EUCAST uudised

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KM ja EUCAST sektsiooni koosolek

Expert rules v. 3.2 consultation – kuni 01.04.2019

- The development of new drugs, the emergence and dissemination of resistance mechanisms, the evolution of testing methods for bacterial resistance, and the increased availability of more accurate bacterial identification by methods such as mass spectrometry, have prompted EUCAST to prepare a new version of the expert rules document.
- A revised version of the first part, intrinsic resistances and exceptional phenotypes (v3.1), was published in **September 2016** (http://www.eucast.org/expert_rules_and_intrinsic_resistance/).
- The revision of the second part, the expert rules, has required longer discussion and is presented on EUCAST website for consultation

Expert rules v. 3.2 consultation – kuni 01.04.2019

Enterobacter* spp., *K. aerogenes*, *Citrobacter freundii*, *Hafnia alvei

cefotaxime, ceftriaxone, ceftazidime

IF susceptible in vitro to cefotaxime, ceftriaxone or ceftazidime, THEN EITHER add a note that monotherapy with cefotaxime, ceftriaxone or ceftazidime as well as combination therapy of these agents with an aminoglycoside should be discouraged owing to risk of selecting resistance, OR **suppress the susceptibility testing results for these agents**

Expert rules v. 3.2 consultation

Serratia spp., Morganella morganii, Providencia spp

cefotaxime, ceftriaxone, ceftazidime

IF susceptible to cefotaxime, ceftriaxone or ceftazidime, THEN **note** that **monotherapy** with cefotaxime, ceftriaxone or ceftazidime may **infrequently select resistant mutants**

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Enterobacter spp., K. aerogenes, Citrobacter freundii, Serratia spp., Morganella morganii, Hafnia alvei

Cefuroxime

IF susceptible to cefuroxime, THEN report cefuroxime and/or any other 2nd generation cephalosporin as resistant

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E. coli, Klebsiella spp. (except K. aerogenes), ***Raoultella*** spp.

- IF resistant to any 3rd generation (cefotaxime, ceftriaxone, ceftazidime) or 4th generation (cefepime) cephalosporin AND susceptible to piperacillin-tazobactam or amoxicillin-clavulanic acid, THEN **report as tested**.
- IF resistant to any 3rd generation (cefotaxime, ceftriaxone, ceftazidime) or 4th generation (cefepime) cephalosporin and susceptible to another 3rd or 4th generation cephalosporin THEN **report each as tested and enclose a warning on uncertain therapeutic outcome for infections other than urinary tract infections.**

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Aminoglükosiidid

Enterobacterales

Breakpoints for aminoglycosides are being revised during 2019 after which all rules pertaining to aminoglycosides will be revisited.

Expert rules v. 3.2 consultation

***Salmonella* spp**

- IF tested susceptible to a 2nd generation cephalosporin THEN report as resistant or not at all
- IF tested susceptible to any aminoglycoside, report as resistant

Expert rules v. 3.2 consultation

Enterococcus faecalis, Enterococcus faecium

- IF vancomycin susceptible but vanA is detected by molecular methods THEN report resistant to vancomycin and teicoplanin

- IF vancomycin susceptible but vanB is detected by molecular methods THEN report resistant to vancomycin and add a warning of resistance development to teicoplanin during therapy

Expert rules v. 3.2 consultation

Campylobacter spp.

- IF susceptible to erythromycin THEN report clarithromycin and azithromycin susceptible

- IF resistant to erythromycin THEN report clarithromycin and azithromycin resistant (there are no separate breakpoints for these agents)

Expert rules v. 3.2 consultation

Corynebacterium spp. (except C. diphtheriae)

- IF resistant to erythromycin AND inducibly resistant to clindamycin THEN report as resistant to clindamycin

- IF susceptible to erythromycin, THEN report clindamycin as tested.

