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Société belge d'infectiologie et de microbiologie clinique

Belgische vereniging voor infectiologie en klinische microbiologie

BAPCOC
Belgian Antibiotic Policy Coordination Committee

Implementation of EUCAST new definitions

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On behalf of the National Antimicrobial Committee (NAC)

SBIMC/BVIKM Symposium 24/05/2022

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

https://www.bvikm.org/national-antimicrobial-committee-fr

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Plan

- ❑ EUCAST new definitions
- ❑ Practical implementation
- ❑ Support activities from the NAC
- ❑ Follow-up of the implementation
- ❑ Varia on the NAC/EUCAST

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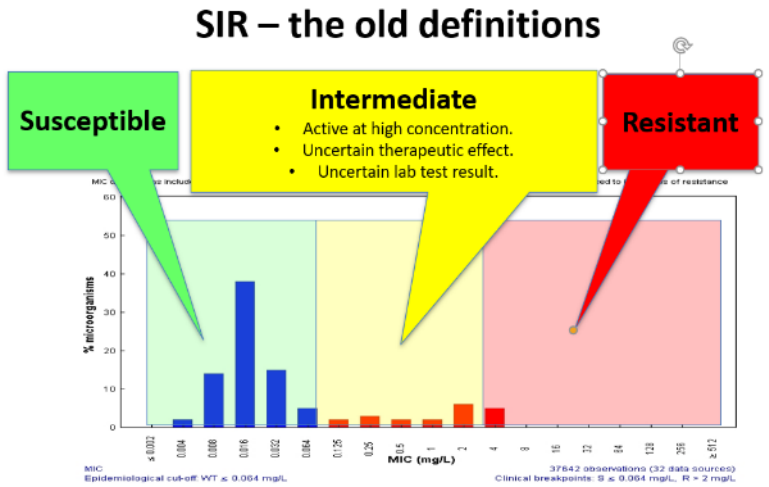
EUCAST SIR – new definitions, new interpretation

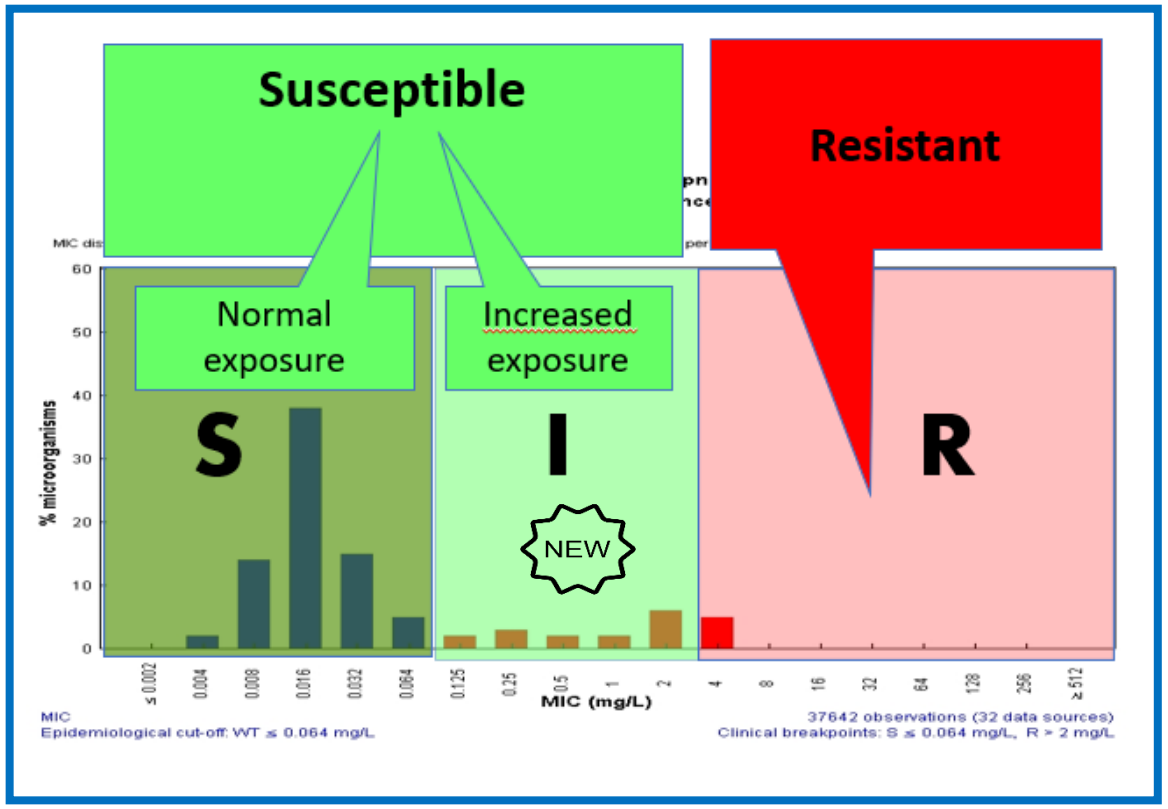
EUCAST v2020:

→ Maintaining letters of the 3 possible categories "S", "I" or "R".

→ **Two "susceptible" categories (S, I)** and **one "resistant" category (R)**:

- susceptible at standard dosage (S) and
- **susceptible at increased exposure (I) = susceptible at high dosage** : high probability of therapeutic success when exposure to the antibiotic is increased by adjusting the dose upwards or if the antibiotic is highly concentrated at the infectious site.





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Dosages

EUCAST dosing tab

EUCAST Clinical Breakpoint Tables v. 12.0, valid from 2022-01-01

EUCAST breakpoints are based on the following dosages (see section 8 in Rationale Documents). Alternative dosing regimens may result in equivalent exposure. The table should not be considered a guidance for dosing in clinical practice, and does not replace specific local, national, or regional dosing guidelines. However, if national practices significantly differ from those listed below, EUCAST breakpoints may not be valid. Situations where less antibiotic is given as standard or high dose should be discussed locally or regionally.

Uncomplicated UTI: acute, sporadic or recurrent lower urinary tract infections (uncomplicated cystitis) in patients with no known relevant anatomical or functional abnormalities within the urinary tract or comorbidities.

Penicillins	Standard dosage	High dosage	Uncomplicated UTI	Special situations
Benzylpenicillin	0.6 g (1 MU) x 4 iv **For S**	1.2 g (2 MU) x 4-6 iv **For I/S**		**Meningitis caused by *S. pneumoniae*:** For a dose of 2.4 g (4 MU) x 6 iv, isolates with MIC≤0.06 mg/L are susceptible. **Pneumonia caused by *S. pneumoniae*: breakpoints are related to dosage:** For a dose of 1.2 g (2 MU) x 4 iv, isolates with MIC ≤0.5 mg/L are susceptible. For a dose of 2.4 (4 MU) g x 4 iv or 1.2 g (2 MU) x 6 iv, isolates with MIC ≤1 mg/L are susceptible. For a dose of 2.4 g (4 MU) x 6 iv, isolates with MIC ≤2 mg/L are susceptible.
Ampicillin	2 g x 3 iv	2 g x 4 iv		**Meningitis:** 2 g x 6 iv
Ampicillin-sulbactam	(2 g ampicillin + 1 g sulbactam) x 3 iv	(2 g ampicillin + 1 g sulbactam) x 4 iv		
Amoxicillin iv	1 g x 3-4 iv	2 g x 6 iv		**Meningitis:** 2 g x 6 iv
Amoxicillin oral	0.5 g x 3 oral	0.75-1 g x 3 oral	0.5 g x 3 oral	
Amoxicillin-clavulanic acid iv	(1 g amoxicillin + 0.2 g clavulanic acid) x 3-4 iv	(2 g amoxicillin + 0.2 g clavulanic acid) x 3 iv		
Amoxicillin-clavulanic acid oral	(0.5 g amoxicillin + 0.125 g clavulanic acid) x 3 oral	(0.875 g amoxicillin + 0.125 g clavulanic acid) x 3 oral	(0.5 g amoxicillin + 0.125 g clavulanic acid) x 3 oral	Amoxicillin-clavulanic acid has separate breakpoints for systemic infections and uncomplicated UTI. When amoxicillin-clavulanic acid is reported for uncomplicated UTI, the report must make clear that the susceptibility category is only valid for uncomplicated UTI.
Piperacillin	4 g x 4 iv	4 g x 4 iv by extended 3-hour infusion		High dosage for more serious infections.
Piperacillin-tazobactam	(4 g piperacillin + 0.5 g tazobactam) x 4 iv 30-minute infusion or x 3 iv by extended 4-hour infusion	(4 g piperacillin + 0.5 g tazobactam) x 4 iv by extended 3-hour infusion		A lower dosage of (4 g piperacillin + 0.5 g tazobactam) x 3 iv, 30-minute infusion, is adequate for some infections such as complicated UTI, intraabdominal infections and diabetic foot infections, but not for infections caused by isolates resistant to third-generation cephalosporins.
Ticarcillin	3 g x 4 iv	3 g x 6 iv		
Ticarcillin-clavulanic acid	(3 g ticarcillin + 0.1-0.2 g clavulanic acid) x 4 iv	(3 g ticarcillin + 0.1 g clavulanic acid) x 6 iv		
Temocillin	2 g x 2 iv	2 g x 3 iv		The 2 g x 2 iv dose has been used in the treatment of uncomplicated UTI caused by bacteria with beta-lactam resistance mechanisms.
Phenoxymethylpenicillin	0.5-2 g x 3-4 oral depending on species and/or infection type	None		
Oxacillin	1 g x 4 iv	1 g x 6 iv		The high exposure dosing regimen pertains to the severity of the infection or drug exposure at the site of infection.
Cloxacillin	0.5 g x 4 oral or 1 g x 4 iv	1 g x 4 oral or 2 g x 6 iv		The high exposure dosing regimen pertains to the severity of the infection or drug exposure at the site of infection.
Dicloxacillin	0.5-1 g x 4 oral or 1 g x 4 iv	2 g x 4 oral or 2 g x 6 iv		The high exposure dosing regimen pertains to the severity of the infection or drug exposure at the site of infection.
Flucloxacillin	1 g x 3 oral or 2 g x 4 iv (or 1 g x 6 iv)	1 g x 4 oral or 2 g x 6 iv		The high exposure dosing regimen pertains to the severity of the infection or drug exposure at the site of infection.
Mecillinam oral (pivmecillinam)	None	None	0.2-0.4 g x 3 oral	

