National introduction of EUCAST breakpoints and methods

Iztok Štrumbelj

- National Laboratory of Health, Environment and Food

Maribor, Slovenia

- Slovenian National Antimicrobial Susceptibility Testing Committee

Disclosure.

No conflict of interest, nothing to disclose.

Purpose:

to describe **the introduction** of European Committee on Antimicrobial Susceptibility Testing (**EUCAST**) bacteriology **breakpoints and methods in Slovenia**.

Slovenia

- Population: 2 million
- Independent since 1991

http://www.slovenia.info/ http://www.itis.si/zemljevid

Hospitals in Slovenia

29 hospitals (26 public, 3 private), most samples from:

- 2 university clinical centres
- 11 general hospitals

Source: Zdravstveni statistični letopis 2012, Nacionalni inštitut za javno zdravje (NIJZ).

Medical microbiology laboratories (12)

are parts of different public institutions

- 1 university laboratory (Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana)
- 8 laboratories are departments of National Laboratory of Health, Environment and Food
- 3 are hospital laboratories

Certified medical microbiology laboratories in Slovenia

Quality system (QS) and certification of diagnostic laboratories

1. Quality system (QS), published in Official Gazette of Republic of Slovenia
2. Audit of laboratory QS by independent Commission
3. If requirements met: “permission to work” issued by Ministry of Health for 5 years.

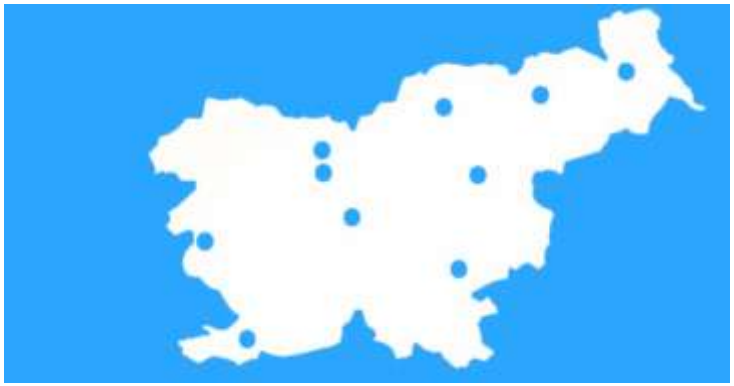
List of certified diagnostic laboratories in the field of clinical bacteriology published at the website of Ministry of Health. (accessed March 19th, 2015)

12 laboratories:

- 1 specialised in mycobacteriology
- 11 perform antimicrobial susceptibility testing of common bacteria

KLINIČNA ALI MEDICINSKA MIKROBIOLOGIJA

1. Bolnišnica Golnik - KOPA - Laboratorij za mikrobakterije
2. Bolnišnica Golnik - KOPA - Laboratorij za respiratorno mikrobiologijo
3. Medicinska fakulteta Ljubljana - Inštitut za mikrobiologijo in imunologijo
4. Nacionalni laboratorij za zdravje, okolje in hrano; Center za medicinsko mikrobiologijo, Oddelek za medicinsko mikrobiologijo Kranj
5. Nacionalni laboratorij za zdravje, okolje in hrano; Center za medicinsko mikrobiologijo, Oddelek za medicinsko mikrobiologijo Maribor
6. Nacionalni laboratorij za zdravje, okolje in hrano; Center za medicinsko mikrobiologijo, Oddelek za medicinsko mikrobiologijo Celje
7. Nacionalni laboratorij za zdravje, okolje in hrano; Center za medicinsko mikrobiologijo, Oddelek za medicinsko mikrobiologijo Murska Sobota
8. Nacionalni laboratorij za zdravje, okolje in hrano; Center za medicinsko mikrobiologijo, Oddelek za medicinsko mikrobiologijo Koper
9. Nacionalni laboratorij za zdravje, okolje in hrano; Center za medicinsko mikrobiologijo, Oddelek za javnozdravstveno mikrobiologijo Ljubljana
10. Nacionalni laboratorij za zdravje, okolje in hrano; Center za klinično mikrobiologijo, Oddelek za medicinsko mikrobiologijo Nova Gorica
11. Splošna bolnišnica Slovenj Gradec - Oddelek za mikrobiologijo
12. Nacionalni laboratorij za zdravje, okolje in hrano; Center za medicinsko mikrobiologijo, Oddelek za medicinsko mikrobiologijo Novo mesto



Slovenian National Antimicrobial Susceptibility Testing Committee

Slovenian acronym: **SKUOPZ**

Slovenska **k**omisija za **u**gotavljanje **o**bčutljivosti za **p**rotimikrobna **z**dravila

- **Established:** at the end of 2010.
- **Members:** at least one member from each certified laboratory and one member from National Institute of Public Health

- **Two working areas:**

a) **Methods** for antimicrobial susceptibility testing (AST)
b) **Surveillance** of antimicrobial resistance (AMR) - three annual national reports were published on web (2011, 2012, 2013).

