Update zu EUCAST 2012

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Agenda

1. Breakpoints
2. Rationale documents and technical notes
3. website (www.eucast.org)

Revision of E.DEF 7.1 → E.DEF 7.2 (susceptibility testing of yeasts)

- DMSO recommended as solvent for caspofungin, micafungin and fluconazole.
- Shelf life microtitre plates extended to 6 months at -80 ˚C
- *Cryptococcus* included (incubation time 48-72 hours at 35 ˚C (30 ˚C if insufficient growth)
- QC ranges provided for anidulafungin and *C. krusei* ATCC 6258, *C. parapsilosis* ATCC 22019

Breakpoints in 2011-12

- *Aspergillus* and amphotericin
- *Aspergillus* and itraconazole
- *Aspergillus* and posaconazole

Rationale Doc.s and combined TN submitted to CMI

- *Aspergillus* and voriconazole - Discussion document

EUCAST-AFST documents

Reference Methods

- Yeast
  - **E.DEF 7.2 (2012)**
  - **TN- E.DEF 7.2 (In Press)**
  - E.DEF 7.1 (2008)
  - TN- E.DEF 7.1 (2008)
- Conidia forming moulds
  - E.DEF 9.1 (2008)
  - TN-E.DEF 9.1 (2008)

Breakpoints

Compound	*Candida*		*Aspergillus*	
	Rationale Doc	Techn. Note CMI	Rationale Doc	Techn. Note CMI
Amphotericin	2010	**2011**	**2012**	**Submitted ***
Anidulafungin	2010	**2011**		
Fluconazole	2007	2008	-	-
Itraconazole			**2012**	**Submitted ***
Posaconazole	2010	**2011**	**2012**	**Submitted ***
Voriconazole	2008	2008	**Discussion Doc.**	

Aspergillus spp.

EUCAST Antifungal Clinical Breakpoint Table v. 4.1, valid from 2012-03-05

MIC method (EUCAST standardised broth microdilution method)
Medium: RPMI1640-2% glucose, MOPS as buffer
Inoculum: Final 1x10(5) – 2.5x10(5) cfu/mL
Incubation: 48h
Reading: Visual
Quality control: *A. fumigatus* ATCC 204305, *A. flavus* ATCC 204304, *A. fumigatus* F 6919, *A. flavus* CM 1813, *C. parapsilosis* ATCC 22019 (read after 18-24 h) or *C. krusei* ATCC 6258 (read after 18-24 h)

Antifungal agent	MIC breakpoint (mg/L)												Notes
	A. flavus		*A. fumigatus*		*A. nidulans*		*A. niger*		*A. terreus*		Non-species related breakpoints[1]		
	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	
													1. 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 organisms that do not have specific breakpoints.
Amphotericin B	IE[2]	IE[2]	1	2	Note[3]	Note[3]	1	2	-	-	IE	IE	**2.** The ECOFFs for these species are in general one step higher than for *A. fumigatus.* **3.** There are too few MIC data to establish ECOFFs and hence to suggest any breakpoints.
Anidulafungin	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	
Caspofungin	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	
Fluconazole	-	-	-	-	-	-	-	-	-	-	-	-	
Itraconazole[4]	1	2	1	2	1	2	IE[2,5]	IE[2,5]	1	2	IE[5]	IE[5]	**4.** Monitoring of itraconazole trough concentrations in patients treated for fungal infection is recommended. **5.** The MIC values for isolates of *A. niger* and *A. versicolor* are in general higher than those for *A. fumigatus*. Whether this translates into a poorer clinical response is unknown.
Micafungin	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	
Posaconazole	IE[2]	IE[2]	0.12[6]	0.25[6]	IE[2]	IE[2]	IE[2]	IE[2]	0.12[6]	0.25[6]	IE	IE	**6.** Provided adequate drug exposure has been confirmed using therapeutic drug monitoring (TDM). There remains some uncertainty regarding cut-off values for posaconazole concentrations that separate patients with a high probability of clinical success from those with a low probability of clinical success. In some circumstances (e.g. patients with persistent and profound neutropenia, large lesions, or those with other features associated with a poor clinical outcome) a relatively high trough concentration should be sought. Preclinical and clinical data suggest this value should be >1 mg/L at steady state. For other patient groups a lower trough concentration may be acceptable. For prophylaxis a target concentration of >0.7 mg/L has been suggested.
Voriconazole	IP	IP	IP	IP	IP	IP	IP	IP	IP	IP	IP	IP	

