

EUCAST Report

EUCAST (the European Committee on Antimicrobial Susceptibility Testing) and its Subcommittee on Antifungal Susceptibility Testing (EUCAST AFST) is convened by ESCMID and the European national breakpoint committees in France, Germany, the Netherlands, Norway, Sweden, and the United Kingdom. It is financed by ESCMID and the national breakpoint committees and by a grant received from DG Sanco of the European Union. EUCAST has four Steering Committee meetings and one General Committee meeting per year. EUCAST activities cover: harmonising breakpoints for existing drugs; setting breakpoints for new antibacterial and antifungal drugs; collecting multiple distributions of MIC values for any antimicrobial agent and species to be published on the EUCAST website for antimicrobial MIC wild type distributions; and collaborating with ESCMID study groups, EARSS, the EMEA, NCCLS and the pharmaceutical and susceptibility testing device manufacturing industries. Further details are given on websites run by EUCAST (see www.eucast.org). Here we briefly present some of our recent activities.

BREAKPOINTS FINALISED FOR AMINOGLYCOSIDES, FLUOROQUINOLONES, GLYCOPEPTIDES AND LINEZOLID

At the Steering Committee meeting held in conjunction with the 15th ESCMID in Prague, May 2004, EUCAST finalised a first set of common European breakpoints. Several rounds of consultation with the EUCAST General Committee, the pharmaceutical industry and antimicrobial susceptibility testing manufacturers were concluded in preparation for the Steering Committee meeting where consensus was reached. The EUCAST breakpoints are available on the EUCAST website (www.eucast.org). EUCAST has commenced work on harmonisation of breakpoints for cephalosporins, the carbapenems and aztreonam. Again we urge anyone in possession of MIC distributions for any of the drugs in these or any other groups or for any bacterial species to contribute them to the EUCAST database. Please contact the chairman of EUCAST.

BREAKPOINT TABLES

The EUCAST breakpoint tables, as exemplified by fluoroquinolones in Figure 1, are organised in such a way that each class of drugs has its own table. EUCAST may decide to omit a drug from a class table, usually because the drug is only marketed in one or two countries, in which case the user is referred to the national breakpoint committee of that country. From the breakpoint table the user can directly access the internet-based EUCAST MIC wild type distribution programme. Later this year the user will also be able to reach the drug-specific documents indicating the rationale for the breakpoint decisions made by EUCAST. The breakpoints are organised according to species or groups of species and the organisation of the table is the same irrespective of drug class. A dash signifies that the drug in question cannot be expected to have any useful activity against the species. The letters IE indicate "insufficient evidence" and suggest the lack of any formal indication and/or insufficient evidence to set a breakpoint. The breakpoints are given in the format 0.5/0.5 (interpreted as $S \leq 0.5$ mg/L, $R > 0.5$ mg/L).

CHANGES TO EUCAST CONSTITUTION 2004

To improve our channels of information and to clarify how EUCAST is

funded, a number of changes were made to the EUCAST constitution, which is available on the EUCAST website.

COLLABORATION BETWEEN EUCAST, EMEA AND THE PHARMACEUTICAL INDUSTRY IS BEING EXPLORED

A formalised collaboration between EUCAST, EMEA, and the pharmaceutical industry is being explored. The goal is to identify a procedure to allow EUCAST to formally address the question of breakpoints in the process of registration of new antimicrobial drugs. A preliminary standard operating procedure is being discussed among the three parties.

