# Empfindlichkeitstestung bei Pilzen – Neuigkeiten? Bericht aus einem EUCAST AFST (yeasts and moulds) Netzwerk-Laboratorium

EUCAST reloaded 6.0
Follow-up Workshop
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# A brief history of antifungal susceptibility testing standardization

1982 Established subcommittee

1986 Develop reproducible method

1992 M27-P method introduced

1997 M27-A method introduced

20% hospitals performing testing for yeast; intra/inter-laboratory agreement poor

Synthetic medium (RPMI)
Broth-based method
0.5-2.5 x$10^3$

Breakpoints


Higher glucose;
24 hour endpoint;
spectrophotometer

2002 M38-A

Conidia forming filamentous fungi

2004 M44-A

Disk-diffusion Method-yeast

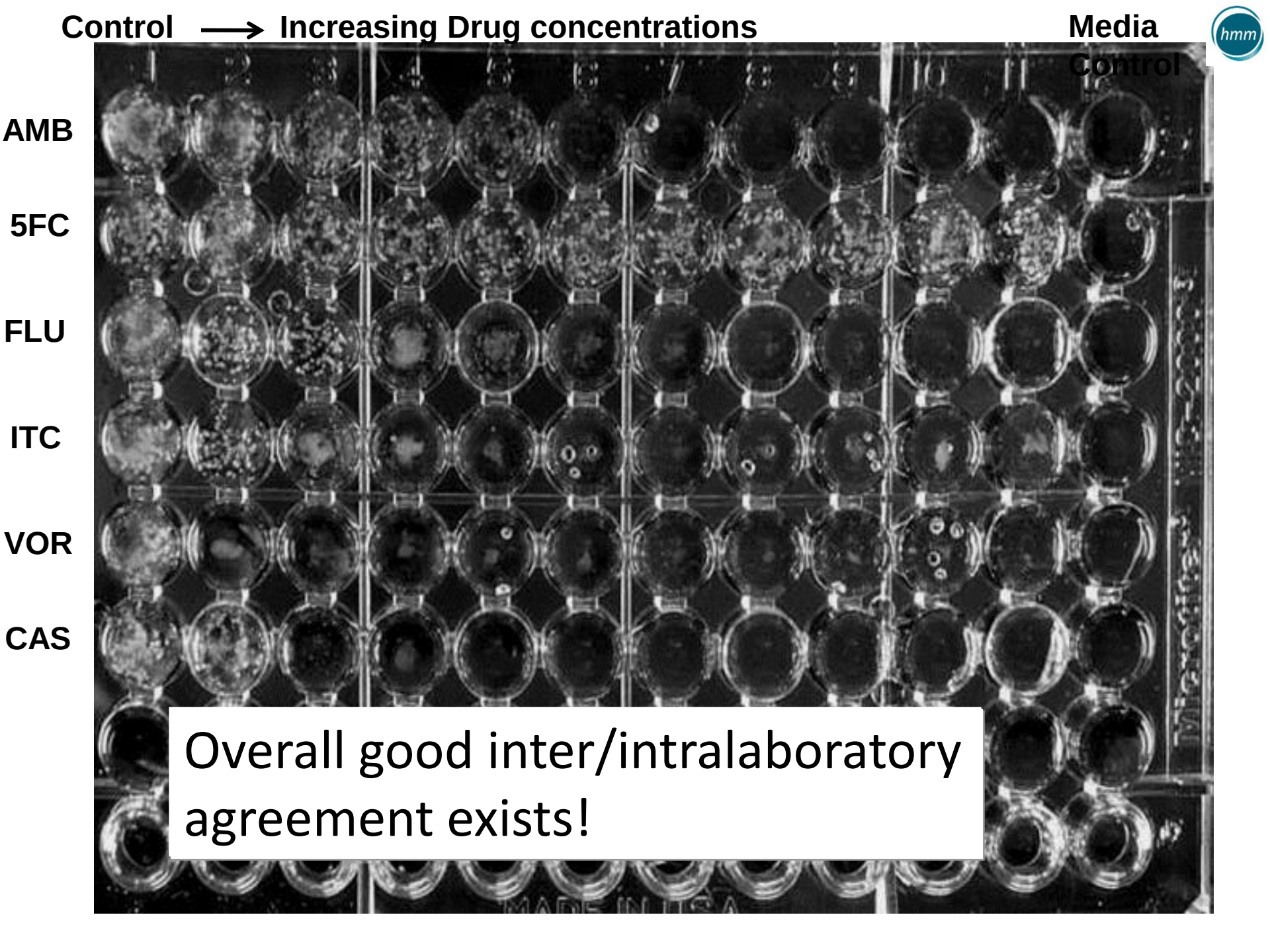
2009

Disk-diffusion method-moulds

Fothergill et al. Infect DisClin N Amer 2006;20:699-709.