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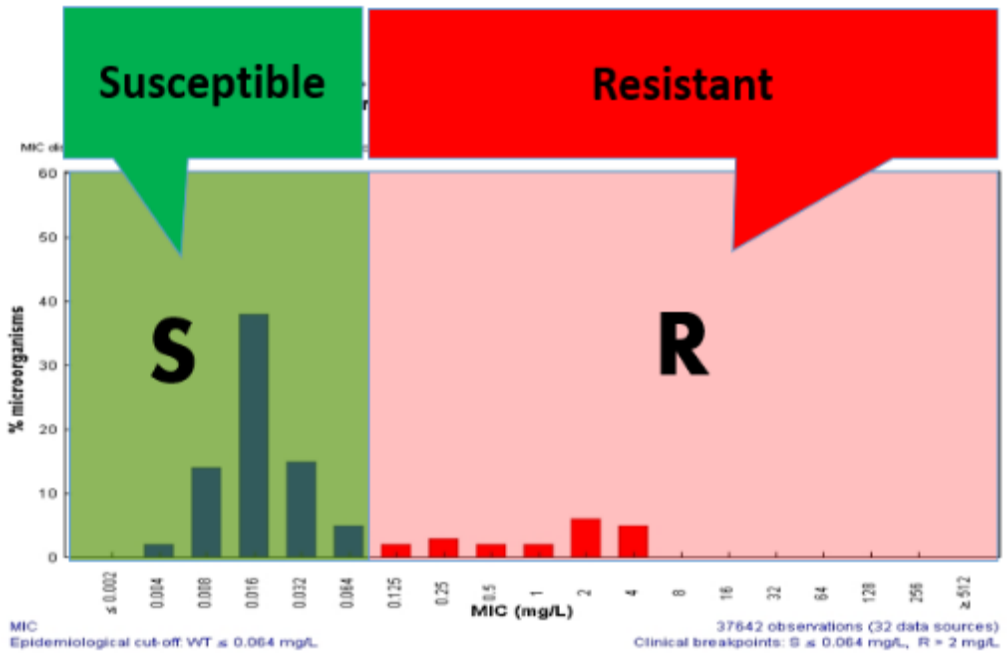
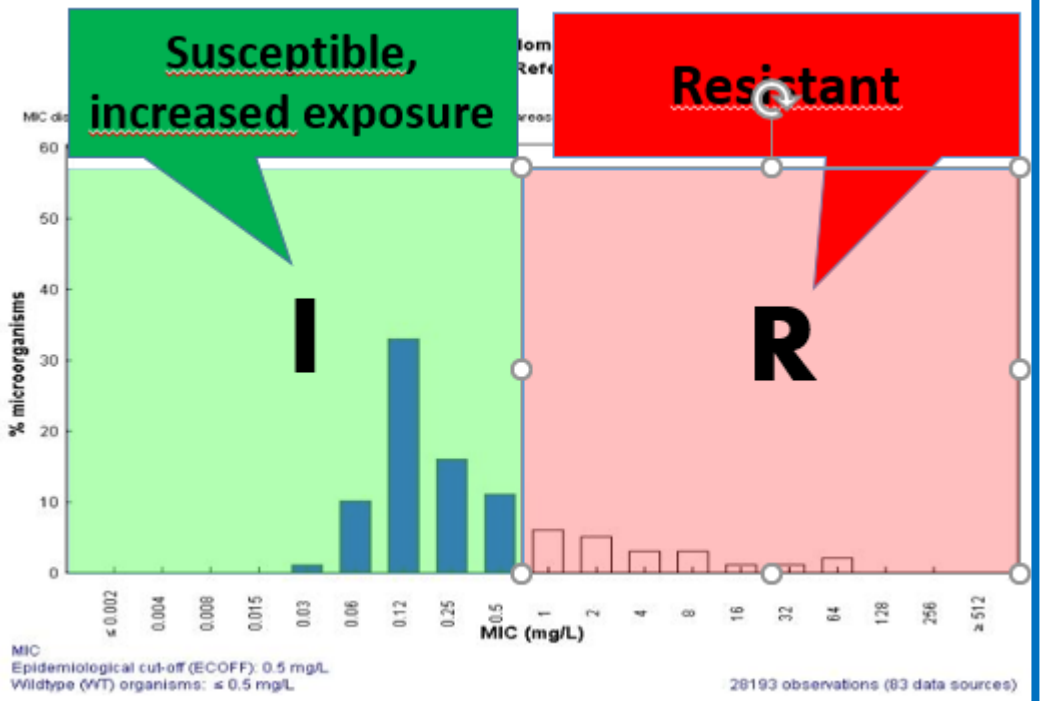
SIR – new definitions 2020



