

European Committee on Antibiotic Susceptibility Testing (EUCAST)

Minutes of the Meeting on 31 May 2000 at the 10th European Congress of Clinical Microbiology and Infectious Diseases, Stockholm, Sweden

Chairman Professor Ian Phillips

Secretary Dr Derek Brown

A list of attendees who signed the register is attached.

1. **Apologies for absence**

Prof. S. Sidorenko

Prof. R. Auckenthaler

Prof. F. Baquero

Dr S. Uzunovic-Kamberovic

Dr F. Drobniewski

Prof. W. Hyrowinowitz

Prof G.C. Schito

Dr P. Urbaskova

Dr A. Bryskier

2. **Minutes of meeting in Berlin, 24 March 1999**

Approved as a correct record.

3. **Matters arising**

3.1 ***Sub-committee membership***

A list of members of sub-committees was sent out with the minutes of the last meeting.

3.2 ***Breakpoint round table meeting at ECCMID 2000***

A session on breakpoints was organised for the ECCMID 2000 and took place on Monday 29 May.

4. **Main Committee membership**

Dr Brown reported on changes to membership as follows:

Bosnia New member Dr Selma Uzunovic-Kamberovic

Hungary Dr Eva Ban replaces Dr Endre Ludwig

Ireland New member Dr Lynda Fenelon

Lithuania New member Prof. Alvydas Laiškonis

Slovenia Dr Jana Kolman replaces Dr A Dragas

For the device manufacturers Dr Jean-Pierre Marcel replaces Dr Hibert unless industry reports otherwise.

The membership of the EUCAST Main Committee is detailed in the Statutes. If there are any changes to representatives on the committee the Scientific Secretary should be informed.

5. Sub-committees

5.1 *Sub-committee structure*

Dr D. Brown outlined the structure of the Sub-committees and an updated list of members, together with contact addresses of chairpersons, will be sent with the minutes of this meeting [**Action Dr D. Brown**].

5.2 *Voting procedure*

Prof. I. Phillips outlined the procedure for voting on EUCAST documents. Any proposal must be made and seconded by Main Committee members. There will be discussion on the proposal. If there is a seconded counter-proposal this will be discussed in turn before a vote is taken. Any individual can take part in the discussion but only members of the Main Committee or their appointed deputy can vote. There must be a two thirds majority of those voting for a proposal to be accepted.

5.3 *Molecular Methods*

Prof. P. Hawkey listed the Sub-committee members and reported that a meeting attended by Prof. Hawkey, Dr M. Struelens, Prof. A. Vatalopolis and Dr A. Tambic had been held the previous day. A questionnaire on molecular methods had been distributed as part of the process of producing a position paper on use of molecular methods in susceptibility testing. Prof. Hawkey asked for the names of any laboratories using such methods. Contact has been made with the NCCLS and input requested. It is intended that the questionnaire will be posted on the ESCMID www site. The aim is to collate questionnaire results by the end of September 2000 and to produce a draft position paper by the end of 2000 [**Action Prof. P. Hawkey**].

5.4 *Terminology*

Prof. Phillips reported on revision of EUCAST definitive document E.Def 1.1 on Terminology, which was published in CMI 1998;4:291. Members of the Main Committee have been sent a list of suggestions for revisions and Prof. Phillips detailed responses to these as attached.

Dr G. Kahlmeter proposed (seconded by Dr D. Brown) that the responses detailed by Prof. Phillips are accepted and a revised version should be published.

In discussion of the proposal Dr D. Denning suggested that with fungi the term "clinically resistant" should be avoided as it gets confused with "microbiologically resistant", and that the terms "refractory" or "clinical failure" might be used. Prof. Phillips felt that as the definitions were in relation to bacteria it was not possible to use these terms. The Fungal Sub-committee were asked to make proposals relating to fungi for inclusion in the next revision. Dr E. Nichols suggested that the definition of culture medium should be in line with that in the ISO Standard. Prof. Phillips indicated that the definition to be used "A preparation used for the cultivation and growth of micro-organisms" came from Oxoid.

The result of the vote on the proposal was 14 for, none against and no abstentions. The revised version will be sent to CMI for publication as E.Def 1.2 [**Action Prof I. Phillips**].

5.5 ***Intracellular pathogens***

Dr G. Ridgway listed the Sub-committee members and reported that a series of documents from various members of the Sub-committee on different pathogens would be combined into a single outline document for wider distribution. The group has no links with NCCLS and Dr C. Thornsberry confirmed that there was no NCCLS activity in this area [**Action Dr G. Ridgway**].

5.6 ***Breakpoints***

Prof. Phillips reported that the Sub-committee had held one meeting. A letter had been submitted to CMI comparing MICs by three methods on a range of organisms in three countries and showed that the susceptible populations have very similar MIC distributions. A letter was also being prepared by Dr J. Degener summarising how the different approaches to setting breakpoints has led to different breakpoints. The objective was to harmonize breakpoints for new agents and for the top 10 established drugs for Gram-positive and Gram-negative organisms [**Action Dr J. Degener**].