Example page from SKUOPZ annual national surveillance report

Staphylococcus aureus

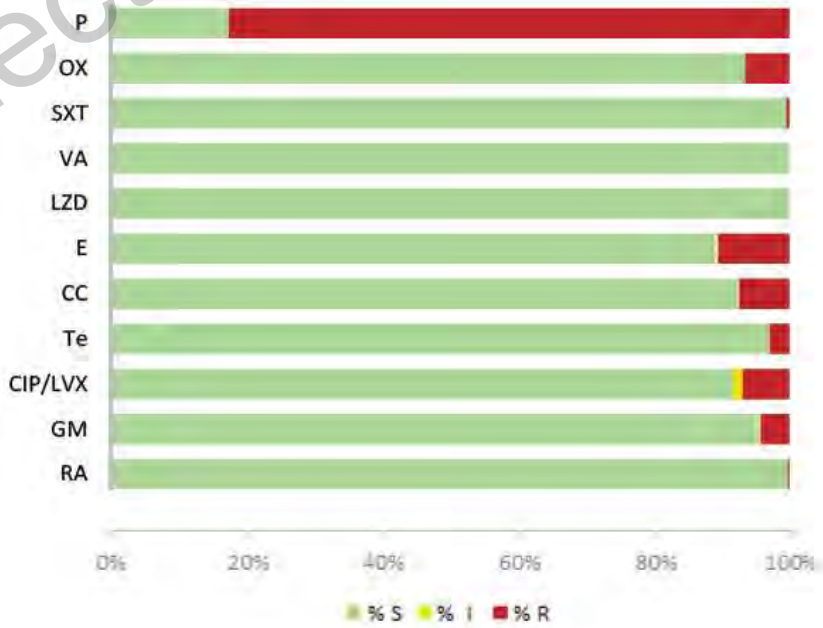
Zajeti izolati: prvi izolati pri bolnikih iz vzorcev, poslanih iz bolnišničnih ambulant in oddelkov, brez nadzornih kužnin.

Obdobje: 1. 1. 2013 - 31. 12. 2013

Poudarki, dodatki, pojasnila: Med 7138 testiranimi izolati je 6 % izolatov odpornih proti oksacilinu (angl. "methicillin - resistant *Staphylococcus aureus*, MRSA"). Odpornost proti oksacilinu pomeni odpornost proti vsem betalaktamskim antibiotikom. Občutljivost MRSA izolatov je prikazana na naslednji strani.

Antibiotik	Okrajšava	% S	% I	% R	Število prvih izolatov
Penicilin	P	17	0	83	7135
Oksacilin	OX	94	0	6	7137
Trimetoprim-sulfametoksazol	SXT	100	0	0	7138
Vankomicin	VA	100	0	0	5943
Linezolid	LZD	100	0	0	3970
Eritromicin	E	89	1	10	6995
Klindamicin	CC	92	0	7	6995
Tetraciklin	Te	97	0	3	5912
Ciprofloksacin / levofloksacin	CIP/LVX	92	1	7	6962
Gentamicin*	GM	95	0	4	6665
Rifampicin*	RA	100	0	0	5793

* gentamicin in rifampicin - pri stafiloknih okužbah se ne uporabljata kot samostojen antibiotik



Antimicrobial susceptiblity testing (AST) methods used in Slovenia

Disk diffusion method used as principal method.

For MIC determination, **gradient diffusion method** is mostly used.
Always for anaerobes.

Standard microdilution method not used routinely.

Automated AST systems used in few laboratories.

Both, MICs and zones, entered and **interpreted** in LIS.

