EUCAST at the ECCMID 1999 in Berlin

Main Committee Meeting, March 24, 1999, at the 9th European Congress of Clinical Microbiology and Infectious Diseases, Berlin, Germany

The meeting was attended by 26 members of the main committee and 39 observers. This newsletter is based largely on the discussions held at the meeting. The main business of the meeting consisted of reports presented by the subcommittee coordinators; updated summaries of these are given here.

EUCAST at the ECCMID 2000 in Stockholm

Plenary Meeting

The next plenary meeting of EUCAST will be held at the 10th ECCMID in Stockholm, 28-31 May 2000. ECCMID will also provide an opportunity for subcommittees to meet.

Round Table Discussion

At the 10th ECCMID in Stockholm, 28-31 May 2000, EUCAST will hold a round table discussion entitled

“Standardisation of Breakpoints for Antimicrobial Susceptibility Testing”.

The session chairmen will be

Prof. John Degener and Prof. Ian Phillips,
coordinators of the EUCAST breakpoint subcommittee.

The following speakers are scheduled:

I. Phillips Microbiological considerations for setting breakpoints.
J.W. Mouton Pharmacological considerations for setting breakpoints.
R. Pallares Significance of in-vitro resistance of Streptococcus pneumoniae; clinical considerations for setting breakpoints.
F. Goldstein Standardisation of breakpoints in France.
J.E. Degener Standardisation of breakpoints in the Netherlands.
Main Committee

The EUCAST main committee membership as of March 24, 1999, is listed below. Nominations for representatives of countries where no official representative is listed should be sent to Prof. Ian Phillips at the EUCAST office.

Country representatives

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Pharmaceutical industry representatives

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Device manufacturers representatives

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Original ESCMID committee members not in other categories

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<td>Prof. Fernando Baquero</td>
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Please send your nominations for representatives from Albania, Belarus, Bosnia-Herzegovina, Latvia, Lithuania or Luxemburg to:

**EUCAST Secretariat**
Cornelia Hasselmann
Martin-Buber-Weg 17
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Phone: + 49-89-8971 20 03
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e-mail: Cornelia.Hasselmann@t-online.de

It is essential that representatives are well recognised nationally by clinical microbiologists and infectious diseases specialists.
EUCAST Subcommittees

Several subcommittees have been established thus far. We hope people will see that this is a very ambitious programme and will appreciate the reasons for our slow, but we believe steady, progress.

Activity has been carried out largely by means of correspondence, partly because we feel that this is appropriate for much of the work, and partly because of financial constraints. Some subcommittees will need to actually meet, rather than correspond, to achieve greater depth of discussion. We should also aim to publish as soon as possible, but the material must be adequately prepared. We shall do so despite difficulties that sometimes very few of us seem to appreciate, but which are becoming overcome.

Fax numbers and E-mail addresses are given for subcommittee coordinators, who would welcome any contribution or comment on the activities of their subcommittees.

Breakpoints Subcommittee

Coordinators: Prof. John Degener
Fax: +31-50-363 35 28
E-mail: J.E.Degener@med.rug.nl

The aim of this subcommittee is to design a standard method to determine susceptibility breakpoints for antibiotics. These breakpoints should be used uniformly in the European Community. When, in addition, consensus is reached on the test methodology, and quality control procedures are established, it should be possible to reach a good level of comparability of the interpretation of test results derived from medical microbiology laboratories within the European Community. Apart from the epidemiological interest, there is an urgent need for such consensus, since the approval of antimicrobial drugs is now conferred centrally by the European Medicines Evaluation Agency (EMEA). Part of the approval requires documentation of the interpretation of antimicrobial susceptibility test results.

A draft document on breakpoint determination has been produced and circulated to EUCAST members for comment. This document is directed at those responsible for producing information on which breakpoints can be determined by the breakpoints group, and is similar to the MIC-based sections of NCCLS M-23. The draft will be published soon. Furthermore, a paper is being prepared on a reference MIC method.

Comparison of MIC distributions for common organisms and common antibiotics, based on information obtained in different parts of Europe, is being undertaken as part of the process of harmonisation of breakpoints. Data received to date from different countries, even though based on different MIC methodologies, shows striking similarities. These findings will, in the future, be helpful in determining common breakpoints as far as these are allowed to be based on microbiological population analysis.

We are trying to promote a multicentre study of MICs determined in parallel on Mueller-Hinton and Iso-Sensitest media for a collection of organisms with well-characterised resistance mechanisms. This is a major project, ideally using an internationally accepted set of strains, which might then provide candidates for better quality control strains as well as demonstrate the comparative performance of the two media for common, non-fastidious (at least, initially) organisms.