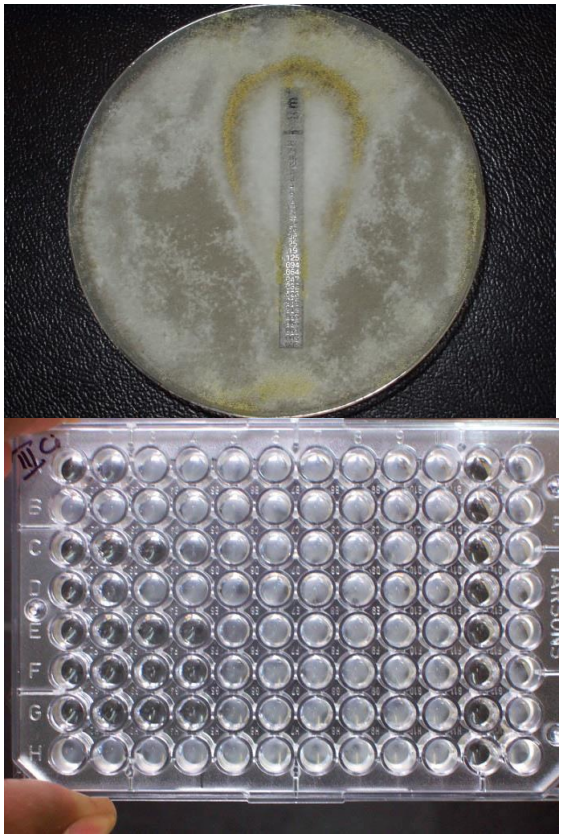
# Reference Methods

| Characteristics | CLSI M27-A3 | EUCAST Def |
|---|---|---|
| Suitability | Yeasts | Fermentative Yeast |
| Inoculum | 0.5-2.5x$10^3$ CFU/ml | 0.5-2.5x$10^5$ CFU/ml |
| Test medium | RPMI 1640 0,2%G | RPMI 1640 G2% |
| Format | Microdilution | Microdiluation |
| Temperature | 35°C | 35°C |
| Duration of incubation | 46-50h<br>24 h for yeasts | 24h |
| Endpoint | 80% inhibition M27-A2<br>50% inhibition M27-A3 (azole) | 80% amphotericin B<br>50% inhibition azole |
| Reading | Visually | Plate reader |


Control ⟶ Increasing Drug concentrations
Media Control
AMB
5FC
FLU
ITC
VOR
CAS
Overall good inter/intralaboratory agreement exists!

# ……MICs obtained differ from method to method!

- **Medium (type, brand, batch)**
  - CLSI vs. EUCAST: glucose conc. 0.2% vs. 2%
- **Inoculum size**
  - the higher  the higher the MIC
- **Inoculum growth phase**
  - the shorter the lag phase  the higher the MIC
- **Incubation temperature**
  - affects growth rate, expression of res mechanisms
- **Incubation time**
  - the longer  the higher the MIC
- **Definition of endpoint (50%, 80%, 100% inhibition)**
  - the more stringent  the higher the MIC
- **Reading variation**
  - visual vs. spectrophotometric
  - trailing
- **Biology of the fungus**



Lass-Flörl et al., 2015

# CLSI versus EUCAST

Breakpoints (BPs): S: ≤X; R:>Y  Revised BPs

| CLSI M27-S3 | | CLSI revised (M27-S4) | | | EUCAST | |
|---|---|---|---|---|---|---|
| **AMB** | ≤1 | ≤1 | | | ≤1;>1 | |
| **ANF** | ≤2 | ≤0.25 | >0.5 | (alb, krus, trop) | ≤0.032; >0.032 | (alb) |
| | | ≤0.125 | >0.25 | (glab) | ≤0.06;>0.06 | (glab, krus, trop) |
| | | ≤2; > 4 | | (para, guillier) | | (para poor target, guillier IE) |
| **CSF** | ≤2 | | | | | |
| **MFG** | ≤2 | ≤0.25; | >0.5 | (alb, krus, trop) | ≤0.016; >0.016 | (alb) |
| | | ≤0.06; | >0.125 | (glab) | ≤0.03; >0.03 | (glab) |
| | | ≤2; | >4 | (para, guillier) | ≤0.02; >2 | (para, krus IE, trop IE, guillier IE) |
| **Fluco** | ≤8; >32 | ≤2; | >4 | (alb, para, trop) | ≤2; >4 | (alb, trop, para) |
| | | SDD ≤32; | >32 | (glab) | | (glab IE) |
| | | | | (krus poor target) | | (krus poor target) |
| **Vori** | ≤1; >2 | ≤0.125; | >0.5 | (alb, para, trop) | ≤0.125; >0.125 | (alb, trop, para) |
| | | ≤0.5; | >1 | (krus) | | (glab/krus IE) |
| | | | | (glab IE) | | |
| **Itra** | ≤0.125; > 0.5 | ≤0.125; | >0.5 | | - | |
| **Posa** | - | | | | ≤0.06; >0.06 | (alb, trop, para) |
| | | | | | | (glab/krus IE) |

www.eucast.org; Pfaller Drug Resist Updat. 2010 & 2011

:MC Arendrup (Chair) WW Hope (Secretary), M. Cuenca-Estrella & C. Lass-Flörl

Organization
EUCAST News
Clinical breakpoints
Expert rules and intrinsic resistance
Resistance mechanisms
Guidance documents
Consultations
MIC distributions and ECOFFs
Zone distributions and ECOFFs
AST of bacteria
AST of mycobacteria
AST of fungi
- Clinical AFST breakpoints
- MIC distributions and ECOFFs
- Methods in antifungal susceptibility
- QC AFST Tables
- Rationale documents for antifungals
- Documents for discussion in AFST
- Publications in journals
- Meetings and Minutes
- Previous versions of documents

AST of veterinary pathogens
Frequently Asked Questions (FAQ)
Meetings
Presentations and statistics

Antifungal susceptibility testing (AFST

# Antifungal susceptibility testing (AFST)

Methods for susceptibility testing of Candida, Aspergillus and other fungi are developed and validated by the EUCAST subcommittee on AFST.

