

# European Committee on Antibiotic Susceptibility Testing (EUCAST)

## Minutes of the Meeting on 20<sup>th</sup> March 1999 at the 9<sup>th</sup> European Congress of Clinical Microbiology and Infectious Diseases, Berlin, Germany

Chairman Professor Ian Phillips  
Secretary Dr Derek Brown  
A list of attendees is attached.

### 1. **Apologies for absence**

Professor B. Wiedemann.  
Dr A. Bryskier

### 2. **Minutes of meeting in London, 10<sup>th</sup> November 1997**

Approved as a correct record.

### 3. **Matters arising**

#### 3.1 **Constitution**

See item 4.

#### 3.2 **Industry representatives on the Main Committee**

Industry representatives were originally appointed for one year and Professor Phillips asked if industry members wished to extend the appointments or elect new members [**Action industry members**].

#### 3.3 **Venue for EUCAST meetings**

Professor Phillips asked whether having EUCAST meetings at the ECCMID was convenient as some members have alternative commitments at the Congress. The reason for having EUCAST meetings at the ECCMID was largely financial as EUCAST does not have funds to support attendance of all committee members and many would be at the ECCMID anyway. It was agreed to investigate the possibility of holding the meeting at the end of the 10<sup>th</sup> ECCMID in Stockholm in May 2000.

### 4 **Constitution**

Professor Phillips reported that the Constitution had been redrafted and a copy of the Statutes was appended to the minutes of the last meeting. This version has been agreed by the Executive Committee of ESCMID and was agreed by the EUCAST Main Committee.

### 5 **Main Committee membership**

A list of Main Committee members was also appended to the minutes of the last meeting and amendments should be notified to the EUCAST Secretary.

Professor Phillips welcomed Dr Mary-Jane Ferraro, Chair of NCCLS Subcommittee on Antimicrobial Susceptibility Testing and thanked her for her helpful discussions regarding the objectives of EUCAST and NCCLS. Dr Ferraro explained that NCCLS welcomed collaboration which contributed to global harmonisation of susceptibility testing methods. Professor Phillips reported that NCCLS was considering an invitation to have formal representation on the EUCAST Main Committee.

### 6. **Sub-committee reports**

In response to a question about membership of sub-committees Dr Brown explained that membership was based on the procedure agreed at the last meeting. Attendees at the last meeting had expressed preferences for particular sub-committees and it was agreed that Prof Phillips and Dr Brown would identify co-ordinators and recommend some sub-committee members, with additional experts being identified by co-ordinator. Sub-committee members have not been published and it was agreed that a list would be distributed with the minutes [ACTION Derek Brown].

6.1 **Terminology** (Co-ordinator Professor Ian Phillips)

Professor Phillips reported that a Discussion Document has been published in CMI (1998;5:291-296) with an invitation for proposals for revision. Several proposals have been received including a need for definitions of pharmacokinetics and pharmacodynamics. Any further comments should be sent to EUCAST via Cornelia Hasselmann (FAX +49 89 8971 2004, Email Cornelia.Hasselmann@t-online.de) An NCCLS group has been set up to consider whether a joint document might be appropriate. It is intended that a revised version will be produced next year.

Abbreviations and codes for antimicrobials have been published in the Newsletter of the International Society of Chemotherapy (June 1997 & January 1998) and comments on these have been invited. A common coding system would be useful both for labelling of disks and for use in Journals. The NCCLS also have a group investigating acronyms. Anne Harris noted that coding relates to official names, which are controlled by three different authorities, and different coding systems are used by disk manufacturers who are reluctant to change long-established codes. Also ASM have a list of acronyms which is widely used in Journals. Dr Bob Badal (Microscan, USA) reported that manufacturers are looking at standardisation, particularly with regard to new agents.

6.2 **Breakpoints** (Co-ordinators Professor Ian Phillips & Dr John Degener)

Professor Phillips reported that a draft document on the procedure for setting breakpoints had been produced and distributed first to members of the Breakpoint Sub-committee and then to all members of EUCAST. Anyone who would like a copy should contact Cornelia Hasselmann. It is intended that the document will be published as a tentative document in CMI. The NCCLS have a similar document and copyright issues are being discussed with NCCLS.

There have been no formal requests for production of European breakpoints from any pharmaceutical company but older agents are being worked on based on data from national groups. Data for discussion will be released as soon as possible. Professor John Degener suggested that priorities need to be identified for newer agents.

Professor Pente Huovenen asked about the status of disc diffusion methods and standardisation of the results of disc diffusion methods. Professor Phillips felt that a reference MIC method should be produced for Europe and that the performance of national disk diffusion methods will need to be related to results with the reference MIC method. The limited value of restricted range MICs was noted because many organisms have MICs recorded as less than the lowest value or greater than the highest value in the restricted range. Dr Fred Goldstein summarised the required data for setting breakpoints, ie MIC distributions,

pharmacokinetic data and comparisons of existing breakpoints.

