which are checked for consistency before incorporation into the database. Some distributions are now based on close to 100,000 MICs. The data are presented as tables and histograms of MIC distributions. Wild-type MIC distributions have several benefits – they assist in setting breakpoints that do not divide the wild-type distributions, which would prevent reproducible susceptibility testing; they are used to define epidemiological cut-off values (microbiological breakpoints) that separate the wild-type from the non-wild type microorganisms; they provide a reference for those who need to calibrate susceptibility testing systems or products; and they provide a reference to the expected MIC value for an organism that has not developed resistance to an agent.

**EUCAST and VetCast**

In December 2004 the Veterinary Committee on Antimicrobial Susceptibility Testing (VetCast) was initiated in Copenhagen at a meeting of representatives of European veterinary reference laboratories. In the EU it is mandatory for all Member States to monitor antimicrobial resistance annually in organisms of public health concern. This monitoring is primarily focused on Salmonella spp and Campylobacter spp from food-producing animals, but may include other organisms. In order to harmonise the results of these monitoring activities in Europe, uniform breakpoints are essential. Hence, setting wild type distributions is very relevant for veterinary laboratories. Through VetCast and the existing network of veterinary reference laboratories close to 1668 MIC data sets, covering a substantial range of organisms and agents of relevance to the veterinary field, have been collected. In January 2006 a Community Reference Laboratory (CRL) was designated for antimicrobial resistance (DFVF, Denmark). The CRL will have a major role in the future implementation of epidemiological cut-off values and breakpoints.

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**Peer Review and Publishing**

**peer, noun:** an equal; one of the same quality or ability

**peer, verb:** to look closely and searchingly, as in trying to see more clearly

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**Authority among equals**

From a young age, we grant to our peers a great deal of authority, to a different degree and of a different nature than that inherent in traditional authority figures. This probably because one way of seeing ourselves is through the eyes of, or in the context of, our peers - those doing the same thing, those behaving the same way, those in the same situation, those with whom we wish to be associated.

Up to a certain point, we have the luxury of deciding who our peers are, based on an understanding of ourselves, or an aspiration. Those who wish to publish in scientific publications, however, are more restricted. Nonetheless, peers remain a mainstay of self-judgment and peer review has become an established institution.

The First International Congress on Peer Review in Biomedical Publication took place in 1989, and the Fifth took place last year. This initiative on the part of the JAMA has been fostered, among others, by the BMJ and The Lancet.

In an editorial following the Second Congress, Drummond Rennie, Deputy Editor at JAMA, explained that the point of the initiative is to stimulate and present research on peer review and the integrity of the publication process, an area of research that seems unlikely to some. According to pre-and post-congress questionnaires, the vast majority of respondents (95% pre-congress and 92% post-congress) agreed that peer review improves the quality of published manuscripts. Prior to the congress survey, 68% of respondents thought journals should adopt more uniform standards for peer review and 81% were of this opinion after the congress. The majority of respondents concurred that editors should contribute to an effort to establish baseline data on the prevalence of scientific fraud (75% pre-congress and 85% post-congress) [1].

Peer review, according to Richard Smith, former editor of the BMJ, currently CEO of United Health Europe and board member of The Public Library of Science (PLoS), is held "absolutely sacred" in a field where people rarely accept anything on "blind faith". Still, there is evidence of the "downside" of peer review. "Even the very best journals have published rubbish they wish they’d never published at all. Peer review doesn’t stop that." And the process can lead to misjudgments in the other direction, failures to recognise promising work; some of the most highly cited papers were initially rejected. Peer review is a "lottery to some extent" says Smith; "it’s very unscientific, really" [2].

Others, however, believe that the process of peer review could be precisely scientific. Richard Horton, Editor of the Lancet, in a presentation at the Second Congress, suggested that a method of argument analysis [3], if applied to the scientific research paper, offers an opportunity for a systematic and logical approach to peer review. In brief, the relation between (1) the primary data and (2) the interpretation of these data (the argument) is determined by (3) the justification or reasonable grounds for the study. Reviewers should focus initially on the validity of the core argument made by the authors to determine whether the study is even warrant- ed. Thus, reviewers should look for a justification for the study (3) before considering the data (1) and the interpretation (2); only then does it make sense to consider the probability (4), the degree of random and systematic error (5) and the ‘generalisability’ (6). Horton proposes these six criteria as an alternative to the usual checklist, which provides ‘a crude normative framework’ for reviewers. Doing so would lead the reviewer through a logical process that would limit the risk of unacknowl-