New and revised documents open for consultation will until accepted be published in the → EUCAST News section together with all other consultations from EUCAST.

Information on subcommittee organisation and members are available on the webpage describing the → Organisation of EUCAST.

Information for industry aiming to bring agents to EUCAST for review and revision of breakpoints or a new agent to EMA for registration is available at → Information for industry.

Development of new methods and validation and calibration of existing methods is performed at the EUCAST Development Laboratory for AFST:
→ The EUCAST Development Laboratory for Antifungal Susceptibility Testing
with the help of
→ The EUCAST AFST Network Laboratories

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- **EUCAST method for susceptibility testing of yeasts** (v 7.3.1 valid from 15 January, 2017).

- **EUCAST method for susceptibility testing of moulds** (version 9.3.1 valid from 15 January, 2017)

- **Routine and extended internal quality control for antifungal susceptibility** as recommended by EUCAST Version 1.0, valid from 2015-11-04

http://www.eucast.org/ast_of_fungi/methodsinantifungalsusceptibilitytesting/susceptibility_testing_of_moulds/

## Epidemiological Cut off (ECOFF)

Define upper limit of “wild type” MIC distribution – no acquired resistance mechanisms

Cutoffs help detecting the emergence of reduced susceptibility (acquired resistance) in the absence of clinical breakpoints - or “in addition to” clinical breakpoints

Helps identify organisms requiring further characterization

In vivo /in vitro correlation?

### Clinical Breakpoint

CBPs are used to indicate those isolates that are likely to respond to treatment with a given antimicrobial agent administered at the approved dosing regimen for that agent

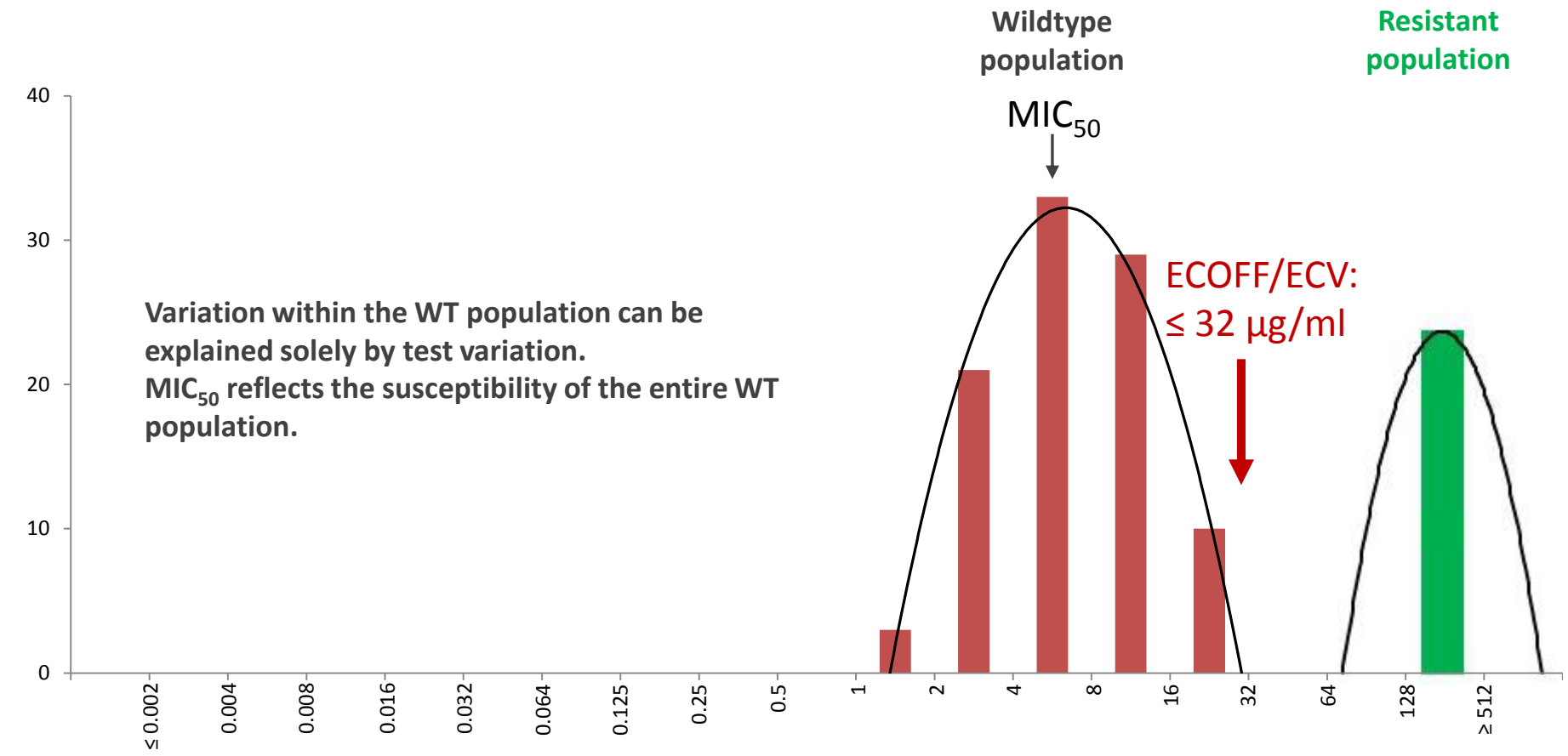
What is you experience?