Transition from CLSI to EUCAST

Introduction, June 2013

- EUCAST presented in ISIS – official journal of Slovenian Medical Chamber
- Symposium about EUCAST for microbiologists and clinicians

The process, June 2013 – April 2014

Three main points

- **Laboratory information system (LIS) upgrade.**
- **Laboratory methods.**
- **Information for clinicians.**

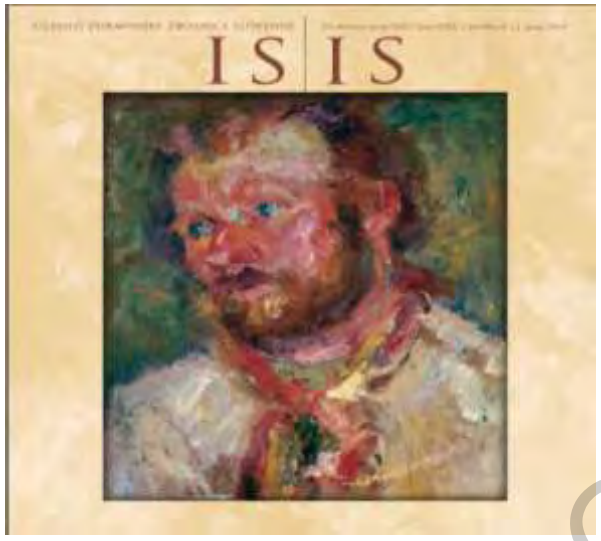
Final control of the process

- **Results of external quality assessment.**

Note: in this presentation, "agent" means "antimicrobial agent".

Introduction, June 2013.

- EUCAST presented in ISIS – official journal of Slovenian Medical Chamber.
- **Symposium** with international speakers for microbiologists and clinicians, round table. Final unanimous decision: **EUCAST should be introduced.**



Novosti za klinične zdravnike in mikrobiologe

Uvajanje testiranja občutljivosti za protimikrobna zdravila po smernicah EUCAST v Sloveniji

Iztok Štrumbelj, Andrej Golle, Miroslav Petrovec, Mateja Pirš, Marta Poljak, Katja Seme

Kako nastanejo smernice za testiranje občutljivosti za protimikrobna zdravila

4. Likarjev simpozij -

UVEDBA SMERNIC EUCAST ZA TESTIRANJE OBČUTLJIVOSTI ZA PROTIMIKROBNA ZDRAVILA V SLOVENIJI

IMPLEMENTATION OF GUIDELINES OF EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING (EUCAST) IN SLOVENIA

sreda, 19. 06. 2013/ Wednesday, June 19th 2013
velika predavalnica Medicinske fakultete v Ljubljani / Great Lecture Hall Faculty of Medicine Ljubljana

PROGRAM / PROGRAMME

08:30–08:45	Pozdrav udeležencem *Welcome address and introduction*
08:45–09:15	**Gunnar Kahlmeter**: EUCAST – predstavitev, kratka zgodovina, sedanjost in svetla prihodnost *EUCAST: background, short history, current situation and bright future*
09:15–09:35	**Rafael Canton**: Metode za detekcijo mehanizmov odpornosti, ki imajo pomembne posledice za javno zdravje *Methods to detect resistance mechanisms of clinical and/or public health importance*
09.35–09.55	**Gunnar Kahlmeter**: Testiranje protimikrobne občutljivosti z metodo disk difuzije po EUCAST-u *Antimicrobial susceptibility testing using the EUCAST disk diffusion method*
09:55–10:15	**Rafael Canton**: Intrinzična odpornost bakterij in interpretativno odčitavanje/poročanje pri testiranju občutljivosti za protimikrobna zdravila *Intrinsic resistance and interpretative reading of antimicrobial susceptibility testing*
10:15–10:35	**Diskusija / *Discussion***
10:35–11:00	Odmor s kavo / *Coffee break*
11:00–11:30	**Rafael Canton, Gunnar Kahlmeter**: Uvedba standardov EUCAST v Evropi in širše: kratka zgodovina, sedanjost in prihodnost *Implementation of EUCAST in Europe and beyond: short history, current situation and bright future*
11:30–11:45	**Arjana Tambić Andrašević, Iva Butić**: Uvedba smernic EUCAST na Hrvaškem: praktične izkušnje in posledice *Implementation of EUCAST in Croatia: Practical experiences and consequences*
11:45–12:00	**Iztok Štrumbelj, Katja Seme:** Aktivnosti in ovire za uvedbo smernic EUCAST v Sloveniji *Current situation activities and obstacles for implementation of EUCAST guidelines in Slovenia*
12:00–12:45	**OKROGLA MIZA / ROUND TABLE** **Gunnar Kahlmeter, Rafael Canton, Iztok Štrumbelj, Katja Seme, Andrej Golle, Bojana Beović, Franc Strle, Tatjana Lejko Zupanc:** Kaj se lahko naučimo iz uspehov in napak drugih: uvedba smernic EUCAST v Sloveniji *Learning from other's success and mistakes: how to implement EUCAST guidelines in Slovenia*

Consensus

During the whole process of EUCAST implementation – all decisions of SKUOPZ were accepted by consensus.