Only S, no I:

- Only one dosage regimen
- When increased exposure cannot be achieved



Only I, no S:

Wild-type intrinsically less sensitive to the agent
”Arbitrary S-breakpoint” always obtain an ”I” rather than an ”S” when testing.

S≤0.001 mg/L
S≥50 mm

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Most common organisms-agents with no S category (only I and R categories)

- *Enterobacterales*:
  - Cefuroxime
  - Temocillin
- *Pseudomonas*:
  - Piperacillin-tazobactam
  - Ceftazidime
  - Cefepime
  - Aztreonam
  - Ciprofloxacin/Levofloxacin
- *Stenotrophomonas*:
  - Cotrimoxazole
- *Staphylococcus*:
  - Cipro/levofloxacin
- *S. pneumoniae*:
  - Levofloxacin
- *H. influenzae*:
  - Amoxicillin oral
  - Amox-clav oral
  - Cefuroxime oral
- *M. catarrhalis*:
  - Cefuroxime oral

- Comments on lab reports for these results
- Active monitoring of antibiotic choice (avoid unnecessary use of broad-spectrum AB)

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Practical examples of antibiogram reports

❑ **Hospital**: ***P. aeruginosa*** with wild-type susceptibility profile

Antibiotic	Result (category)
Piperacillin-tazobactam	**I**
Ceftazidime	**I**
Cefepime	**I**
Aztreonam	**I**
Ciprofloxacin	**I**
Meropenem	**S**
Ceftazidime-avibactam	**S**
Ceftolozane-tazobactam	**S**
Cefiderocol	**S**

❑ **Community**: ***H. influenzae*** with wild-type susceptibility profile (sputum of a patient with bronchopneumonia)

Antibiotic	Result (category)
Amoxicillin oral	**I**
Amoxicillin-clavulanic acid oral	**I**
Cefuroxime oral	**I**
Ciprofloxacin oral	S

➢ **AB stewardship:**

Narrow-spectrum at HD with "I" should be preferred over a broader spectrum at SD with "S" (such as meropenem for *P. aeruginosa*).