CBPs are missing for most drug-bug combinations

Turnidge J, Paterson DL. Clin Microbiol Rev. 2007; 20: 391

# E.g. EUCAST fluconazole MIC C. glabrata

## Fluconazole / Candida glabrata EUCAST
## Antimicrobial wild type distributions of microorganisms – reference database
## EUCAST MIC Distribution




807 observations (12 data sources)
Clinical breakpoints

http://www.eucast.org/mic_distrubitions_of_wild_type_microorganisms/

**Breakpoint (BP).** Specific values of MICs on the basis of which fungi can be assigned to the clinical categories „susceptible“, „intermediate“ and „resistant“. The breakpoints can be altered due to changes in circumstances (e.g. changes in commonly used drug dosages) or when additional data/knowledge emerges.

a) **Susceptible (S).** A mould is defined as susceptible by a level of antimicrobial activity associated with a high likelihood of therapeutic success.
b) **Intermediate (I).** A mould is defined as intermediate by a level of antimicrobial activity associated with a high likelihood of therapeutic success but only when a higher dosage of the agent than normal can be used or when the agent is physiologically concentrated at the site of infection.
c) **Resistant (R).** A mould is defined as resistant by a level of antimicrobial activity associated with a high likelihood of therapeutic failure.

**Wild type (WT).** A mould isolate is defined as WT for a species by the absence of phenotypically detectable acquired and mutational resistance mechanisms to the agent in question.

**Non-wild type (NWT).** A mould isolate is defined as NWT for a species by the presence of phenotypically detectable acquired or mutational resistance mechanisms to the agent in question.

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## 1. Technical notes on susceptibility testing of fungi

EUCAST DEFINITIVE DOCUMENT E.DEF 9.1: Method for the determination of broth dilution minimum inhibitory concentrations of antifungal agents for conidia forming mould
EUCAST technical note on the EUCAST definitive document EDef 7.2: method for the determination of broth dilution minimum inhibitory concentrations of antifungal agents for yeasts EDef 7.2 (EUCAST-AFST).

EUCAST Definitive Document EDef 7.1: method for the determination of broth dilution MICs of antifungal agents for fermentative yeasts

## 2. Technical notes on antifungal breakpoints

**Breakpoints for *Candida***
Amphotericin B
Voriconazole
Posaconazole
Micafungin, anidulafungin and fluconazole
**Breakpoints for *Aspergillus***
Amphotericin B, itraconazole, and posaconazole
Voriconazole

# Species-specific EUCAST ECOFFs and breakpoints (mg/L) for isavuconazole and itraconazole against *Aspergillus* and *Candida* species, respectively

| Species | ECOFF (mg/L) | Clinical breakpoints [a] (mg/L) | |
|---|---|---|---|
| | | S ≤ | R > |
| **Isavuconazole** | | | |
| *A. flavus* | 2 | IE[b] | IE[b] |
| *A. fumigatus* | 2 | 1 | 1 |
| *A. nidulans* | 0.25 | 0.25 | 0.25 |
| *A. niger* | 4 | IE[b] | IE[b] |
| *A. terreus* | 1 | 1 | 1 |
| **Itraconazole** | | | |
| *C. albicans* | 0.06 | 0.06 | 0.06 |
| *C. dubliniensis* | 0.06 | 0.06 | 0.06 |
| *C. glabrata* | 2 | IE[b] | IE[b] |
| *C. guilliermondii* | 2 | IE[b] | IE[b] |
| *C. krusei* | 1 | IE[b] | IE[b] |
| *C. lusitaniae* | 0.125 | 0.125 | 0.125 |
| *C. parapsilosis* | 0.125 | 0.125 | 0.125 |
| *C. tropicalis* | 0.125 | 0.125 | 0.125 |

ECOFF, epidemiological cutoff value; EUCAST, European Committee on Antimicrobial Susceptibility Testing; MIC, minimum inhibitory concentration.

[a] For simplicity, the intermediate category is not listed. It is readily interpreted as the values between the S and the R breakpoint. For MIC breakpoints listed as S ≤ 1 and R > 1, there is no intermediate category. There is insufficient clinical evidence to set breakpoints for other species than those listed.

[b] The MIC values are in general higher than those for *A. fumigatus* and *C. albicans*, respectively. Whether this translates into a poorer clinical response is unknown. There is insufficient evidence (IE) to set breakpoints for these species.

Arendrup et al, CMI 2016;22:571

# Acceptable MIC ranges (mg/L) of antifungal agents for quality control strains

| Antifungal agent | *Candida krusei* ATCC 6258 | *Candida parapsilosis* ATCC 22019 | *Candida albicans* CL-CNM F 8555 | *Candida krusei* CL-CNM CL3403 |
|---|---|---|---|---|
| Amphotericin B | 0.12–1.0 | 0.12–1.0 | 0.06–0.5 | 0.25–1.0 |
| Flucytosine | 1.0–4.0 | 0.12–0.5 | 0.06–0.25 | 2.0–8.0 |
| Fluconazole | 16.0–64.0 | 0.5–2.0 | 32.0–128.0 | 16.0–64.0 |
| Isavuconazole | 0.015–0.06 | ≤0.015–0.03 | NA | NA |
| Itraconazole | 0.03–0.12 | 0.03–0.12 | 0.25–1.0 | 0.12–0.5 |
| Voriconazole | 0.03–0.25 | 0.015–0.06 | 0.5–2.0 | 0.12–0.5 |
| Posaconazole | 0.015–0.06 | 0.015–0.06 | 0.12–0.5 | 0.06–0.25 |
| Caspofungin | NA | NA | NA | NA |
| Anidulafungin | 0.015–0.06 | 0.25–1.0 | NA | NA |
| Micafungin | 0.03–0.125 | 0.5–2 | NA | NA |

ATCC, American Type Culture Collection; CL-CNM, yeast collection of the Spanish National Centre of Microbiology; MIC, minimum inhibitory concentration; NA, not available.