DOCUMENTS DESCRIBING THE RATIONALE BEHIND BREAKPOINT DECISIONS TO BE PUBLISHED ON WEBSITE

The rationale behind each of the EUCAST breakpoint decisions will be published on the website in 2004. Background data has been obtained from scientific papers, the six national breakpoint committees, experts within and outside the EUCAST Steering Committee and General Committee, the pharmaceutical industry, antimicrobial resistance surveillance organisations and national reference laboratories. In setting breakpoints the Steer-

Fluoroquinolones - EUCAST clinical MIC breakpoints

| Fluoroquinolone ¹ | Species related breakpoints (S/R) ² | | | | | | | | | | No. species related breakpoints by EC ⁷ | |
|------------------------------|--|--------------------------|----------------------------|-----------------------------|---------------------------|------------------------------------|---------------------------------|-----------------------------|---------------------------------|----------------------------|--|-------|
| | Enterobacteriaceae ³ | Pseudomonas ³ | Acinetobacter ³ | Staphylococcus ³ | Enterococcus ³ | Streptococcus A,B,G,I ³ | Enterobacteriaceae ³ | Staphylococcus ³ | Enterobacteriaceae ³ | Streptococcus ³ | | |
| Ciprofloxacin | 0.5/1 | 0.5/1 | 1/1 | 1/1 | — | — | 0.125/2 | 0.5/0.5 | 0.030/0.030 | 0.030/0.05 | — | 0.5/1 |
| Letrofloxacin | 1/2 | 1/2 | 1/2 | 1/2 | — | 1/2 | 2/2 | 1/1 | IE | IE | IE | 1/2 |
| Moxifloxacin | 0.5/1 | — | — | IE | — | IE | 0.5/0.5 | 0.5/0.5 | IE | IE | IE | 0.5/1 |
| Norfloxacin | 0.5/1 | — | — | — | — | — | — | — | IE | — | — | 0.5/1 |
| Ofloxacin | 0.5/1 | — | — | 1/1 | — | — | 0.125/4 | 0.5/0.5 | 0.120/25 | IE | — | 0.5/1 |

1. For breakpoints for other fluoroquinolones (eg. gatifloxacin and sarafloxacin) - refer to breakpoints determined by national breakpoint committees.
 2. Enterobacteriaceae spp.: there is clinical evidence for significance to indicate a poor response in systemic infections caused by Enterobacteriaceae spp. exhibiting low fluoroquinolone resistance (MIC < 0.016 mg/L).
 3. Staphylococcus spp.: breakpoints for ciprofloxacin and ofloxacin relate to high dose therapy.
 4. Staphylococcus pneumoniae - all type 3 pneumonias are not considered susceptible to ciprofloxacin or ofloxacin and are therefore categorized as non-susceptible. For ofloxacin the S/R breakpoint was increased from 1/2 to 4/0 mg/L, and for ciprofloxacin the S/R breakpoint from 1/2 to 2/0 to avoid using the wild type MIC distribution. The breakpoints for bedaquiline relate to high dose therapy.
 5. Streptococcus pneumoniae - fluoroquinolone low-level resistance (parfloxacin MICs of 0.125-0.5 mg/L) may occur in N. meningitis. There is no evidence that low-level resistance is of clinical importance in respiratory tract infections with N. meningitis. An intermediate category was not defined since only few clinically resistant strains have been reported.
 6. Resistant pneumonias: breakpoints apply to the use of ofloxacin in the prophylaxis of meningococcal disease.
 7. Non-species related breakpoints have been determined mainly on the basis of PK/PD data and are independent of MIC distributions of specific species. They are for use only for species that have not been given a species-specific breakpoint and not for those species where susceptibility testing is not recommended (marked with - or IE in the table).
 — = Susceptibility testing not recommended as the species is a poor target for therapy with the drug.
 IE = There is insufficient evidence that the species is a good target for therapy with the drug.
 Breakpoints finalized at EUCAST Steering committee meeting 2004-04-09

EUCAST 2003 (The European Committee on Antimicrobial Susceptibility Testing)
 Updated 2004-05-11, G. Hoogkamp

Figure 1: EUCAST breakpoint table for fluoroquinolones (www.eucast.org)

ing Committee, in collaboration with the national breakpoint committees, has followed the procedure set down in the EUCAST document European antimicrobial MIC breakpoints through EUCAST and the National Breakpoint Committees, which is available on the EUCAST website.