The subcommittee is preparing an open EUCAST round table discussion on the different aspects of breakpoint determination. The meeting will take place during the ECCMID in Stockholm in May 2000.

There is a need to meet more frequently than annually, and members have been asked to investigate sources of funding, including their own institutions or personal sponsors.

Intracellular Pathogens Subcommittee

Coordinator: Dr. Geoff Ridgway
Fax: +44 171 388 8514
E-mail: g.ridgway@academic.uclh.nthames.nhs.uk

A document is being produced with contributions as follows. Prof. J.C. Péchère will write a section on pharmacokinetic considerations, Mr. D. Felmingham on Legionella, Prof. D. Raoult on Rickettsia, Bartonellaceae and related organisms, Prof. E. Rubenstein on Brucella, Prof. C. Bébéar on mycoplasmas and Dr. G. Ridgeway on Chlamydia. Any individuals or groups with an interest in this area are invited to contact Dr. Ridgway directly.
EUCAST Subcommittees continued

Terminology Subcommittee

Coordinator: Prof. Ian Phillips
Fax: + 44-171-735 24 89
E-mail: phillips@escmid.freeserve.co.uk

The EUCAST discussion document has now been published as a definitive document. "Methods for the determination of susceptibility of bacteria to antimicrobial agents. Terminology" appeared in Clinical Microbiology and Infection (1998;5:291-296) with an invitation for proposals for revision. Several proposals have been received, including one that pointed out the need for definitions of pharmacokinetics and pharmacodynamics. Any further comments should be sent to EUCAST via Cornelia Hasselmann (Fax: +49-89-89 71 20 04, E-mail Cornelia.Hasselmann@t-online.de). A considerable amount of correspondence will be reviewed; suggested revisions will be circulated to the breakpoints subcommittee initially and then to EUCAST. A vote on formal agreement will be held at the next EUCAST meeting at the 10th ECCMID, May 2000, in Stockholm. An NCCLS group has been set up to consider whether a joint document might be appropriate.

Dilution Methods Subcommittee

Coordinator: Prof. Bernd Wiedemann
Fax: + 49-228-73 52 67
E-mail: unc301@ibm.rhrz.uni-bonn.de

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 description of a proposed agar dilution method was sent to EUCAST members for comment earlier this year, and several comments have been received. It is intended that a tentative document will be published soon. Following further discussion of this document, a vote to ratify it as a definitive document will be held at the next EUCAST meeting at the 10th ECCMID, May 2000, in Stockholm.

Mycobacteria Subcommittee

Coordinator: Dr. Francis Drobniewski
Fax: +44 181 346 6477
E-mail: francis.drobniewski@kcl.ac.uk

Dr. Drobniewski is producing a draft position paper. The views of major agencies in this area—expert groups at the WHO, the International Union Against Tuberculosis and the European Society for Mycobacteriology—will be sought. The position paper will include the following points. 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 supernational 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.
Fungi Subcommittee

Coordinator: Dr. Juan-Luis Rodriguez-Tudela
Fax: +34 91 509 7966
E-mail: juanl.rodriguez-tudela@isciii.es

The subcommittee met on 22 July 1999. The subcommittee will be expanded to give greater geographical representation, and reciprocal representation with the NCCLS will be sought. The approach to antifungal testing will follow the NCCLS methods as closely as possible. The yeasts will include Candida spp. (draft method at an advanced stage), non-fermentative organisms such as Cryptococcus neoformans (work underway to establish a reference method) and other fermentative yeasts. Filamentous fungi will be dealt with separately. A microdilution method will be used, with photometric reading for yeasts. Sources of variation in testing will be examined. Collaborative work on quality control strains and establishment of breakpoints is proposed. Potential sources of funding for subcommittee activities are being pursued.

Automated Methods Subcommittee

Coordinator: Prof. Raymond Auckenthaler
Fax: +41 22 372 73 04
E-mail: raymond.auckenthaler@hcuge.ch

The subcommittee has only recently been formed. Representatives of system manufacturers and pharmaceutical companies are needed, and individuals will be invited to participate.

The objective is to define the automated systems and to define an optimal procedure for evaluation including strains with specific resistance mechanisms.

Molecular Methods Subcommittee

Coordinator: Prof. Peter Hawkey
Fax: +44 113 233 5649
E-mail: p.m.hawkey@leeds.ac.uk

Since this subcommittee has only recently been set up, the importance of input from commercial sources was emphasised. The intention is to produce a position paper that outlines the current scope and limitations of molecular methods and, possibly, defines 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 subcommittee 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 between the use of molecular methods in research and epidemiological areas and their use in the management of individual patients.