Arendrup et al, CMI 2016;22:571

# *Candida* spp.

| Antifungal agent | MIC breakpoint (mg/L) | | | | | | | | | | | | | | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *C. albicans* | | *C. glabrata* | | *C. krusei* | | *C. parapsilosis* | | *C. tropicalis* | | *C. guilliermondii* | | Non-species related breakpoints[1] | | |
| | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | S ≤ | R > | |
| Amphotericin B | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | IE | IE | IE | IE | **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. |
| Anidulafungin | 0.032 | 0.032 | 0.064 | 0.064 | 0.064 | 0.064 | 0.002 | 4 | 0.064 | 0.064 | 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] | Note[3] | Note[3] | IE[2] | IE[2] | IE | IE | **3.** Isolates that are susceptible to anidulafungin as well as micafungin should be considered susceptible to caspofungin, until caspofungin breakpoints have been established. Similarly, *C. parapsilosis* isolates intermediate to anidulafungin and micafungin can be regarded intermediate to caspofungin. EUCAST breakpoints have not yet been established for caspofungin, due to significant inter-laboratory variation in MIC ranges for caspofungin. |
| Fluconazole | 2 | 4 | 0.002 | 32 | - | - | 2 | 4 | 2 | 4 | IE[2] | IE[2] | 2 | 4 | |
| Isavuconazole | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | **4.** MICs for *C. tropicalis* are 1-2 two-fold dilution steps higher than for *C. albicans* and *C. glabrata*. In the clinical study successful outcome was numerically slightly lower for *C. tropicalis* than for *C. albicans* at both dosages (100 and 150 mg daily). However, the difference was not significant and whether it translates into a relevant clinical difference is unknown. MICs for *C. krusei* are approximately three two-fold dilution steps higher than those for *C. albicans* and, similarly, those for *C. guilliermondii* are approximately eight two-fold dilutions higher. In addition, only a small number of cases involved these species in the clinical trials. This means there is insufficient evidence to indicate whether the wild-type population of these pathogens can be considered susceptible to micafungin. |
| Itraconazole | 0.064 | 0.064 | IE[2] | IE[2] | IE[2] | IE[2] | 0.125 | 0.125 | 0.125 | 0.125 | IE[2] | IE[2] | IE | IE | |
| Micafungin | 0.016 | 0.016 | 0.032 | 0.032 | IE[4] | IE[4] | 0.002 | 2 | IE[4] | IE[4] | IE[4] | IE[4] | IE | IE | |
| Posaconazole | 0.064 | 0.064 | IE[2] | IE[2] | IE[2] | IE[2] | 0.064 | 0.064 | 0.064 | 0.064 | IE[2] | IE[2] | IE | IE | **5.** Strains with MIC values above the S/I breakpoint are rare or not yet reported. The identification and antifungal 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 they should be reported resistant. |
| Voriconazole | 0.125[5] | 0.125[5] | IE | IE | IE | IE | 0.125[5] | 0.125[5] | 0.125[5] | 0.125[5] | IE[2] | IE[2] | IE | IE | |

http://www.eucast.org/clinical_breakpoints/

# *Aspergillus* spp.

| 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 > | |
| Amphotericin B | IE[2] | IE[2] | 1 | 2 | Note[3] | Note[3] | 1 | 2 | - | - | IE | IE | **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. |
| Anidulafungin | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | **2.** The ECOFFs for these species are in general one step higher than for *A. fumigatus*. |
| Caspofungin | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | **3.** There are too few MIC data to establish ECOFFs and hence to suggest any breakpoints. |
| Fluconazole | - | - | - | - | - | - | - | - | - | - | - | - | **4.** Monitoring of azole trough concentrations in patients treated for fungal infection is recommended. |
| Isavuconazole | IE[2] | IE[2] | 1 | 1 | 0.25 | 0.25 | IE[2] | IE[2] | 1 | 1 | IE | IE | **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. |
| Itraconazole[4] | 1 | 2 | 1 | 2 | 1 | 2 | IE[2,5] | IE[2,5] | 1 | 2 | IE[5] | IE[5] | **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. |
| Micafungin | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | IE | |
| Posaconazole[4] | IE[2] | IE[2] | 0.125[6] | 0.25[6] | IE[2] | IE[2] | IE[2] | IE[2] | 0.125[6] | 0.25[6] | IE | IE | |
| Voriconazole[4] | IE[2] | IE[2] | 1 | 2 | IE | IE | IE[2] | IE[2] | IE[2] | IE[2] | IE | IE | |

http://www.eucast.org/clinical_breakpoints/

# Conclusions

## *in vitro* susceptibility testing:

- **Yeasts**
  - sterile body site
    plus non-*C. albicans*
  - azole (?)
  - non-responder
  - rare species

- **Molds**
  - non *A. fumigatus*
  - all: non responder
  - long treatment & azole
  - rare species