ATU kategooria

- Area of Technical Uncertainty (ATU) in antimicrobial susceptibility testing
- The Area of Technical Uncertainty (ATU) is a term coined by EUCAST to warn laboratories of uncertain interpretation of antimicrobial susceptibility testing (AST) results. These may be by MIC determination or disk diffusion using EUCAST methodology and breakpoints.
- The ATU is a warning to laboratory staff that the value is in an area where there are interpretative difficulties. **The reason is that a breakpoint is in a place where reproducible interpretation cannot be achieved.**
- The ATU is not related to uncertainties in the testing procedures although the **natural unavoidable variation in testing** will influence the actions that may need to be taken. The ATU assumes that the test (MIC, inhibition zone diameter) is correctly performed and that the value obtained is correct in itself

ATU kategooria

- If the decision is to act on the warning there are always several alternatives and the appropriateness of each will vary with the sample in which the organism was identified (UTI vs. septicemia), and the number of available antimicrobial alternatives
- The individual laboratory may decide that results in the ATU should prompt laboratory technicians to consult with medical staff.

ATU report - alternatives

- repeat the test – this is only if there is reason to suspect a technical error.
- perform an alternative test (perform an MIC, a PCR, a test to determine the resistance mechanism) – this is relevant when the alternative test is conclusive (PCR to detect a mecA or mecC gene in Staphylococci, a vanA or vanB gene in enterococci).
- report results in the ATU as "uncertain" with a comment:
  - accept and include the interpretation but add a warning to the report
  - leave interpretation blank and add an explanation to the report
  - report results in the ATU as **"R". If there are several good alternatives in the AST report this may be the easiest and safest option**
  - take the opportunity to discuss the results with the clinical colleague

Rapid AST directly from blood culture bottles

- EUCAST has published recommendations for short incubation (4, 6 and 8 hours) AST directly from positive blood culture bottles:

- direct inoculation of disk diffusion plates (MH, MH-F) using 100 - 150 µL directly from a positive blood culture bottle (BD, bioMerieux and Thermo Fisher).
- no centrifugation or dilution of the inoculum - streak plates as for standard EUCAST disk diffusion.
- shortened incubation - 4, 6 and 8 hours with breakpoints adapted to each incubation time.
- zone diameters are read from the front of the plate after removal of the lid.
- breakpoints for each species and each reading time.
- identity of species must be known prior to interpretation of AST results.

Rapid AST directly from blood culture bottles

- the method is **currently validated** for the following species
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Pseudomonas aeruginosa*
  - *Staphylococcus aureus*
  - *Streptococcus pneumoniae*
  - *Enterococcus faecalis* and *Enterococcus faecium*
- ***Ongoing work*** *(to be finalised 2019-20):*
  - *Criteria for Acinetobacter baumannii (2019)*
  - *Interpretive criteria for more antibiotics than those currently available (2019-20).*

Rapid AST directly from blood culture bottles

- a positive blood culture bottle should be processed 0 - **18 hours after the positive signal.**
- each species has its own TAB in the table and each reading time (4, 6 and 8 hours) its own section.
- not all zone diameters can be read after 4 hours. Read again after 6 and 8 hours. Incubation can not be extended over night. If needed, perform a regular AST overnight.
- read zone diameters ONLY when an obvious zone edge can be identified - otherwise re-incubate and read after 6 or 8 hours.
- **the breakpoint table is specific for EUCAST Rapid AST** - do not use the regular breakpoint table and do not use for rapid AST on an inoculum prepared from colonies.

New definitions of S, I and R

- S - Susceptible, standard dosing regimen: A microorganism is categorised as "Susceptible, standard dosing regimen", when there is a high likelihood of therapeutic success using a standard dosing regimen of the agent.
- I – **Susceptible, increased exposure***: A microorganism is categorised as "Susceptible, Increased exposure*" when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.
- R - Resistant: A microorganism is categorised as "Resistant" when there is a high likelihood of therapeutic failure even when there is increased exposure.
- ***Exposure** is a function of how the mode of administration, dose, dosing interval, infusion time, as well as distribution and excretion of the antimicrobial agent will influence the infecting organism at the site of infection.

