

## European Committee on Antimicrobial Susceptibility Testing (EUCAST)

### **Ratified minutes of the Meeting on 31 March 2007 17<sup>th</sup> European Congress of Clinical Microbiology and Infectious Diseases, Munich, Germany**

A list of attendees who signed the register is attached.

**1. Apologies for absence**

None received.

**2. Minutes of meeting in Nice, 1 April 2006**

The minutes were approved as a true record.

**3. Matters arising**

Dr Brown reported that the dates of the Steering Committee meetings for the following year were on the EUCAST website at <http://www.eucast.org>.

**4. EUCAST Steering Committee membership**

Prof Kahlmeter reported that the current membership of the Steering Committee is:

Chairman	Prof Gunnar Kahlmeter	Sweden	2008
Scientific Secretary	Dr Derek Brown	UK	2008
Clinical Data Coordinator	Dr Rafael Canton	Spain	2008
BSAC	Prof Alasdair MacGowan	UK	2008
CRG	Dr Johan W. Mouton	Netherlands	2008
DIN	Dr Arne Rodloff	Germany	2008
NWGA	Dr Martin Steinbakk	Norway	2008
SFM	Dr Fred Goldstein	France	2008
SRGA	Dr Ingrid Nilsson-Ehle	Sweden	2008
General Committee	Prof. Waleria Hryniewicz	Poland	2008
General Committee	Prof. Pietro Varaldo	Italy	2008

The General Committee representatives will finish their terms on the Steering Committee in April 2008.

**5. Confirmation of membership of EUCAST General Committee**

Membership was reviewed (the current list is attached). Representatives were asked to inform the Scientific Secretary if the current representative of their country has changed. They were also asked to ensure that they keep their national societies informed of EUCAST activities and to take part in the consultation process. Anyone in the pharmaceutical and susceptibility device manufacturing industries may be part of the industry email network that is included in the consultation process.

**6. EUCAST progress report**

Prof Kahlmeter summarised activities over the past year.

- 6.1 There have been four meetings of the Steering Committee. In addition there have been numerous presentations at a variety of meetings.
- 6.2 Harmonized breakpoints for aminoglycosides, fluoroquinolones, glycopeptides and linezolid were completed in 2005-6. Harmonized breakpoints for cephalosporins, carbapenems and aztreonam were completed in 2006-7. All are on the EUCAST website.
- 6.3 Work on penicillins and macrolides is in progress and will be completed later this year following general consultation, which will be soon after this meeting. Work on miscellaneous remaining agents has been started and should be completed by April 2008.
- 6.4 Using the agreed EMEA SOP (available on the EUCAST website) breakpoints have been proposed for garenoxacin, which is currently under consideration by EMEA. The procedure was previously used to set breakpoints for daptomycin and tigecycline, and five more are in the pipeline. The SOP allows EUCAST, in concert with EMEA and the Pharmaceutical industry, to determine clinical breakpoints for new antimicrobials as part of the approval process. The SOP has recently been revised as follows:
  - EUCAST can revise breakpoints for existing drugs (the initiative may come from EMEA, Rapporteur, EUCAST or the Pharmaceutical company);
  - New indications for a drug will be evaluated by EUCAST to determine whether new breakpoints are required;
  - The pharmaceutical companies can ask EUCAST for provisional breakpoints prior to initiating clinical trials;
  - EUCAST breakpoints are included as the only breakpoints in the SPC;
  - Prior to finalisation of opinion, EMEA will forward to EUCAST the proposed SPC for a final check on breakpoints.
- Dr Tulkens asked if other countries than those represented in the Steering Committee or manufacturers of generic agents could suggest revision of breakpoints. Prof. Kahlmeter replied that anyone could suggest revision by contacting EUCAST with supporting evidence. If there is a submission to EMEA for a new clinical application or modification of the SPC then EUCAST will consider the implications for breakpoints.
- 6.5 Rationale documents explaining the basis of breakpoints are being prepared for each agent and will be added to the EUCAST website as they are completed. They are accessed through links in breakpoint tables. Technical notes giving the background to EUCAST breakpoints will be published in CMI. New drugs will each have a technical note. Existing drugs will have a technical note for each class of agents. To date, technical notes for tigecycline, daptomycin and linezolid have been published. Others will be published soon.
- 6.6 Collaboration and sharing of information with other groups including EARSS, expert groups on meningococci, gonococci and anaerobes and veterinary groups, EFSA, "Prosafe" and unofficial contacts with CLSI have continued. Prof. Phillips asked whether how discrepancies in breakpoints used by veterinary and food groups were being resolved. Prof. Kahlmeter and Dr Mervius noted that veterinary and food groups linked to EUCAST were being encouraged to use epidemiological cut-offs.
- 6.7 The slideshow outlining EUCAST activity and processes can be downloaded