**TABLE 2** In vitro susceptibilities of Candida species to anidulafungin, caspofungin and micafungin determined by EUCAST, ETest and Sensititre after 24 hours including VME, ME and MIN

| Drug and species | Number of isolates | EUCAST MIC | | | ETest MIC | | | Sensititre MIC | | | EA | EA | CA EUCAST | | CA CLSI | | Etest EUCAST | | | ETest CLSI | | | Sensititre EUCAST | | | Sensititre CLSI | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Range | 50% | 90% | Range | 50% | 90% | range | 50% | 90% | Etest | Sensititre | Etest | Sensititre | Etest | Sensititre | VME | ME | MIN | VME | ME | MIN | VME | ME | MIN | VME | ME | MIN |
| Anidulafungin | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Total | 104 | 0,002-0,5 | 0,009 | 0,016 | 0,002-1,5 | 0,003 | 0,016 | 0,015-1 | 0,015 | 0,108 | 97% | 92% | 99% | 93% | 99% | 100% | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 7 | 0 | 0 | 0 | 0 |
| *C. albicans* | 63 | 0,002-0,016 | 0,002 | 0,016 | 0,002-0,006 | 0,003 | 0,004 | 0,015-0,06 | 0,015 | 0,030 | 100% | 100% | 100% | 97% | 100% | 100% | | | | | | | | 2 | | | | |
| *C. dubliniensis* | 2 | 0,002-0,002 | 0,002 | 0,002 | 0,002-0,006 | 0,004 | 0,006 | 0,015-0,12 | 0,068 | 0,110 | 100% | 50% | 100% | 50% | 100% | 100% | | | | | | | | 1 | | | | |
| *C. glabrata* | 18 | 0,002-0,031 | 0,016 | 0,016 | 0,002-0,25 | 0,007 | 0,008 | 0,015-0,12 | 0,015 | 0,030 | 94% | 100% | 94% | 94% | 94% | 100% | | 1 | | | | 1 | | 1 | | | | |
| *C. kefyr* | 1 | 0,016 | 0,016 | 0,016 | 0,016 | 0,016 | 0,016 | 0,015 | 0,015 | 0,015 | 100% | 100% | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| *C. krusei* | 5 | 0,016-0,031 | 0,016 | 0,025 | 0,012-0,023 | 0,016 | 0,020 | 0,03-0,06 | 0,030 | 0,048 | 100% | 100% | 100% | 100% | 100% | 100% | | | | | | | | | | | | |
| *C. lusitaniae* | 1 | 0,016 | 0,016 | 0,016 | 0,032 | 0,032 | 0,032 | 0,12 | 0,120 | 0,120 | 100% | 0% | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| *C. orthopsilosis* | 1 | 0,031 | 0,031 | 0,031 | 0,38 | 0,380 | 0,380 | 0,25 | 0,250 | 0,250 | 0% | 0% | 100% | 100% | 100% | 100% | | | | | | | | | | | | |
| *C. parapsilosis* | 4 | 0,125-0,5 | 0,375 | 0,500 | 0,38-1,5 | 1,000 | 1,350 | 0,5-1 | 0,750 | 1,000 | 75% | 75% | 100% | 100% | 100% | 100% | | | | | | | | | | | | |
| *C. pararugosa* | 1 | 0,002 | 0,002 | 0,002 | 0,032* | 0,032* | 0,032* | 0,06* | 0,06* | 0,06* | 100% | 0% | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| *C. tropicalis* | 8 | 0,002-0,016 | 0,016 | 0,016 | 0,003-0,008 | 0,006 | 0,007 | 0,015-0,12 | 0,060 | 0,120 | 100% | 63% | 100% | 63% | 100% | 100% | | | | | | | | 3 | | | | |
| Caspofungin | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Total | 104 | 0,002-0,25 | 0,031 | 0,063 | 0,023-0,5 | 0,094 | 0,354 | 0,015-0,5 | 0,060 | 0,120 | 74% | 98% | n.a. | n.a. | 92% | 99% | n.a. | n.a. | n.a. | 0 | 0 | 8 | n.a. | n.a. | n.a. | 0 | 0 | 1 |
| *C. albicans* | 63 | 0,002-0,062 | 0,031 | 0,062 | 0,023-0,125 | 0,064 | 0,094 | 0,015-0,06 | 0,060 | 0,090 | 71% | 100% | n.a. | n.a. | 100% | 100% | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |
| *C. dubliniensis* | 2 | 0,031-0,031 | 0,031 | 0,031 | 0,047-0,094 | 0,071 | 0,089 | 0,03-0,12 | 0,075 | 0,111 | 100% | 100% | n.a. | n.a. | 100% | 100% | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |
| *C. glabrata* | 18 | 0,016-0,125 | 0,062 | 0,063 | 0,064-0,38 | 0,125 | 0,190 | 0,03-0,25 | 0,060 | 0,120 | 89% | 100% | n.a. | n.a. | 83% | 94% | n.a. | n.a. | n.a. | | | 3 | n.a. | n.a. | n.a. | | | 1 |