New definitions of S, I and R

- Eestikeelse termini osas pole siiani kindlat otsust tehtud
- Infektsionistidega arutatud, esialgu lükatud edasi

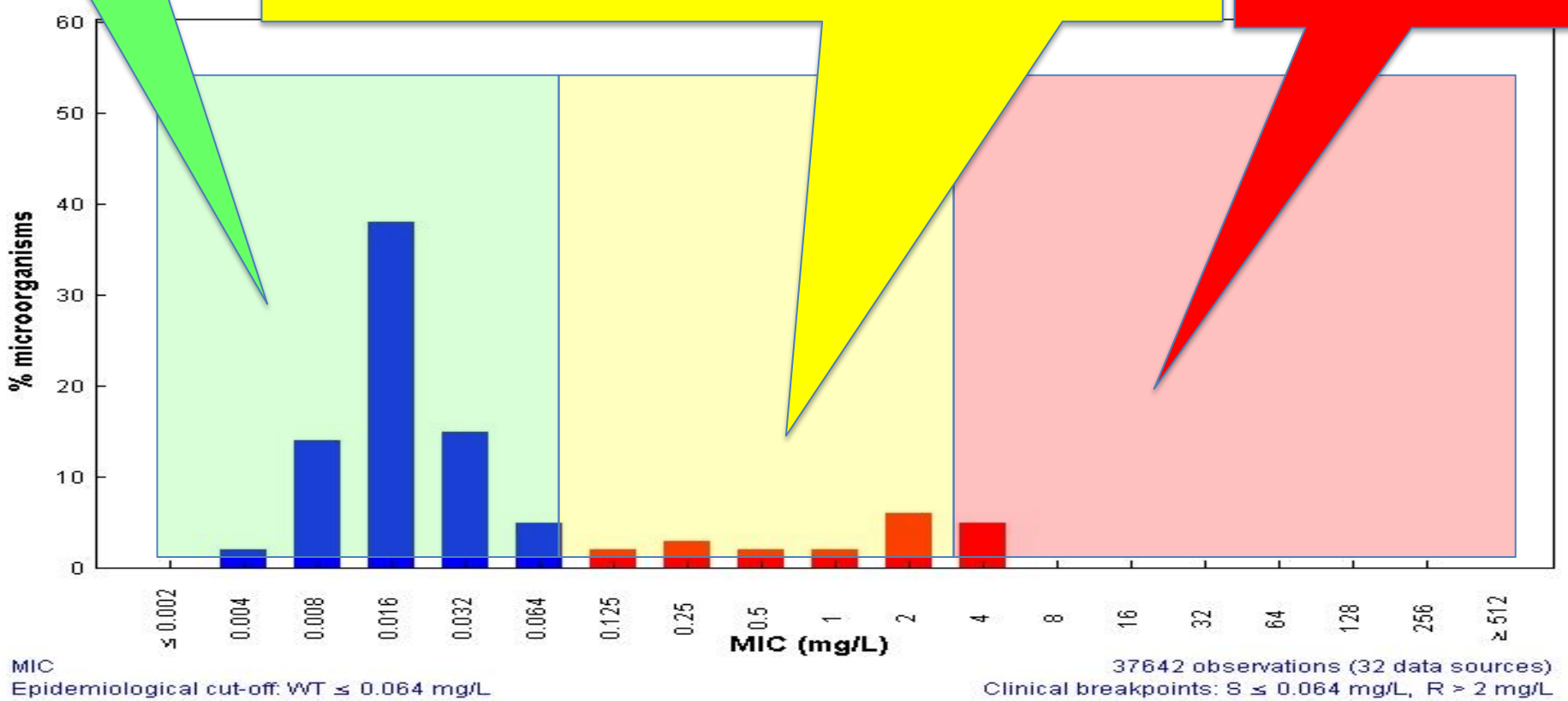
SIR – the old definitions