EUCAST DOCUMENTS

Discussion Documents will no longer be printed as inserts in Clinical Microbiology and Infection. From now on they will be published on the EUCAST website for at least 3 months, during which comments will be invited. Definitive documents will continue to be published in CMI and will also be available on the EUCAST website.

FUNDING OF EUCAST

EUCAST is funded by the national breakpoint committees of France, Germany, Norway, Sweden, the Netherlands and the United Kingdom, the ESCMID and, since May 2004, by a grant from DG Sanco of the European Union. The available funds cover EUCAST Steering Committee meetings (four meetings per year), activities of the EUCAST AFST, website activities and two workshops in 2005 and 2006.

POWERPOINT PRESENTATION OF EUCAST TO GO ON WEBSITE

The Steering Committee is preparing a PowerPoint presentation of EUCAST to go on the EUCAST website. It should provide an opportunity to present to audiences the ongoing process of harmonising European breakpoints. It can be run on the website or be downloaded from the website. The presentation will be updated regularly.

REFERENCE METHODOLOGY FOR MIC DETERMINATION THROUGH CEN AND ISO

Following an initiative in CEN, and through an ensuing collaboration between CEN and ISO, a joint international reference method for the determination of MIC in non-fastidious microorganisms will be published. It will be based on the broth microdilution method already published by EUCAST and NCCLS.

SUBCOMMITTEE ON ANTIFUNGAL SUSCEPTIBILITY TESTING (AFST)

The AFST is continuing its excellent work by setting European breakpoints for *Candida* species. Wild type MIC distributions are being collected and will eventually be made available on the EUCAST website. The EUCAST document Determination of minimum inhibitory concentrations by broth microdilution of fermentative yeasts will now be submitted for publication in CMI as a Definitive Document.

EUCAST SUSCEPTIBILITY DEFINITIONS

The EUCAST definitions of clinical and epidemiological categories of susceptibility are shown in Table 1.

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Table 1: EUCAST definitions of susceptibility categories and breakpoints

Clinical Susceptibility Categories and Breakpoints

Clinically Susceptible (S)

- a micro-organism is defined as susceptible by a level of antimicrobial activity associated with a high likelihood of therapeutic success.
- a micro-organism is categorized as susceptible (S) by applying the appropriate breakpoint in a defined phenotypic test system.

Clinically Intermediate (I)

- a micro-organism is defined as intermediate by a level of antimicrobial activity associated with indeterminate therapeutic effect.
- a micro-organism is categorized as intermediate (I) by applying the appropriate breakpoints in a defined phenotypic test system.

Clinically Resistant (R)

- a micro-organism is defined as resistant by a level of antimicrobial activity associated with a high likelihood of therapeutic failure.
- a micro-organism is categorized as resistant (R) by applying the appropriate breakpoint in a defined phenotypic test system.

Clinical breakpoints may be altered with legitimate changes in circumstances. Clinical breakpoints are presented as $S < x$ mg/L; $I > x, < y$ mg/L; $R > y$ mg/L

Epidemiological Susceptibility Categories and Cut-off Values

Wild type (WT)

- a micro-organism is defined as wild type (WT) for a species by the absence of acquired and mutational resistance mechanisms to the drug in question.
- a micro-organism is categorized as wild type (WT) for a species by applying the appropriate cut-off value in a defined phenotypic test system.
- wild type micro-organisms may or may not respond clinically to antimicrobial treatment.

Microbiological resistance - Non-Wild Type (NWT)

- a micro-organism is defined as non-wild type (NWT) for a species by the presence of an acquired or mutational resistance mechanism to the drug in question.
- a micro-organism is categorized as non-wild type (NWT) for a species by applying the appropriate cut-off value in a defined phenotypic test system.
- non-wild type micro-organisms may or may not respond clinically to antimicrobial treatment.

Epidemiological cut off values will not be altered by changing circumstances. The wild type is presented as $WT < z$ mg/L and non-wild type as $NWT > z$ mg/L