| *C. kefyr* | 1 | 0,031 | 0,031 | 0,031 | 0,023 | 0,023 | 0,023 | n.a. | 0,015 | 0,015 | 100% | 100% | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |
| *C. krusei* | 5 | 0,063-0,125 | 0,125 | 0,125 | 0,38-0,5 | 0,380 | 0,452 | 0,12-0,25 | 0,250 | 0,250 | 60% | 100% | n.a. | n.a. | 0% | 100% | n.a. | n.a. | n.a. | | | 5 | n.a. | n.a. | n.a. | | | |
| *C. lusitaniae* | 1 | 0,063 | 0,063 | 0,063 | 0,25 | 0,250 | 0,250 | n.a. | 0,060 | 0,060 | 100% | 100% | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |
| *C. orthopsilosis* | 1 | 0,031 | 0,031 | 0,031 | 0,38 | 0,380 | 0,380 | n.a. | 0,250 | 0,250 | 0% | 0% | n.a. | n.a. | 100% | 100% | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |
| *C. parapsilosis* | 4 | 0,062-0,25 | 0,125 | 0,213 | 0,38-0,38 | 0,380 | 0,380 | 0,12-0,5 | 0,250 | 0,425 | 75% | 100% | n.a. | n.a. | 100% | 100% | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |
| *C. pararugosa* | 1 | 0,002 | 0,002 | 0,002 | 0,19* | 0,19* | 0,19* | 0,12* | 0,12* | 0,12* | 0% | 0% | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |
| *C. tropicalis* | 8 | 0,016-0,063 | 0,031 | 0,063 | 0,032-0,094 | 0,079 | 0,094 | 0,03-0,06 | 0,060 | 0,060 | 75% | 100% | n.a. | n.a. | 100% | 100% | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |
| Micafungin | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Total | 104 | 0,002-0,25 | 0,002 | 0,016 | 0,003-0,5 | 0,006 | 0,064 | 0,008-1 | 0,015 | 0,060 | 92% | 92% | 99% | 97% | 99% | 100% | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 3 | 0 | 0 | 0 | 0 |
| *C. albicans* | 63 | 0,002-0,016 | 0,002 | 0,016 | 0,003-0,012 | 0,006 | 0,008 | 0,008-0,03 | 0,008 | 0,015 | 100% | 100% | 100% | 98% | 100% | 100% | | | | | | | | 1 | | | | |
| *C. dubliniensis* | 2 | 0,002-0,002 | 0,002 | 0,002 | 0,004-0,008 | 0,006 | 0,008 | 0,015-0,06 | 0,038 | 0,056 | 100% | 100% | 100% | 50% | 100% | 100% | | | | | | | | 1 | | | | |
| *C. glabrata* | 18 | 0,002-0,016 | 0,002 | 0,016 | 0,004-0,064 | 0,006 | 0,008 | 0,008-0,06 | 0,015 | 0,015 | 94% | 100% | 94% | 94% | 94% | 100% | | 1 | | | | 1 | | 1 | | | | |
| *C. kefyr* | 1 | 0,016 | 0,016 | 0,016 | 0,032 | 0,032 | 0,032 | 0,03 | 0,030 | 0,030 | 100% | 100% | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| *C. krusei* | 5 | 0,016-0,062 | 0,016 | 0,043 | 0,064-0,094 | 0,064 | 0,094 | 0,12-0,12 | 0,120 | 0,120 | 20% | 20% | n.a. | n.a. | 100% | 100% | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |
| *C. lusitaniae* | 1 | 0,016 | 0,016 | 0,016 | 0,032 | 0,032 | 0,032 | 0,03 | 0,030 | 0,030 | 100% | 100% | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| *C. orthopsilosis* | 1 | 0,016 | 0,016 | 0,016 | 0,19 | 0,190 | 0,190 | 0,5 | 0,500 | 0,500 | 0% | 0% | 100% | 100% | 100% | 100% | | | | | | | | | | | | |
| *C. parapsilosis* | 4 | 0,062-0,25 | 0,188 | 0,250 | 0,25-0,5 | 0,315 | 0,464 | 0,25-1 | 0,750 | 1,000 | 75% | 50% | 100% | 100% | 100% | 100% | | | | | | | | | | | | |
| *C. pararugosa* | 1 | 0,002 | 0,002 | 0,002 | 0,032* | 0,032* | 0,032* | 0,12* | 0,12* | 0,12* | 100% | 0% | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| *C. tropicalis* | 8 | 0,002-0,016 | 0,016 | 0,016 | 0,008-0,12 | 0,012 | 0,047 | 0,015-0,03 | 0,030 | 0,030 | 88% | 100% | n.a. | n.a. | 100% | 100% | n.a. | n.a. | n.a. | | | | n.a. | n.a. | n.a. | | | |