Input is invited 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, to produce performance standards, organise laboratory studies to test the standards, and encourage studies of the clinical correlation and relevance of results of molecular methods. The importance of links with other groups, including the ESCMID diagnostic groups and groups in the USA, is recognised.
EUCAST Subcommittees continued

Quality Assurance Subcommittee

Coordinator: Dr. Derek Brown
Fax: +44 1223 242775
E-mail: dfjb2@cam.ac.uk

The group aims to establish a collection of reference strains. Most of the recognised control strains are of limited value in testing performance of methods because they are largely susceptible to antimicrobial agents.

An extended set of strains with different susceptibilities and different resistance mechanisms is required. 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 of any other method, could then be compared in relation to the standard method by testing the extended set of strains.

It is intended to examine criteria for routine control of susceptibility with a view to producing guidelines for use of control strains and, possibly, to examine whether results obtained with sensitive control strains can provide useful information on differences among methods.

The use of “expert rules” can improve the quality of routine testing. Because many of the rules are not specific to particular methods, a list of such rules will be produced. The input of device manufacturers, some of whom have extensive rule bases in their systems, is invited.

Finance

EUCAST is very grateful for funds or travel expenses from the following commercial sources. It is intended that these funds will be used to provide some resources for subcommittees. More will be needed, and support for specific EUCAST activities is being sought.

AB Biodisk, Sweden
Bayer AG, Germany
bioMérieux, France
Oxoid Ltd, UK
Pfizer Central Research, UK
Sanofi Diagnostics Pasteur, France
SmithKline Beecham, UK
Zeneca, UK
NCCLS Subcommittee on Antimicrobial Susceptibility Testing

13-15 June 1999, Reston, VA, USA

Once again, I attended the meeting of the Subcommittee as one of the 16 advisers, all of whom, with the exception of Bob Rennie from Canada and myself from Europe, are from the USA, as are the 12 voting members. The very efficient Mary Jane Ferraro serves as the Subcommittee's Chairholder.

These meetings always start with Working Groups on the previous day, but on this occasion I was unable to attend them. The subjects discussed included text revision of M2-A, M7-A5 and M23-A2, all due out next year; Stenotrophomonas and Burkholderia; recording and reporting antimicrobial susceptibility data; fastidious organisms; anaerobes; and quality control. Members were all therefore well prepared for the full meeting on the following day.

The meeting included the usual complement of requests for MIC and disk quality control ranges – for cefditoren, cefotaxime and pneumococci, gatifloxacin and gonococci, clinafloxacin and P. aeruginosa, and daptomycin – and there was the usual complement of minor variation from requested ranges in final decisions. The fastidious organisms group report gave rise to prolonged debate on beta-lactam breakpoints for pneumococci, and especially on penicillin. In the end, the latter was left at 0.06, 0.12-1.0 and 2, on the grounds that current confusion might be better than that resulting from site-specific (i.e. meningitis and possibly otitis) breakpoints. Clearly this is not the end of the story, which we too should debate at our next meeting in Stockholm. The anaerobe group is clearly concerned about the comparative performance of Brucella and Wilkens Chalgren broths and was made aware of problems experienced in Europe, communicated to me by Prof. Dubreul. There was also discussion on MRSA QC strains ATCC 43300 and 33591, the former of which does not grow well but which offers a more stringent test. More discussion is to follow, as I understood the conclusion!

The next meeting of the subcommittee will be in Orlando (not my favourite city!) on 9-11 January 2000.

After the meeting and subsequently, I discussed with Dr. Ferraro our intention to publish a document on an agar dilution MIC reference method (recently circulated to EUCAST members) to further our own consultation process, and our wish to produce a document on breakpoint determination (which EUCAST members have already seen) as similar to relevant sections of their M23 as possible without running into copyright problems. I hope to have information on this soon.

Ian Phillips, Chairman EUCAST

Workshop on Achieving Consensus in Antimicrobial Susceptibility Testing

21st International Congress of Chemotherapy, 4-7 July 1999, Birmingham, UK

This ICC workshop brought together Mary Jane Ferraro, NCCLS Subcommittee Chairholder, Ann Harris of Glaxo Wellcome, my-self as Chairman of EUCAST, and about 40 participants to discuss progress in achieving consensus on susceptibility testing.

I started by outlining the activities of EUCAST in trying to get agreement on MIC reference methods. Mary Jane talked about the role of NCCLS and its attempts to work with us. Ann outlined the needs of the pharmaceutical industry for a consistent approach to surveillance, breakpoint determination and drug licensing. Although there was impatience with the pace of our activities, there was general support for our approach, including our attempts to document agreement where it already exists. There is a need to include colleagues in parts of the world other than Europe and North America in our discussions.

Ian Phillips, Chairman EUCAST