from the EUCAST website.

- 6.8 The EUCAST website covers most EUCAST activity and includes breakpoint tables, documents and guidelines. The data in the wild type distribution program on the website continues to be expanded. There are now over 11,000 organism-antibiotic distributions from different sources. Developments of the websites including current links from the breakpoint tables to MIC distributions and documents were described. Current developments to mark wild type MICs on distributions and to download all wild type distributions in one go were outlined. Dr Livermore suggested that it would be useful to indicate MICs for isolates with known resistance mechanisms. While the value of this was acknowledged the non-wild type in the MIC distributions would not be downloadable as they could give false impressions of resistance rates and there was frequently truncation of MIC distributions at the high end. In reply to a question from Dr Tulkens, it was explained that some wild type distributions are slightly asymmetrical because the distributions are based on combined data from different sources that may vary slightly, but never more than one dilution (or they are excluded).
- 6.9 EUCAST continues to be financially supported by ESCMID, the National Breakpoint Committees of Steering Committee members and a grant from DG SANCO of the EU. The EU grant finishes in April, 2007. ECDC has been reviewing the possibility of including EUCAST within its remit and very recently has agreed to continue the EU part of the funding, but the activity will go to tender (Dr Peter Tüll of ECDC explained that this is a legal requirement for any project costing more than 60,000 Euros).

## 7. EUCAST sub-committee report

- 7.1 Prof. Kahlmeter reported that the Antifungal Susceptibility Testing Sub-committee, chaired by Prof. Juan-Luis Rodriguez-Tudela, has almost completed the process for fluconazole breakpoints and these, together with a rationale document and technical note, will be published very soon. Breakpoints for other agents will then be considered. The EMEA is drafting a modification of the SPC for antifungals to include breakpoints based on EUCAST methodology for *Candida* spp.
- 7.2 Dr Leclercq (Chairman of the Expert Rules Subcommittee) reported that a first draft comprising four tables of intrinsic resistances, three tables of exceptional phenotypes and six tables of interpretive rules had been produced. This draft was being updated following comments from national committees and the second draft would be released for wider comment within a month. The wide consultation will include the EUCAST General Committee, national committees, the industry networks and any others who wish to comment. The draft will be put on the EUCAST website. Comments will be required by the end of August 2007.
- 7.3 Prof. Phillips asked if tentative EUCAST documents on cell-associated pathogens and mycobacteria had been progressed. Dr Brown explained that the authors of the document on cell-associated pathogens did not wish to update their document but that an updated version of the document on susceptibility testing of *M. tuberculosis* had been submitted to CMI for publication.

## 8. CLSI

8.1 The internal problems regarding the relationship of CLSI to FDA impeding the revision of CLSI breakpoints and the question of whether only FDA had the legal authority to set and revise breakpoints in the USA were noted in the minutes of the EUCAST General Committee meeting in April 2006. Prof. Kahlmeter explained that he had invited CLSI to outline the current situation.