The first major decision was critical.

- Request of some clinicians: to supplement EUCAST breakpoints with breakpoints from other AST systems, if EUCAST has no breakpoint for an agent / species
  (e.g. ampicilin-sulbactam and *Acinetobacter baumannii*)
- **SKUOPZ decision: unacceptable. "Mixing" breakpoints would lead to a confusion.**

Strict use of EUCAST interpretations was followed:

(-) dash in the EUCAST breakpoint tables: no testing or resistant result.
(IE) insufficient evidence in the breakpoint tables: if necessary (rarely) MIC can be determined, but without interpretation into SIR category.

Laboratory information system (LIS) upgrade (1)

REVIEW OF THE PROCESS:

All laboratories use **the same LIS** provided by a Slovenian software company.
The software development was started by **Jana Kolman**, MD and **Alenka Štorman**, MD, clinical microbiologists, in mid-nineties.

Identification of need:

- **SKUOPZ:** what do we want from LIS
- **SKUOPZ:** comments which appear in the results form were written

Software changes:

- dedicated clinical microbiologist and software expert Alenka Štorman **communicated** the need for changes to software provider
- software provider **implemented** all software changes.

Databases and comments entered in LIS, validation. Alenka Štorman:

- entered all breakpoint values (MICs and zones)
- wrote all comments into LIS
- linked them to the proper AST result for different species / agents
- validated LIS after changes were implemented.

Laboratory information system (LIS) upgrade (2)

INTERPRETATION OF ZONES AND MICs (into S, I, R category).

Result of upgrade:

- all zones (calliper is used) and MICs are entered into LIS
- automatically interpreted as S, I or R according to EUCAST breakpoints.

Automatic interpretation of zones / MICs is especially helpful if:

1. one MIC/disk zone is interpreted differently for different species in the bacterial group
2. interpretation of MIC /zone is limited only to few species within bacterial group.

However, manual correction of the result is sometimes necessary.

LIS precludes S, I, R interpretation if there are no EUCAST breakpoints.

1.Breakpoints for the agent are different for different species within a group

Software precludes use of inappropriate breakpoints for the species tested.

Example: *Staphylococcus* spp. - breakpoints for cefoxitin screen disk (surrogate disk for "methicillin " susceptibility / resistance)

Species	Zone – methicilin susceptible
S. aureus, S. lugdunensis and *S. saprophyticus*	S ≥ 22
S. pseudintermedius	S ≥ 35
Other coagulase-negative staphylococci	S ≥ 25

2.Breakpoints for the agent are limited to some species within a group

There is no interpretation (no breakpoints) for other species in the group.

Software precludes interpretation for species without breakpoints.

Example 1. Systemic infections.

Group	Agent	Breakpoints limited to
Enterobacteriaceae	Cefuroxime iv	*E. coli, Klebsiella* spp. and *P. mirabilis*

Example 2. Uncomplicated urinary tract infections only.

Group	Agent	Breakpoints limited to
Enterobacteriaceae	Nitrofurantoin	*E. coli*
Enterococcus spp.	Nitrofurantoin	*E. faecalis*
Staphylococcus spp.	Nitrofurantoin	*S. saprophyticus*
Streptococcus spp.	Nitrofurantoin	*S. agalactiae*

Manual correction of results

Example 1. ***Staphylococcus*** spp., inducible clindamycin resistance.

Agent, disk	"Zone test result"	Reason for change	Final result for the agent
Clindamycin	Zone ≥ 22 mm, S – susceptible.	Positive D-phenomenon.	R – resistant*

**manual comment about possible use of clindamycin in minor soft tissue infections is also added*

Example 2. ***S.aureus, S. lugdunensis***, penicillinase.

Agent, disk	"Zone test result"	Reason for change	Final result for the agent
Penicillin	Zone ≥ 26 mm, S - susceptible	The zone edge is sharp.	R - resistant

Laboratory information system (LIS) upgrade (3)

COMMENTS OF RESULTS APPEAR ON THE RESULTS FORM

Background:

•for proper interpretation of many EUCAST results (S, I or R), comments are essential.