Prof. I. Phillips reported that the Sub-committee has been requested to establish a breakpoint for linezolid. A meeting for this will be convened by Dr F. Goldstein as soon as possible [**Action Dr F. Goldstein**].

Prof. I. Phillips reported that there had been no comments on discussion document E.Dis 2, Determination of antimicrobial susceptibility test breakpoints published as a CMI insert in November 1999. Prof. L. Verbist proposed (seconded by Dr D. Brown) that the Discussion Document should be accepted and published as a Definitive Document E.Def 2.1.

In discussion Dr A. Harris asked what the voting procedure was in setting breakpoints and what involvement industry had in the process. Prof. Phillips explained that all members of the Breakpoint Sub-committee were entitled to vote. The company produces written evidence in the form of a dossier, which is sent to all Sub-committee members before the meeting. The evidence is also presented by the company at the meeting. The dossier includes information on MIC distributions, pharmacological and pharmacodynamic information, clinical information, particularly in relation to response to treatment with organisms having borderline susceptibility. The company withdraw and following discussions in the Sub-committee, breakpoints are proposed to the company. Following further discussion with the company the Sub-committee votes on the breakpoints. If accepted the breakpoint is published as provisional before ratification by the Main Committee. Dr A. Harris, Dr P. Hayle, Dr J. Fung Tomc and Dr C. Thornsberry all spoke in favour of all discussions being open to the company as in NCCLS, as this is felt to be more productive, more efficient and avoids objections to secrecy. Prof. T. Bergan felt that the open discussion with the company before and after the Sub-committee proposes a breakpoint is adequate and that a period of discussion without the vested interests of industry is important. Dr J. Fung Tomc asked what happens if the company disagrees with the Sub-committee. Prof. Phillips stated that this had happened only one in eight previous cases. The rationale for the breakpoint is given in the Sub-committee report, which may say that further information is desirable and will reconsider the breakpoint at a later date. It was questioned whether there might be a conflict of interest with the industry representative on the Sub-committee, but it was agreed that in this case the representative would not vote. Dr C.

Thornsberry suggested that the process of setting the breakpoints be defined in detail so that all companies follow exactly the same procedure. Prof. I. Phillips agreed to work on a checklist to make the process clearer. **[Action Prof. I. Phillips]**. Dr J. Fung Tomc asked if distributions of MICs were to be based on specific media and methods. Prof. I. Phillips indicated that the EUCAST reference method (to be discussed later), or a method shown to give equivalent results, should be used. Dr G. Kahlmeter suggested that proposed breakpoints be sent to different reference groups in Europe for comment. Prof. Phillips indicated that all groups had the opportunity to comment as breakpoints were initially provisional. Dr D. Denning pointed out that there are particular problems with antifungal agents where there are large inter-patient variations with new azoles, and that animal models are becoming more important, particularly when resistance is rare.

The result of the vote on the proposal to accept and publish the Discussion Document as a Definitive Document was 14 for, none against and no abstentions. The revised version will be sent to CMI for publication as E.Def 2.1 **[Action Prof I. Phillips]**.

After further discussion of the issue of whether all discussion by the Subcommittee was open to the company, Prof T. Bergan proposed (seconded by Prof. L. Verbist) that present practice should be continued in that when setting breakpoints on new agents, a brief separate discussion by the Breakpoint Subcommittee should not be open to the pharmaceutical company involved. The result of the vote on the proposal was 10 for, 4 against and no abstentions. The proposal was therefore agreed.

5.7 ***Dilution methods***

Dr D. Brown reported that a draft discussion document on determination of minimum inhibitory concentrations (MICs) of antibacterial agents by agar dilution was distributed to Main Committee members for comment in January 1999. Comments returned to EUCAST have been incorporated into a revised version published as an inset in CMI in May 2000. Copies of the comments and responses to comments have been distributed to Main Committee members. Prof. B. Wiedemann proposed (seconded by Prof. L. Verbist) that the Discussion Document, with agreed minor modifications, be accepted and published as a Definitive Document.

In discussion, accepted alterations were the inclusion of a reference to a Norwegian breakpoint document (Prof. T. Bergan), inclusion of "of bacteria" in the title of the document (Dr D. Denning), and inclusion of "Target MIC" in the title of table 4 (Dr J. Fung Tomc). It was queried whether the referenced NCCLS document M6 on Mueller-Hinton agar could be applied to suppliers from outside the USA. Dr D. Brown felt that it could and this was confirmed by Dr R. Jones and Dr J. Jorgensen. It was suggested that the effects of atmosphere were not sufficiently specific, but it was noted that the document requires the effects of any changes in atmosphere to be established.

The result of the vote on the proposal was 13 for, none against and no abstentions. The revised version will be sent to CMI for publication as E.Def 3.1 **[Action Dr D. Brown]**.