VME very major error; ME major error; MIN minor error; MIC minimal inhibitory concentration; MIC 50%, 90% MICs for which 50% and 90% of isolates are inhibited; EA essential agreement; CA categorical agreement; n.a. not applicable as no breakpoints defined; *read after 48 hours

ETest® versus Sensititre YeastOne® versus EUCAST
Aigner et al, submission 2017

## Candidämie nach Spezies für die Jahre 2007 bis 2015

| Species | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|---|---|---|---|
| *Candida albicans* | 96 (60,8%) | 95 (57,9%) | 105 (59,3%) | 111 (63,4%) | 95 (55,6%) | 81 (51,9%) | 138 (58,2%) | 106 (58,9%) | 124(54,1%) |
| *Candida glabrata* | 24 (15,2%) | 31 (18,9%) | 28 (15,8%) | 27 (15,4%) | 35 (20,5%) | 32 (20,5%) | 57 (24,1%) | 42 (23,3%) | 40(17,5%) |
| *Candida parapsilosis* | 17 (10,8%) | 12 (7,3%) | 10 (5,6%) | 14 (8%) | 16 (9,4%) | 18 (11,5%) | 12 (5,1%) | 11 (6,1%) | 25(10,9%) |
| *Candida tropicalis* | 7 (4,4%) | 4 (2,4%) | 13 (7,3%) | 10 (5,7%) | 8 (4,7%) | 7 (4,5%) | 12 (5,1%) | 8 (4,4%) | 13 (5,7%) |
| *Candida krusei* | 6 (3,8%) | 5 (3%) | 6 (3,4%) | 5 (2,9%) | 10 (5,8%) | 6 (3,8%) | 9 (3,8%) | 1 (0,6%) | 6 (2,6%) |
| *Candida dubliniensis* | | | 3 (1,7%) | 1 (0,6%) | | 4 (2,6%) | 4 (1,7%) | 2 (1,1%) | 4 (1,7%) |
| *Candida lipolytica* | | | 1 (0,6%) | | | 1 (0,6%) | | | |
| *Candida lusitaniae* | 1 (0,6%) | 5 (3%) | 5 (2,8%) | 1 (0,6%) | 1 (0,6%) | 1 (0,6%) | 2 (0,8%) | 1 (0,6%) | 2 (0,9 %) |
| *Candida orthopsilosis* | | | | | | 1 (0,6%) | | 2 (1,1%) | |
| *Candida pseudotropicalis (kefyr)* | 2 (1,3%) | 1 (0,6%) | | 1 (0,6%) | | 1 (0,6%) | | | |
| *Candida species* | 1 (0,6%) | 3 (1,8%) | | 1 (0,6%) | | 1 (0,6%) | | | |
| *Candida pararugosa* | | | | | | | | | 3 (1,3%) |
| *Candida inconspicua* | | | | | | | | | 2 (0,9%) |
| *Candida kefyr* | | | | | | | | | 2 (0,9%) |
| *Trichosporon mucoides* | | | | | | | | | 1 (0,4%) |
| *Cryptococcus neoformans* | | 2 (1,2%) | | 1 (0,6%) | 2 (1,2%) | 1 (0,6%) | | | 1 (0,4%) |
| *Saccharomyces cerevisae* | | | 1 (0,6%) | | | 1 (0,6%) | 1 (0,4 %) | | 1 (0,4%) |
| *Trichosporon asahii* | | | | 1 (0,6%) | 1 (0,6%) | 1 (0,6%) | | 1 (0,6%) | |
| *Candida famata* | | | 1 (0,6%) | | 1 (0,6%) | | | 1 (0,6%) | 1 (0,4%) |
| *Candida guilliermondii* | 2 (1,3%) | 1 (0,6%) | 1 (0,6%) | 1 (0,6%) | 1 (0,6%) | | | 1 (0,6%) | 3(1,3%) |
| *Candida pelliculosa* | | | | 1 (0,6%) | | | | | 1 (0,4%) |
| *Candida pulcherrima* | 1 (0,6%) | | | | | | | | |
| *Candida rugosa* | 1 (0,6%) | | | | | | 1 (0,4%) | | |
| *Candida sake* | | 4 (2,4%) | | | | | | | |
| *Candida sphaerica* | | 1 (0,6%) | | | | | | | |
| *Candida utilis* | | | | | 1 (0,6%) | | | | |
| *Saccharomyces species* | | | 3 (1,7%) | | | | | 1 (0,6%) | |
| *Geotrichum capitatum* | | | | | | | 1 (0,4%) | | |
| *Candida melibosica* | | | | | | | | 1 (0,6%) | |

**Aures, 2015**

**Resistenzraten nach Substanz für durch Hefepilze verursachte Fungämien von 2007 bis 2015 (EUCAST-Breakpoints)**

| Substanz | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|---|---|---|---|
| AMB | 0,7%(149) | 0%(147) | 0%(159) | 0%(166) | 0%(162) | 0%(137) | 0%(216) | 0%(169) | 0%(183) |
| AND | | 6,7%(45) | 27,9%(68) | 15,2%(79) | 8%(88) | 4,8%(62) | 3,5%(86) | 2,1%(146) | 1,6%(186) |
| MIC | | | | | 15,7%(102) | 16,2%(111) | 15,5%(71) | 17,9%(39) | 4,9%(41) |
| FLU | 6%(150) | 5,8%(156) | 7,2%(166) | 3%(167) | 4,5%(155) | 4,3%(139) | 5%(218) | 1,1%(174) | 4,3%(211) |
| POS | 34,6%(104) | 17,4%(92) | 13,4%(119) | 15,7%(134) | 9,2%(119) | 3,8%(105) | 11,8%(127) | 9,2%(119) | 4,1%(146) |
| VOR | 2,5%(118) | 4,5%(111) | 6,3%(127) | 3%(135) | 4,2%(119) | 2,1%(95) | 2,6%(153) | 0,8%(128) | 3,1%(163) |
| ITR | | | | | | | | 80% (15) | 22,9%(35) |

**Resistenzraten nach Substanz für durch Hefepilze verursachte Fungämien von 2007 bis 2015 (CLSI-Breakpoints)**

| Substanz | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|---|---|---|---|
| CAS | 2,2%(134) | 2,9%(140) | 2,7%(146) | 3,9%(155) | 3,8%(105) | 7,7%(65) | 3,7%(81) | 6,2%(65) | 2,5%(79) |

**Aures, 2015**

**Vielen Dank für Ihre Aufmerksamkeit!**