Basic idea was to make comments as **user friendly** as possible:

- for laboratories (automatic comment)
- clinicians (as short and as clear as possible).

Considerable amount of work and discussions was necessary to integrate (or split) guidelines and rules from different EUCAST documents into software rules so that comments are added to laboratory reports automatically - **99 different comments** were entered into LIS.

Comments / notes in the report

• Comments are **linked to the results** so that appropriate comment is automatically linked to the agent or agent result.

• Few comments are added **manually**, e.g. when resistance mechanism is determined.

Automatical comments are linked to the:

1. species (e.g. “AmpC” comment linked to group 2. *Enterobacteriaceae*)
   OR
1. to an element. “Element” is bacterial species and:

- the agent or
- S, I or R result of the agent or
- MIC of the agent.

Comments linked to the agent, examples (1)

Applicability of the result of an agent to other agents

- Isolate: *Staphylococcus* spp. Agent: erythromycin
- Comment: Result of erythromycin applies also to azithromycin, clarithromycin and roxithromycin.

- Isolate: *Streptococcus agalactiae.* Agent: penicillin.
- Comment: *Streptococcus agalactiae* - result of penicillin applies also to other penicillins (with the exception of phenoxymethylpenicillin and isoxazolylpenicillins), to cephalosporins (with the exception of cefixime and ceftazidime) and to carbapenemes.

Explanation about the agent tested

- Isolate from urine: *Enterococcus* spp. Agent: norfloksacin disk is tested.
- Comment: *Enterococcus* - result of norfloksacin disk is valid for ciprofloxacin and levofloxacin, not for norfloxacin. Result applies to uncomplicated urinary tract infections only.

Comments linked to the agent, dose (2)

General comment about high dose.

- Isolate: *Pseudomonas* spp. Agent: ceftazidime
- Comment: Result applies to high dose therapy.

Specific once-daily application of high daily dose.

- Isolate: *Pseudomonas* spp. Agent: gentamicin.
- Comment: Result applies to once-daily administration of high aminoglycoside dosages.

Specific dose of an agent for the isolate.

- Isolate: isolate without species specific breakpoint, PK/PD breakpoints used. Agent: imipenem.
- Comment: Breakpoints apply to imipenem 500 mg x 4 daily administered intravenously over 30 minutes as the lowest dose. 1 g x 4 daily was taken into consideration for severe infections and in setting the R breakpoint.

Comments linked to the SIR result of an agent

Comment is **different for S or R or I result**.

Example: genus *Stapylococcus,* **methicillin** (tested with cefoxitin disk).

Isolate: any staphylococcus. Result: S.
Comment: Oxacillin susceptible staphylococcal isolate is also susceptible to other antistaphyloccal penicillins (e.g. cloxacillin, flucloxacillin), to penicillins with betalactamase inhibitors, to carbapenemes and to cephalosporins - except for ceftazidime, cefixime and ceftibuten, which should not be used for staphylococcal infections.

Isolate: *Stapylococcus aureus** Result: R.
Comment: *Stapylococcus aureus*, resistant to oxacillin, is resistant to all beta-lactam agents; exceptions are ceftaroline and ceftobiprole if their antimicrobial susceptibility result is susceptibility (S).

**Note: Comment for CNS are slightly different - no ceftaroline and ceftobiprole breakpoint.*

Comments linked to the MIC of an agent

Isolate: *Streptococcus pneumo*niae.

Comment is **different** for **different MIC results** in the table.

Result and comment for parenteral penicillin, **pneumonia**, non-meningeal criteria:

MIC (mg / L)	Category	Comment in the report (related to MIC)
>0,06 AND ≤0,5	I	Pneumonia: when a dose of 1.2 g x 4 is used, isolate should be regarded as susceptible.
>0,5 AND ≤1	I	Pneumonia: when a dose of 2.4 g x 4 or 1.2 g x 6 is used, isolate should be regarded as susceptible.
>1 AND ≤2	I	Pneumonia: when a dose of 2.4 g x 6 is used, isolate should be regarded as susceptible.

Sources.

Links to following »basic« documents are provided on the EUCAST web site http://www.eucast.org (current versions, accessed 25th March 2015).