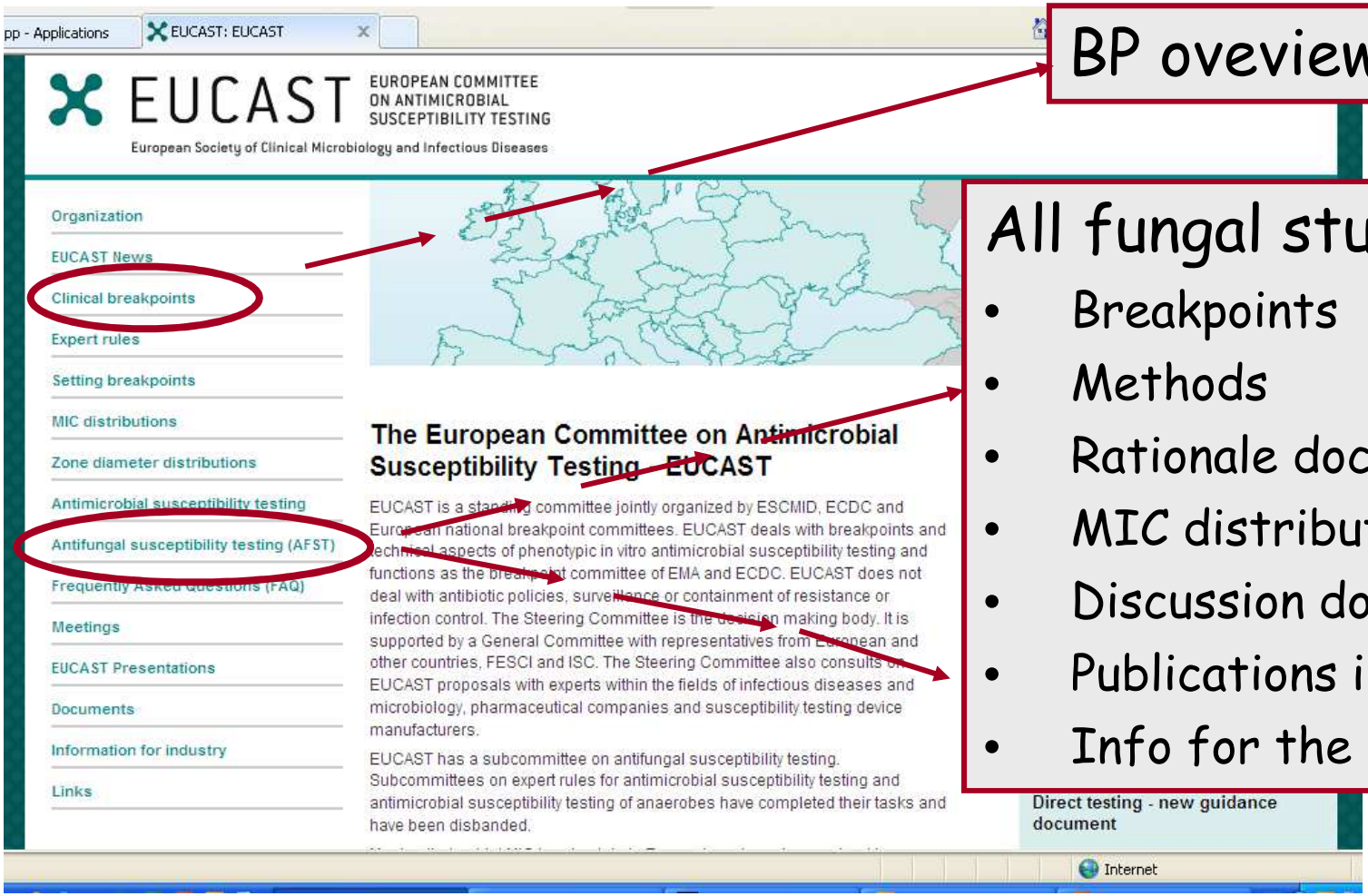
Candida spp.

EUCAST Antifungal Clinical Breakpoint Table v. 4.1, valid from 2012-03-05

MIC method (EUCAST standardised broth microdilution method)
Medium: RPMI1640-2% glucose, MOPS buffer
Inoculum: Final $0.5x10^5$ – $2.5x10^5$ cfu/mL
Incubation: 18-24h
Reading: Spectrophotometric, full inhibition for amphotericin B but 50% growth inhibition for other compounds
Quality control: *C. parapsilosis* ATCC 22019 or *C. krusei* ATCC 6258

Antifungal agent	MIC breakpoint (mg/L)														Notes
	C. albicans		*C. glabrata*		*C. krusei*		*C. parapsilosis*		*C. tropicalis*		*C. guillermondii*		Non-species related breakpoints[1]		
	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	
															1. 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 organisms that do not have specific breakpoints.
Amphotericin B	1	1	1	1	1	1	1	1	1	1	IE	IE	IE	IE	
Anidulafungin	0,03	0,03	0,06	0,06	0,06	0,06	-	-	0,06	0,06	IE[2]	IE[2]	IE	IE	**2.** The ECOFFs for these species are in general higher than for *C. albicans*.
Caspofungin	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	-	-	Note[3]	Note[3]	IE[2]	IE[2]	IE	IE	**3.** Due to significant inter-laboratory variation in MIC ranges for caspofungin, EUCAST breakpoints have not yet been established.
Fluconazole	2	4	IE[2]	IE[2]	-	-	2	4	2	4	IE[2]	IE[2]	2	4	
Itraconazole	IP	IP	IP	IP	IP	IP	IP	IP	IP	IP	IP	IP	IP	IP	
Micafungin	IP	IP	IP	IP	IP	IP	-	-	IP	IP	IE[2]	IE[2]	IP	IP	
Posaconazole	0,06	0,06	IE[2]	IE[2]	IE[2]	IE[2]	0,06	0,06	0,06	0,06	IE[2]	IE[2]	IE	IE	
Voriconazole	0.12[4]	0.12[4]	IE	IE	IE	IE	0.12[4]	0.12[4]	0.12[4]	0.12[4]	IE[2]	IE[2]	IE	IE	**4.** Strains with MIC values above the S/I breakpoint are rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC above the current resistant breakpoint (in italics) they should be reported resistant.

- Web site update



BP oveview tables

All fungal stuff

- Breakpoints
- Methods
- Rationale doc. for BPs
- MIC distributions
- Discussion documents
- Publications in Journals
- Info for the industry

- Voriconazole Aspergillus RD
- Breakpoint for Micafungin and *Candida*
    - Collecting MICs for ECOFF determinations
- Isavuconacole
    - Collecting MICs for ECOFF determinations
- *Aspergillus* – echinocandin testing
- Remaining BPs
  - *Candida* and itraconazole
  - *Candida* and topical agents
- Systematic revision of existing documents