The breakpoint group will meet in the near future.

6.3 **Dilution methods** (Co-ordinator Professor Bernd Wiedemann)

In the absence of Professor Wiedemann, Dr Brown reported that dilution methods are important because they are the reference to which other methods are related. It is intended that reference microdilution and agar dilution methods will be defined by EUCAST. A draft agar dilution method was sent to EUCAST members for comment about two months ago and several comments have been received. It is intended that a tentative document will be published later this year.

Professor Houvenen asked how close the method was to the NCCLS method. Dr Brown replied that it is very similar with the exception of blood+NAD supplementation for *H. influenzae* and in details for methicillin/oxacillin susceptibility testing of *S. aureus*. Professor Tom Bergan asked that the method should be as close to NCCLS as possible to avoid the undesirable situation of two reference methods.

6.4 **Intracellular pathogens** (Co-ordinator Dr Geoff Ridgway)

Dr Ridgway reported that a document will be produced with several contributors. Professor J.C. P  ch  re will write a section on pharmacokinetic considerations, Mr D. Felmingham on *Legionella*, Professor D. Raoult on *Rickettsia*, Bartonellaceae and related organisms, Professor E Rubenstein on *Brucella*, Professor C B  b  or on mycoplasmas and Dr G. Ridgeway on *Chlamydia*. When the sections have been combined a report will be submitted to EUCAST.

Professor Phillips mentioned that other ESCMID groups will have an interest in this area and Dr Ridgway invited them to contact him directly. Professor Phillips asked if these organisms were covered by NCCLS and Dr Ferraro replied that they were not and could be an area for collaboration between EUCAST and NCCLS.

6.5 **Mycobacteria** (Co-ordinator Dr Francis Drobniowski)

Dr Drobniowski reviewed his approach to producing a draft position paper on this area. The major agencies are expert groups at the WHO, the International Union Against Tuberculosis and the European Society for Mycobacteriology. The heads of the various national agencies for mycobacteria will be meeting in June and their views will be sought. Details of different systems will be reviewed including manual, semi-automated and automated methods. The three basic standardised approaches are the absolute concentration method, the resistance ratio method, and the 1% proportion method. A vast body of clinical data is available validating results of in-vitro tests. Reproducibility studies involving reference laboratories have produced good results whereas studies in small laboratories have shown poor reproducibility. An ongoing WHO international study involving 24 super-national reference centres has shown reproducibility among these laboratories to be good. There is also a network involving 51 laboratories in Europe. Genotypic methods are also being developed.

6.6 **Fungi** (Co-ordinator Dr Jean-Luis Rodriguez-Tudela)

Dr Rodriguez-Tudela reported that the approach to antifungal testing follows the NCCLS M27-A method as close as possible but there are several problems. The

yeasts will be divided into fermentative and non-fermentative organisms as *Cryptococcus neoformans* does not grow without agitation or oxygen. Filamentous fungi will be dealt with separately. A microdilution method will be used and details were reviewed.

Dr H Mauerich reported that a DIN method is to be published soon and Dr Rodriguez-Tudela agreed to look at that. Dr Rodriguez-Tudela is also in contact with the chairman of the NCCLS antifungal group.

6.7 **Automated methods** (Co-ordinator Professor Raymond Auckenthaler)

Professor Auckenthaler reported that the sub-committee has only recently been formed. He requested representatives of system manufacturers Microscan and Phoenix, together with pharmaceutical companies and suggested Professor Krasemann (Bayer), Anne Harris (Glaxo) and Dr André Bryskier (HRP). The requirement is to define the automated systems and define a procedure for evaluation including strains with specific resistance mechanisms.

Anne Harris noted that the availability of new agents for development in automated systems is often difficult at an early stage because only small quantities of the agent may be produced. Dr Anne Butler from TREK Diagnostics (Sensititre) offered to join the sub-committee.

6.8 **Molecular Methods** (Co-ordinator Professor Peter Hawkey)

Professor Hawkey reported that this sub-committee had only just been set up and four members have met before this meeting. The membership was listed and the importance of input from commercial sources was emphasised. The intention is to produce a position paper outlining the current scope and limitations of molecular methods, and possibly define standard methods. There are two approaches to molecular methods, an organism/mechanism approach and a methodological approach and both will be needed. Overlap with other groups such as the Mycobacterial Sub-committee will need to be avoided. Account must be taken of the rapid commercial developments which are in progress, as well as the methods published by research groups in individual laboratories. There are differences in the use of molecular methods in the research and epidemiological areas as opposed to their use in the management of individual patients.