Susceptible

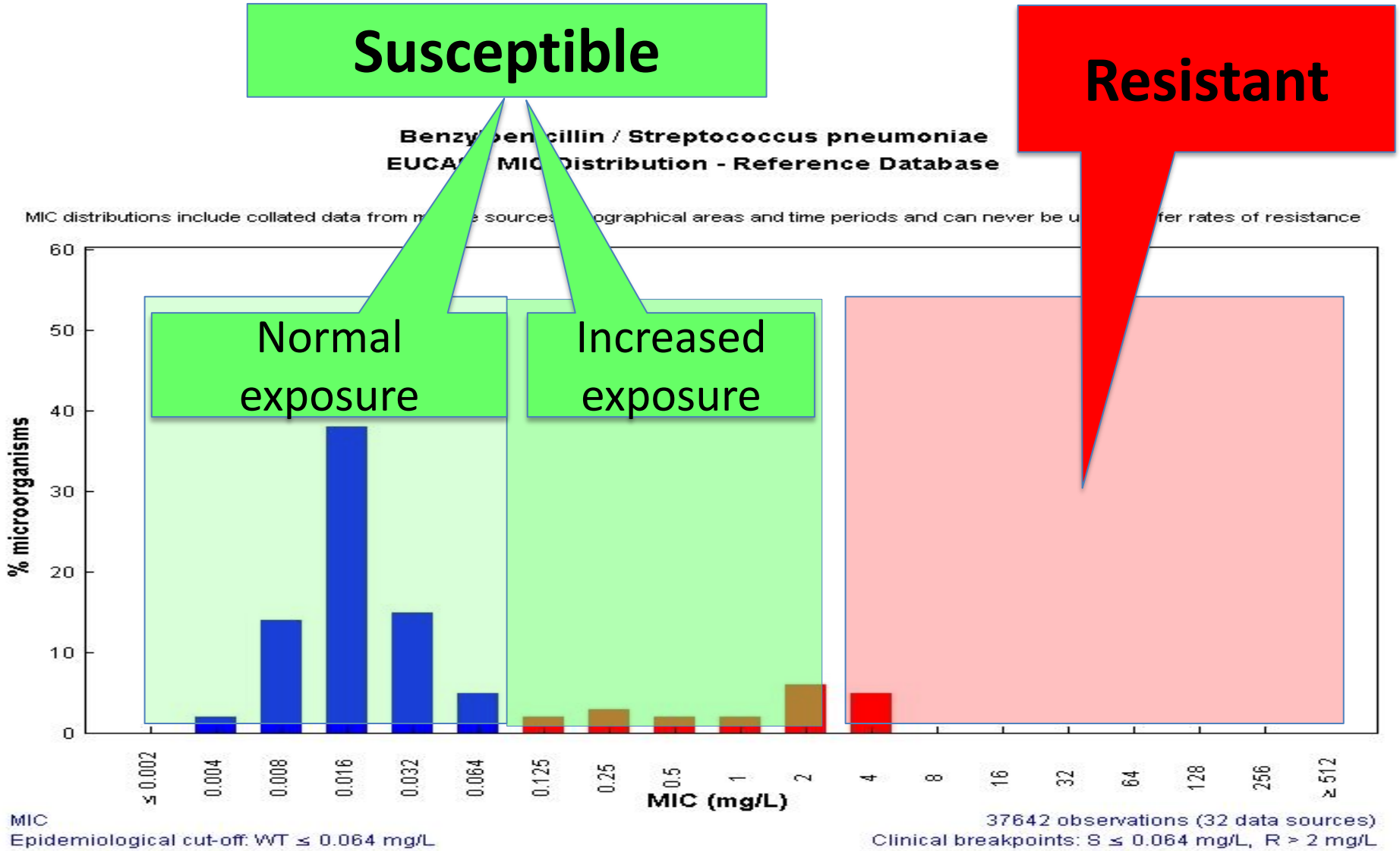
Intermediate

Uncertain effect.
Buffer zone for technical variation.
For a high dose.
Where concentrated for pharmacokinetic reasons.