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Importance of the implementation of the new EUCAST recommendations in Belgium

- **Important for:**
  - Harmonization of the interpretation of AST results at National/European levels (transfer of patients)
  - Continued participation and inclusion of standardized data into international/national AMR surveillance programs (EARS-Net/ECDC, NSIH-AMR,…)
  - Successful participation to international EQA (UK NEQAS)

- **New deadline of implementation: July 1st, 2022** (post-COVID delay)

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Practical implementation of new changes in EUCAST guidelines

✓**Review of local antibiotics dosage regimen** (antibiotic management team)

- Belgium already use HD in general (limited impact)
- Compliance of local/national dosage guidelines with EUCAST dosages used to set breakpoints
- Information of updated posology guidelines (clinical pharmacist)

✓**Reporting layout of antimicrobial susceptibility testing AST results**

- AST devices (manufacturers, microbiology lab)
- Laboratory information system LIS (Microbiology lab, IT)
- Patient medical records system (IT)
- Information in results reporting (electronic/hardcopy)

✓**Follow-up of impact after implementation**

- Monitoring of antibiotic usage and consumption
- Monitoring of antimicrobial resistance AMR data

➔**Multidisciplinary approach required**

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Support activities and guidance by the NAC for the switch

- **Information, communication and training of laboratories and clinicians aiming to:**
  - Provide links to the support documents of EUCAST
  - Promote locally the disposal of dosing tables (SD/HD) of most used agents
  - Organize presentations during staff meetings for labs and clinicians (eg: NAC webinar 24/9/2021)*
  - Encourage cascade reporting (mask results) by labs: test/report list for group of pathogens*
  - Send information letters addressed to
    - laboratories (EQA by Sciensano)
    - antibiotic management teams (by BAPCOC)
    - frontline healthcare workers, GPs (simplified mails)
  - Use other communication channels…
    - BCFI/CBIP-Folia
    - HOST project

* https://www.bvikm.org/national-antimicrobial-committee

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Follow-up on the implementation of the new EUCAST guidelines

- Effective degree of implementation by Belgian labs (survey via Sciensano EQA)
- Structural difficulties for some labs in reporting
  - Automated AST : some AB with insufficient concentration range for interpretation
  - IT layout: add comments, change S/I/R color, mask drugs
  - Different formulations of same AB (IV vs PO)
  - Different clinical contexts (UTI, cUTI, sepsis, meningitis…)
  - New concepts: “ATU”, “(in brackets)”…

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Follow-up on the implementation of the new EUCAST guidelines

- Experience feedbacks & expectations from clinicians
  - Pediatric dosages (EUCAST/ESPID joint WG ongoing*)
  - Lack of rationale for some antibiotics in setting breakpoints
  - Need more PK/PD studies with clinical impact
  - Correlation to define dosages in relation to MIC
  - Concerns on inadequate prescriptions/consumption
  - Difficulties of stewardship for ambulatory patients

* Aguilera-Alonso Ped Inf Dis J 2022

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Follow-up on the implementation of the new EUCAST guidelines

- **Indicators for antibiotic usage and consumption**
  - BAPCOC surveillance
  - Local surveys on adequate choice of AB spectrum/dosage
    - CHU UCL Namur: 3% (1/29) of unnecessary meropenem for *P. aeruginosa*
    - UZ Gent: 1 case for 3 weeks of unnecessary meropenem for *P. aeruginosa*
  - NAC survey: setup ongoing

  → **AB stewardship interventions**: mainly for *P. aeruginosa,* but also for others (i.e. for *Enterobacterales*)

- Impact on epidemiological surveillance of AMR
  - National (Sciensano NSIH) and international (EARS, WHO) AMR surveillance programs
  - Infection control practioners: definition of MDRO

  → **Must clearly separate R from S/I** (no more « non-susceptible » of I/R)