8.2 Dr Mary-Jane Ferraro reported on behalf of CLSI. Two-three years ago FDA asserted their legal right as the only authority in US to set breakpoints for antimicrobial drug label and those used in commercial AST devices, which makes it difficult for laboratories with commercial AST devices to use CLSI breakpoints. An “AST alignment meeting” was held on 16th January 2007 between invited FDA and CLSI representatives. The meeting made a series of recommendations:

Breakpoints for new agents will be set by FDA. If the breakpoints are not considered acceptable by CLSI there will be a gap in CLSI documents as no breakpoint will be published.

CLSI will consider proposals to update CLSI breakpoints for existing drugs when issues of emerging resistance or other compelling evidence arise. Data demonstrating a need for a change must be presented as described in the CLSI M23 document in order to modify existing breakpoints. CLSI will not vote to change breakpoints less than 2 years from the date of the initial FDA drug approval unless there is a compelling public health issue.

CLSI will establish a Microbiology Area Committee Working Group to explore a process with both a US and global perspective to manage and resolve discrepancies in breakpoints. This is to include all interested parties (e.g., drug sponsors, regulatory agencies, device manufacturers, generic drug sponsors, professions, etc.)

8.3 There was discussion and comment on the presentation:

It was unclear what the status of the comments was and the timescale for action. The CLSI M23 document is currently under review.

In order to change an FDA breakpoint a “citizens petition” is required. Such action by CLSI would require a vote at the CLSI subcommittee. There has been no response from FDA to a petition presented by CLSI more than six months ago regarding vancomycin breakpoints for *S. aureus*.

Dr Ferraro considered it unlikely that there will be many gaps in the CLSI documents because of disagreement with the FDA over breakpoints.

The CLSI may give an opinion on breakpoints for agents used in some countries but not available in the US.

FDA documents include MIC breakpoints, equivalent zone diameters and quality control limits.

## 9. ESCMID views on EUCAST

Dr Giuseppe Cornaglia (ESCMID President Elect) reported that the ECMID Executive strongly supported EUCAST and felt that very good progress had been made. EUCAST was considered to be “added value” for ESCMID.

## 10. Future activities

Prof Kahlmeter reported that priorities for the next year were:

- 10.1 Completion of harmonization of breakpoints for penicillins and macrolides.
- 10.2 Complete the process of harmonization of miscellaneous outstanding breakpoints for tetracyclines nitrofurantion, fusidic acid, colistin, chloramphenicol, trimethoprim, trimethoprim-sulphamethoxazole and rifampicin.
- 10.3 Apply the EMEA SOP to breakpoint setting for four to five new drugs.
- 10.4 Continue to develop the rationale documents on the EUCAST website and technical notes in CMI.

## **11. Any other business**

- 11.1 Implementation of EUCAST breakpoints in automated systems.

Dr Tulkens asked when EUCAST breakpoints will be incorporated into machines. Thierry Leonard (BD) noted that if breakpoints were within existing test ranges there was no reason why EUCAST breakpoints could not be incorporated into their system immediately as breakpoints can be individually changed. If breakpoints are outside existing ranges additional work is necessary. Expert rules may be a problem if they are method-related. Barbara Zimmer (Dade-Behring) also confirmed that EUCAST breakpoints could be included in their system if customers requested. Dr Mouton noted that some users are waiting for a full set of breakpoints before changing to EUCAST.

## **12. The next meeting of the EUCAST Committee**

Scheduled for 18<sup>th</sup> ECCMID, Barcelona, Spain 19-22 April 2008.