Resistant



SIR - new definitions 2019



EUCAST technical guidance on the use of the combination disk test (CDT) for confirmation of ESBL in Enterobacterales

- **New disk potencies** for combination disks containing cefotaxime and ceftazidime without and with clavulanic acid
- EUCAST recommends laboratories to introduce combination disks containing cefotaxime 5 µg and ceftazidime 10 µg without and with clavulanic acid 10 µg for routine phenotypic confirmation of ESBL production in Enterobacterales.
- **EUCAST tasks manufacturers of disks** for diagnostic use to make available the cefotaxime 5 µg ± CLAV 10 µg and the ceftazidime 10 µg ± CLAV 10 µg disks AND to ascertain that the biological activity of cefotaxime and ceftazidime in disks without and with clavulanic acid is identical.
- For this purpose, disks without and with clavulanic acid must be produced in parallel and sold as a diagnostic kit.

EUCAST technical guidance on the use of the combination disk test (CDT) for confirmation of ESBL in Enterobacterales

- New disk potencies for combination disks containing cefotaxime and ceftazidime without and with clavulanic acid
- A total of 45 Escherichia coli and 5 Klebsiella pneumoniae were tested blindly according to EUCAST disk diffusion methodology at three laboratories using Oxoid (Thermo Fisher Scientific) Mueller-Hinton agar. Three sets of combination disks were evaluated; CTX 5 µg ± CLAV 10 µg and CAZ 10 µg ± CLAV10 µg produced by **MAST** and **Liofilchem** were compared to CTX 30 µg ± CLAV 10 µg and CAZ 30 µg ± CLAV 10 µg from MAST.
- Isolates were considered ESBL positive if, for one or both agents, the increase in zone diameter in the presence of clavulanic acid was ≥ 5 mm compared with the cephalosporin alone.

BP table version 9.0, valid from 01.01.2019

- General changes
  - Link to EUCAST Expert Rules and Intrinsic Resistance Tables added to each table
  - Columns for Area of Technical Uncertainty (ATU) added (MIC and zone diameters)
  - Comments relating to high-dose therapy have been exchanged with HE (High Exposure) superscript on the antimicrobial name
  - Meropenem-vaborbactam breakpoints added
  - Eravacycline breakpoints added
  - Doripenem breakpoints removed. In countries that still have access to doripenem, use the breakpoints and dosages in EUCAST Breakpoint Tables v 8.1 (2018)
  - Links to rationale documents for nitroxoline and trimethoprim-sulfamethoxazole added

BP table version 9.0, valid from 01.01.2019

- Taxonomy

• Enterobacteriaceae changed to Enterobacterales
• *Enterobacter aerogenes* changed to *Klebsiella aerogenes*
• *Clostridium difficile* changed to *Clostridioides difficile*
• *Propionibacterium acnes* changed to *Cutibacterium acnes*

Species previously listed as "*E. coli*, *Klebsiella* spp. and *P. mirabilis*" are now listed as "*E. coli*, Klebsiella spp. (except K. aerogenes), *Raoultella* spp. and *P.* mirabilis" due to changes in taxonomy.
• *Morganella* spp. changed to *Morganella morganii*.

Enterobacterales

- General
  - Species limitation added to cefuroxime oral.
- New breakpoints
  - Meropenem-vaborbactam (MIC)
  - Eravacycline (MIC)
- Revised breakpoints
  - Ertapenem (MIC and zone diameter)
  - Imipenem (MIC and zone *diameter)*. *Separate breakpoints for Morganella morganii, Proteus spp. and Providencia* spp.
  - Ciprofloxacin (zone diameter)
  - Tigecycline (MIC and zone diameter). Species limitation added (breakpoints valid for *E. coli* and *C. koseri*).
- ATUs added
  - Amoxicillin-clavulanic acid, piperacillin-tazobactam, ceftaroline and ciprofloxacin.