Prof. B. Wiedemann reported that a draft discussion document on determination of minimum inhibitory concentrations (MICs) of antibacterial agents by broth microdilution, was distributed to Dilution Methods Sub-committee members for comment in February 1999. Few comments have been received to date. Dr J. Fung Tomc asked if there would be any differences in target MICs between agar dilution and broth microdilution methods. Prof. B. Wiedemann indicated that although there are some differences many will be similar. It was agreed to update the draft and publish it as a discussion document in the form of an insert in CMI [**Action Prof. B. Wiedemann**].

5.8 ***Mycobacteria***

Dr F. Drobniowski was not present but sent a note which was presented by Dr D. Brown. An outline position document prepared last year will be updated following a WHO meeting in June 2000 to discuss testing of second line drugs. The intention is to produce a discussion document later this year [**Action Dr F. Drobniowski**].

5.9 ***Fungi***

Dr J.L. Rodriguez Tudela reported that there had been three meetings of the Sub-committee. Three standards were being prepared on fermentative yeasts, non-fermentative yeasts and filamentous fungi. Work on *Candida* has been completed comparing results with 60 strains tested by the EUCAST microdilution method in RPMI medium + 2% glucose and the NCCLS method, which is similar but uses RPMI + 0.2% glucose. The EUCAST method permits reading at 24h. A procedure has been outlined for a microdilution method with spectrophotometric reading of endpoints and two NCCLS strains as controls. Inter-laboratory reproducibility studies involving several European countries and the USA are underway. For *Cryptosporidium* a new method is needed and for filamentous fungi work has just started on the details. It is expected that discussion documents will be produced by the end of the year [**Action Dr J.L. Rodriguez Tudela**].

Dr D. Denning felt that progress will also be needed on developing breakpoints. The procedure will be based on that described for bacteria. He suggested that it might be useful to include a member of the Fungi Sub-committee on the breakpoint group and *vice versa*. A representative from industry might also be desirable and Dr D Sheen (Pfizer) offered to join the Sub-committee. Dr J.L. Rodriguez Tudela suggested that anyone working actively in the field who would be interested in joining the Sub-committee should contact him.

5.10 ***Automation***

Dr D. Brown reported for Prof. R. Auckenthaler, who could not attend the meeting. It is intended to produce a discussion document and an outline of the document was presented. Any comments or contributions should be sent to Prof. R. Auckenthaler [**Action Prof. R. Auckenthaler**].

5.11 ***Quality Assurance***

Dr D. Brown reported that the collection of reference strains had been expanded, and included organisms originally from "the CDC set". As reference MIC methods were close to being agreed the work of characterising the strains would commence when funding was obtained [**Action Dr D. Brown**]. A future problem of the cost of maintenance and distribution of any collection was raised.

The issue of safety in sending resistant organisms through the post was raised last year and Dr D. Brown has discussed the matter with those routinely involved in distributing strains for proficiency testing. It was felt that this was not a particular problem because the identities and resistance profiles of all isolates would be known to sender and receiver (unlike proficiency testing strains), the organisms were no different to organisms currently accessible in culture collections, and resistant organisms can already be obtained from individual laboratories if details have been published. Organisms would only be sent to recognised laboratories, and receiving laboratories could be asked to sign a document acknowledging that they understand that they are receiving known resistant organisms.

6. Relationships with other organisations

- 6.1 Prof. I. Phillips reported that he had attended the last NCCLS meeting and would also attend the next two meetings. Prof. Phillips felt that documents were not received soon enough to collect comments from EUCAST members. Dr J. Jorgensen commented that 6 months was allowed for comments, which should be adequate and NCCLS would be happy to receive any comments. Following discussion it was apparent that while both organizations were interested in harmonization of methods it would be inappropriate for either to be a member of the other.
- 6.2 Links with EMEA had been strengthened. Prof. I. Phillips and Prof. R. Finch had met Dr B. Arondson and it was agreed that EUCAST should provide the EMEA with information on proposed breakpoints.

7. Finance

Prof. I. Phillips reported that EUCAST had limited resources, which would be sufficient to continue to support secretarial expenses. Unfortunately there are not funds to cover the cost of travel of members to meetings separate from international symposia. The Committee was grateful for support received from industry.

8. Any other business

8.1 *EUCAST Newsletter*

Dr D. Brown reported that The EUCAST Newsletter will be produced annually inbetween ECCMID meetings.

8.2 *ESCMID web site*

The ESCMID web site (www.escmid.org) includes a section for EUCAST and it is available for use by Sub-committees (through the EUCAST Scientific Secretary, Dr D. Brown).

8.3 *ECCMID 2001*

A EUCAST session on Quality Assurance for ECCMID 2001 was suggested. Other groups including INSPEAR and HARMONY would also take part in this

session.

8.4 ***EUCAST and CEN***

Dr E. Nichols suggested that EUCAST and CEN standards should be the same. Prof. I. Phillips felt that CEN had made no positive progress in this area and it was not intended to link our professional consensus documents with CEN standards. Prof. Phillips is in contact with Prof K. Shinton of CEN and will send copies of our documents to him.

8.5 ***The next meeting of the EUCAST Main Committee***

This will take place at ECCMID 2001, Istanbul, Turkey, 1-4 April 2001. If possible the EUCAST meeting will be held at the beginning of the congress.