Professor Hawkey invited input from members of EUCAST and from any interested commercial sources. A survey of methods in Europe will be undertaken and EUCAST national representatives may be asked to distribute this. It is planned to produce a draft report later this year and perhaps subsequently produce performance standards, organise laboratory studies to test the standards, and encourage studies of the clinical correlation and relevance of results of molecular methods.

Professor Phillips emphasised the importance of links with other groups including the ESCMID diagnostic groups and groups in the USA. Dr Ferraro commented that there are NCCLS groups for molecular methods in virology and diagnostics, and molecular methods are being considered by the antimicrobial susceptibility testing group. Professor Phillips also mentioned that there are other groups in Europe with whom activities should be co-ordinated.

6.9 **Quality Assurance** (Co-ordinator Dr Derek Brown)

Dr Brown listed the Sub-committee membership. Most of the recognised control strains are of limited value in testing performance of methods as they are largely susceptible to antimicrobial agents. The group aims to collect an extended set of strains with different susceptibilities and different resistance mechanisms. The problems of assembling and maintaining such a collection were outlined. The susceptibility of the strains will be defined by the EUCAST reference dilution methods (agar dilution and broth microdilution). The performance of routine methods used in Europe, or any other method, could then be compared in relation to the standard method by testing the extended set of strains. Criteria for routine control of susceptibility tests will be examined with a view to producing guidelines for use of control strains and possibly examining whether results with sensitive control strains can provide useful information on differences among methods. The use of "expert rules" can improve the quality of routine testing and many of the rules are not specific to particular methods, so a list of such rules will be produced. The input of device manufacturers, some of whom have extensive rule bases in their systems, was invited.

Anne Harris reported that generally MICs of ATCC control strains are similar in different methods and such comparisons might be the basis of examination of similarities among methods, although it is recognised that such data give no indication of the performance of methods with organisms having specific resistance mechanisms.

Dr Fred Tenover reported that several years ago CDC established sets of Gram-positive (100 strains) and Gram-negative (180 strains) organisms for device manufacturers to test methods. The sets can be purchased from CDC. Limited numbers of sets of 50 pneumococci and 50 enterococci have also been produced. Dr Brown suggested that as maintenance and supply of an extended set of strains would be a large amount of work it would be appropriate for them to be deposited in a culture collection so they are widely available and Dr Tenover agreed to talk further about this. Prof Baquero felt that the collection was key to comparisons among methods and that there should be co-operation between the Quality Assurance and Breakpoint Committees, and with NCCLS. Dr Badel emphasised the value of control strains with reduced susceptibility. It was agreed to distribute a draft document, now being produced by the Quality Assurance Sub-committee, on a collection of strains **[ACTION Derek Brown]**.

Dr Drobniowski raised the issue of safety of sending resistant control strains, particularly category 3 organisms, to countries where there are no resistant strains at present, and asked what would be the legal liability if that strain subsequently caused infections. Professor Auchenthaler also expressed concerns about sending out highly resistant organisms. Dr Brown felt that it was important to distinguish between sending such strains as unknown quality assessment (proficiency testing) strains, and making them available as known strains with defined resistances. Prof Baquero also stated that it is necessary to distinguish between the small number of strains used for routine quality control and the extended set with various known resistances for testing new systems. Advice on liability will be sought from the Director of the UK Quality Assessment Scheme **[ACTION Derek Brown]**. Dr Tenover reported that, through the WHO, resistant strains have been widely distributed but strains selected are low pathogenicity and not multi-resistant. Dr Tenover also emphasised the difference between unknown strains sent for proficiency testing and strains with known

specific resistances used to test methods.

- 6.10 Professor Phillips suggested that an issue of the Newsletter later this year should give an update on the activities of the sub-committees.

## **7 NCCLS**

Professor Phillips reported that he had been to two meetings of NCCLS in the last year. The objective is to co-ordinate our activities with those of the NCCLS. Dr Ferraro explained that NCCLS meetings are open to all. Professor Phillips has also attended a meeting of the Prudent Use of Antibiotics Group although there was nothing specific to report.

## **8 Finance**

Professor Phillips reported that support for travel to NCCLS meetings had been obtained specifically for that purpose. EUCAST is very grateful for funds donated by some commercial sources and it is intended that these will be used to provide some support for sub-committees. More will be needed and Professor Phillips will continue with fundraising.

## **9 Any other business**

- 9.1 Professor Phillips had a request from the organisers of the ECCMID 2000, in Stockholm next May, for ideas for a symposium. Following discussion it was agreed to offer a forum session on breakpoints and suggest that other Sub-committees might also offer symposia [**ACTION Derek Brown**].

- 9.2 Next meeting of the Main Committee will be at ECCMID 2000, Stockholm, May 28-31, 2000.