Pseudomonas spp

- General
  - Information added on species included in the table
- New breakpoints
  - Meropenem-vaborbactam (MIC)
- Revised breakpoints
  - Imipenem (MIC and zone diameter)
  - Aztreonam (MIC and zone diameter)
- ATUs added
  - Piperacillin-tazobactam, ceftazidime-avibactam and colistin.

Acinetobacter spp

- General
  - Information added on species included in the table
- Revised breakpoints
  - Imipenem (MIC and zone diameter)
  - Ciprofloxacin (MIC and zone diameter)

Staphylococcus spp

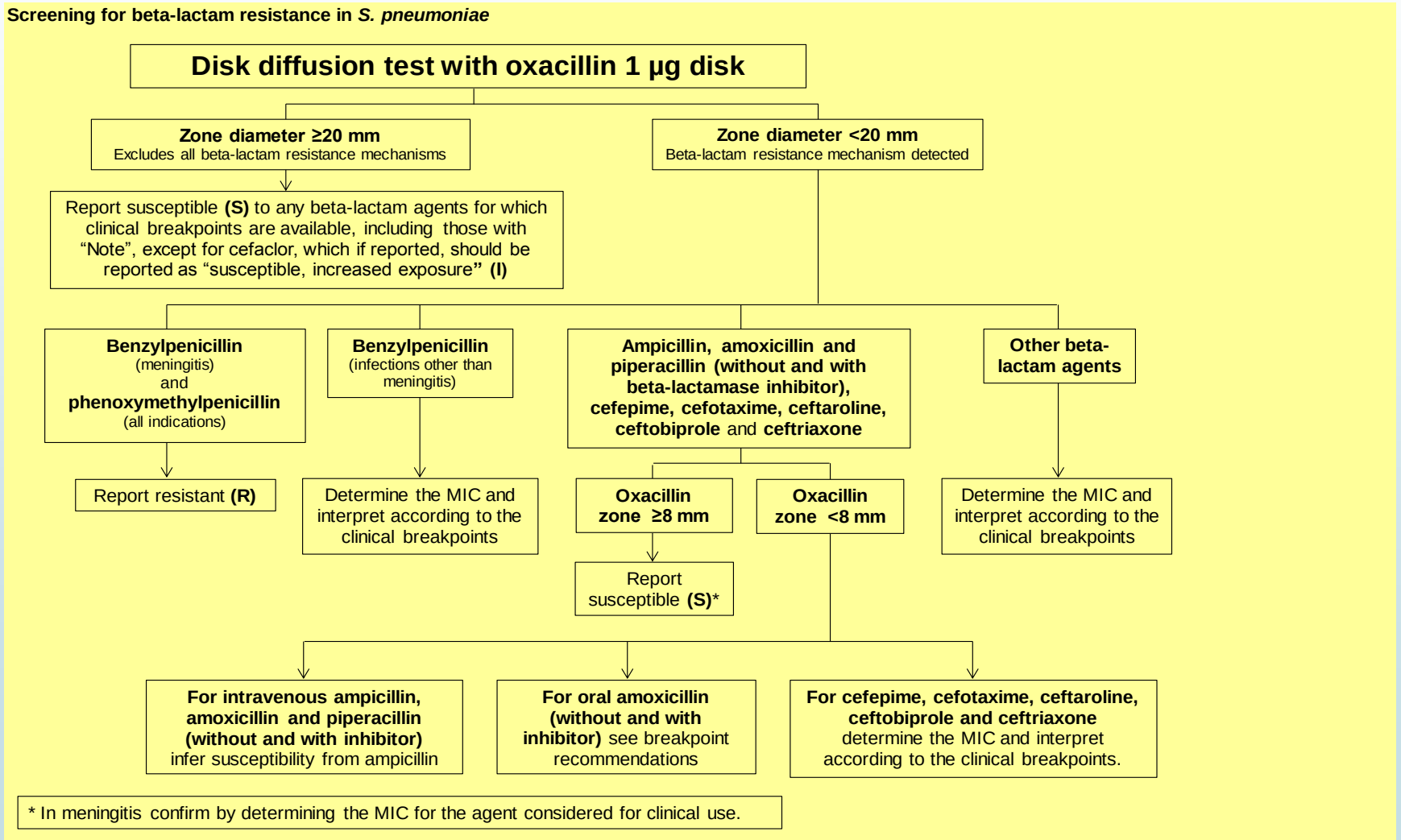
- General
  - Information added on species included in the table
  - "High Exposure" (HE) added to cefotaxime and ceftriaxone
- New breakpoints
  - Eravacycline (MIC)
- ATUs added
  - "Cefoxitin screen S. epidermidis", ceftaroline, ceftobiprole and "amikacin *S. aureus*".