**General Meeting attendees signing the register, 31 March 2007**

Prof Arvydas Ambroziatis	Vilnius, Lithuania
Dr Derek Brown	Cambridge, UK
Dr Rafael Canton	Madrid, Spain
Dr Giuseppe Cornaglia	Verona, Italy
Dr Manuel Cuenca-Estrella	Majadahonda, Spain
Dr Philippe Dufour	La Balme Les Grottes, France
Dr Mike Dudley	San Diego, USA
Dr Anette Engelhardt	Solna, Sweden
Dr Sheila Farnham	Hazelwood, USA
Dr Mary-Jane Ferraro	Boston, USA
Dr Cynthia Fowler	Durham, USA
Dr Niels Frimodt-Moller	Copenhagen, Denmark
Dr Markus Heep	Switzerland
Dr Pat Hogan	New York, USA
Dr Regine Horre	Bonn, Germany
Dr Manette Juvin	Marnes-la-Coquette, France
Prof Gunnar Kahlmeter	Vaxjo, Sweden
Dr Roland Leclercq	Caen, France
Mr Thierry Leonard	Le-Pont-de-Claix, France
Dr David Livermore	London, UK
Dr Konstanze Machka	Munich, Germany
Prof Alasdair MacGowan	Bristol, UK
Prof Krassimir Metodiev	Varna, Bulgaria
Dr Dik Mervius	Lelystad, Netherlands
Dr Linda Miller	Collegeville, USA
Prof Helmut Mittermayer	Linz, Austria
Dr Enrico Montrucchio	Buccinasco, Italy
Dr Mary Motyl	Merck, USA
Dr Johan Mouton	Nijmegen, Netherlands
Dr Gerard Notario	Abbott Park, USA
Prof Ian Philips	Malaga, Spain
Dr Anne Pinault	Marcy L'Etoile, France
Dr James Poupard	Philadelphia, USA
Dr Bob Rennie	Alberta, Canada
Dr Juan-Luis Rodriguez-Tudela	Majadahonda, Spain
Dr Helio Sader	North Liberty, USA
Dr Dee Shortridge	St Louis, USA
Dr Robert Skov	Copenhagen, Denmark
Dr John Turnidge	Adelaide, Australia
Dr Arjana Tambic-Andrasevic	Zagreb, Croatia
Prof Paul Tulkens	Brussels, Belgium
Mr Thierry Vidalenc	Paris La Defence, France
Dr Giles Zambardi	La Balmes Les Grottes, France
Dr Barbara Zimmer	West Sacramento, USA

**EUCAST General Committee April 2007**

<b>Chairman</b>	Dr Gunnar Kahlmeter
<b>Scientific Secretary</b>	Dr Derek Brown
<b>Clinical Data Coordinator</b>	Dr Rafael Canton
<b>National representatives</b>	
Austria	Prof. Helmut Mittermayer
Belgium	Prof. Jan Verhaegen
Bosnia	Dr Selma Uzunovic-Kamberovic
Bulgaria	Prof. Krassimir Metodiev
Croatia	Dr Arjana Tambic-Andrasevic
Czech Republic	Dr Pavla Urbaskova
Denmark	Dr Niels Frimodt-Møller
Estonia	Dr Paul Naaber
Finland	Dr Antti Nissinen
France	Prof. Claude-James Soussy
Germany	Prof. Bernd Wiedemann
Greece	Prof. Alkiviadis Vatopoulos
Hungary	Dr Éva Bán
Iceland	Dr Karl Gustaf Kristinsson
Ireland	Dr Martin Cormican
Italy	Prof. Pietro Varaldo
Latvia	Dr A. Balode
Lichtenstein	No representative
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 Lazar Ranin
Slovak Republic	Prof. Milan Niks
Slovenia	Dr Jana Kolman
Spain	Dr Francisco Soriano
Sweden	Dr Barbro Olsson-Liljequist
Switzerland	Prof. Jacques Bille
Turkey	Dr Deniz Gür
UK	Prof Alasdair MacGowan
<b>ISC</b>	Dr Paul Tulkens
<b>FESCI</b>	Dr David Livermore
<b>Pharmaceutical Industry</b>	Email network of any with an interest in antimicrobials
<b>Device Manufacturers</b>	Email network of any with an interest in antimicrobials