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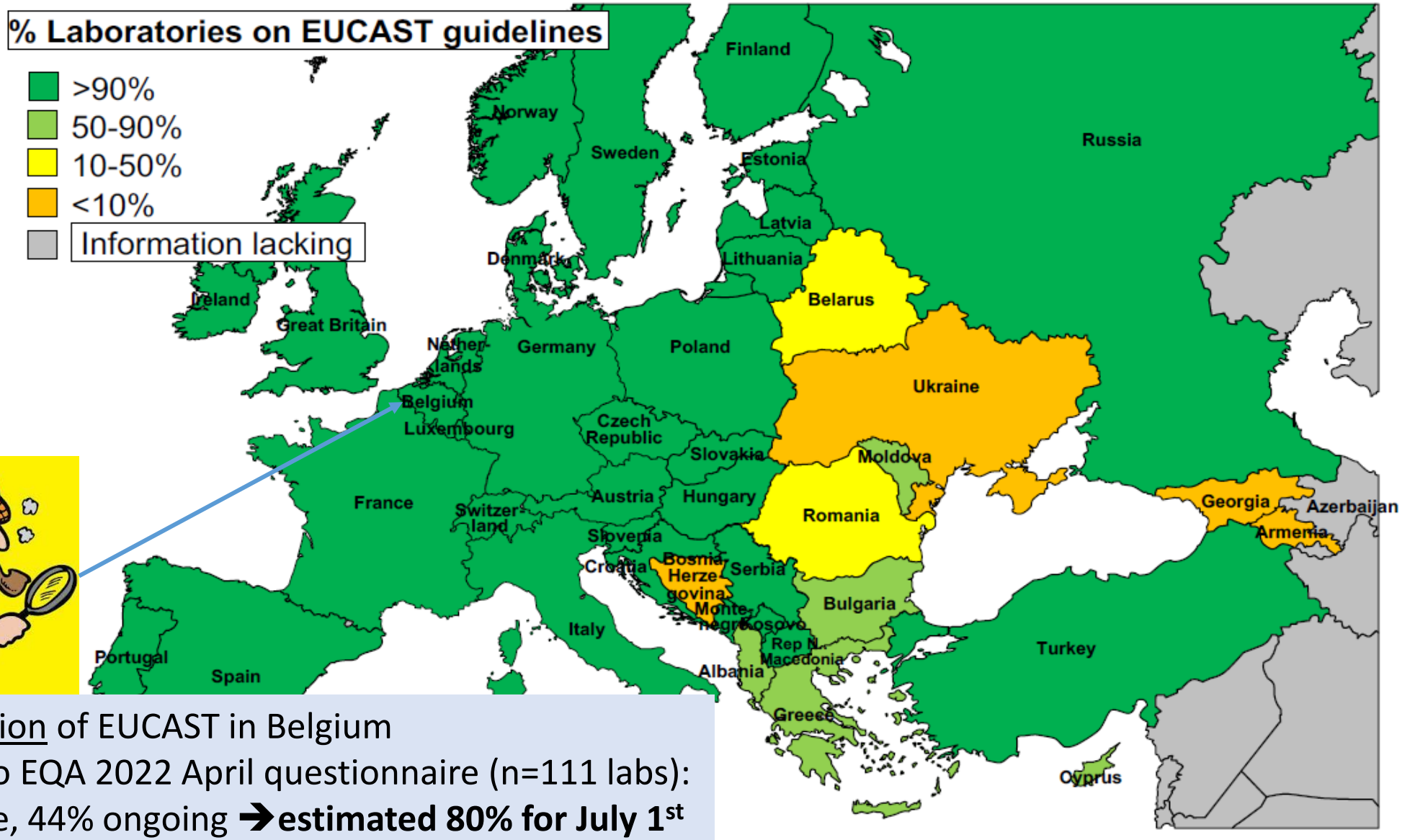
Implementation of EUCAST breakpoints/guidelines, March 2022



New version of EUCAST in Belgium

Sciensano EQA 2022 April questionnaire (n=111 labs):

37% done, 44% ongoing ➔**estimated 80% for July 1st**

Countries not on the map: Australia | Brazil | China | Canada | Iceland | Israel | Malta | Morocco | New Zealand | South Africa | USA

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Ongoing activities in the NAC

- ❑NAC panel 2.0 : collection strains (MDRO) for AST validation
  - Short communication in JGAR*
  - Distribution to labs by Sciensano in 2022 T4
- ❑**AST methods interlaboratory evaluation:**
  - **Temocillin**
  - ***S. pneumoniae*…**
- ❑EUCAST new AST DD method for anaerobes
  - 2022 EUCAST guidelines: more drug/bug combinations ongoing
  - Method validation project
- ❑Links to NAC documents at BVIKM website:

https://www.bvikm.org/national-antimicrobial-committee-fr

* Deckers et al. J Glob Antimicrob Res 2022;28:125-129

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Acknowledgments

Current members of the NAC (2022)

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Stefanie Desmet, Apr. Biol., Dr.	UZ Leuven
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