Enterococcus spp

- General
  - Information added on species included in the table
- New breakpoints
  - Eravacycline (MIC)
- Revised breakpoints
  - Tigecycline (MIC and zone diameter)
  - Trimethoprim-sulfamethoxazole (MIC and zone diameter). Breakpoints replaced with Note: activity of trimethoprim and trimethoprim-sulfamethoxazole is uncertain against enterococci, and it is not possible to predict clinical outcome. The **ECOFF** to categorise isolates as wild type or non-wild type for both *E. faecalis* and E. faecium is 1 mg/L, with a corresponding zone diameter ECOFF of **23 mm** for trimethoprim-sulfamethoxazole.

Streptococcus pneumoniae

- Flow chart updated

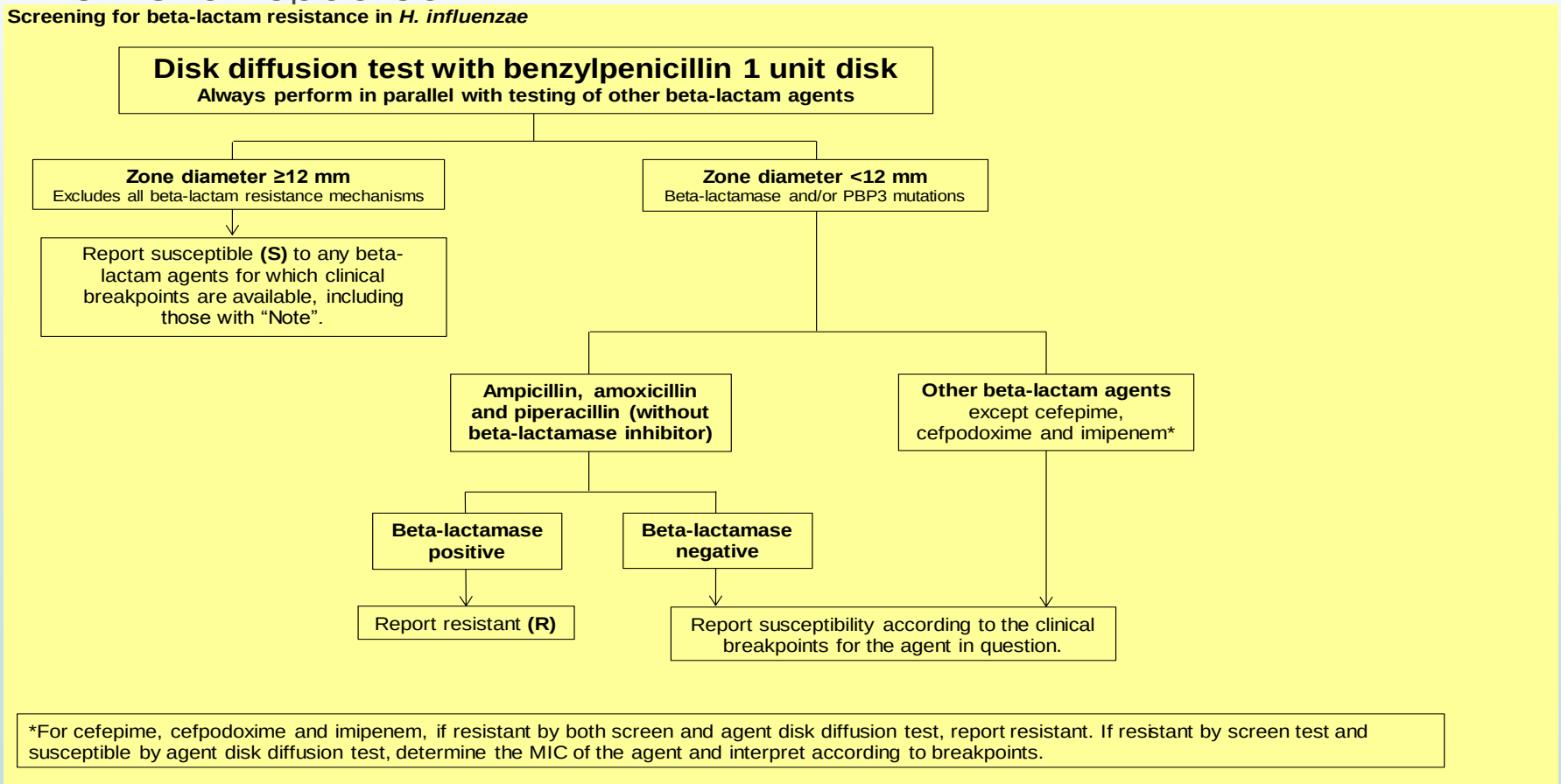


Streptococcus pneumoniae

- New breakpoints
  - Ampicillin (zone diameter)
  - Amoxicillin oral (MIC)
  - Amoxicillin-clavulanic acid oral (MIC)
- Revised breakpoints
  - Meropenem meningitis (MIC)
  - Norfloxacin screen (zone diameter)
  - Trimethoprim-sulfamethoxazole (zone diameter)

Haemophilus influenzae

- Flow chart updated



Haemophilus influenzae

- New breakpoints
  - Amoxicillin oral (MIC)
  - Amoxicillin-clavulanic acid oral (MIC and zone diameter)
  - Piperacillin (changed from Note to IE)
  - Piperacillin-tazobactam (MIC and zone diameter)
- Revised breakpoints
  - Cefpodoxime (MIC and zone diameter)
  - Ceftriaxone (zone diameter)
  - Cefuroxime iv (zone diameter)
  - Cefuroxime oral (zone diameter)
  - Ertapenem (zone diameter)
  - Meropenem meningitis (MIC)
- ATUs added
  - Ampicillin, amoxicillin-clavulanic acid (iv and oral), piperacillin-tazobactam, cefepime, cefotaxime, cefpodoxime, ceftriaxone, cefuroxime (iv and oral) and imipenem.

Gram-positive and Gram-negative anaerobes

- Gram-positive
  Staphylococcus saccharolyticus added to species list.
  Revised breakpoints
  - Ertapenem
  - Imipenem
- Gram-negative
  Parabacteroides added to species list.
  Revised breakpoints
  - Ertapenem
  - Imipenem

Corynebacterium spp

- Breakpoints for corynebacteria were developed for species other than C. *diphtheriae*.
- In an ongoing study, the preliminary results indicate that the current breakpoints for benzylpenicillin and rifampicin are not useful for C. *diphtheriae*.

Dosages

- Comments relating to high-dose therapy have been exchanged with HE (High Exposure) superscript on the antimicrobial name.
- Palju muudatusi, eriti oluline HE märkuse korral
- Esineb erinevusi Eesti praktikaga

Tervitused meie sektsioonile EUCAST SC poolt