General information at: http://www.eucast.org

- The European Committee on Antimicrobial Susceptibility Testing. ***Breakpoint tables for interpretation of MICs and zone diameters.*** Version 5.0, 2015.
- Leclercq R et al. *EUCAST expert rules in antimicrobial susceptibility testing* (2011)
- Giske CG et al. *EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance*. (Version 1.0. December 2013)
- Guidance Document on *Stenotrophomonas maltophilia* (1 Feb 2012)
- Guidance Document on *Burkholderia cepacia group* (20 July, 2013)
- Guidance Document on *Breakpoints for topical use of antimicrobial agents* (2014)
- *Check list to facilitate implementation of antimicrobial susceptibility testing with EUCAST breakpoints* (2010)
- *EUCAST QC table v 5.0* (2015-01-11)
- *Preparation of plates and media for EUCAST AST* (v 4.0, 19 June, 2014)
- *Compliance of manufacturers of susceptibility testing devices and materials* (25 September, 2014)

Disk-diffusion documents at: http://www.eucast.org
(current versions, accessed 25th March 2015).

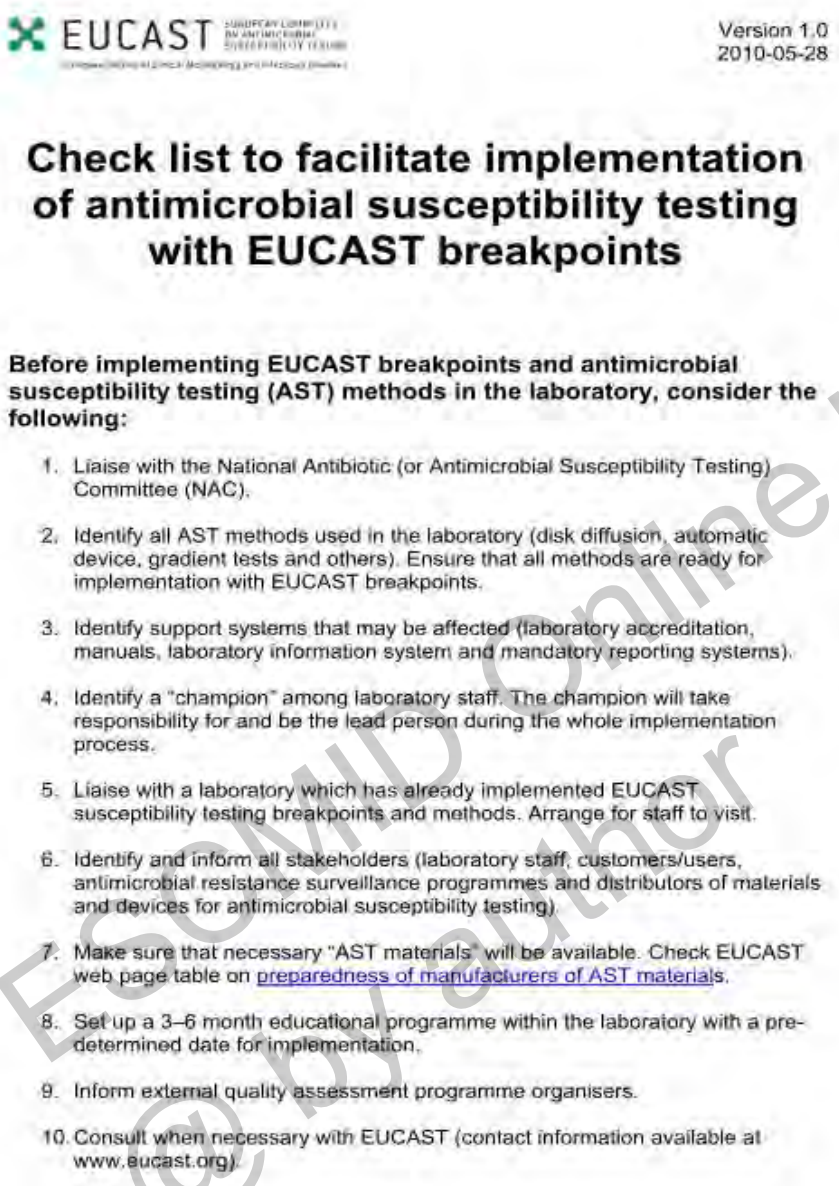
- *EUCAST Disk Diffusion - Manual* (v 5.0, 26 January, 2015)
- *EUCAST Disk Diffusion - Slide Show* (v 5.0, 26 January, 2015)
- *EUCAST Disk Diffusion - Reading Guide* (v. 4.0, 19 June, 2014)
- Matuschek E et al. *Development of the EUCAST disk diffusion antimicrobial susceptibility testing method and its implementation in routine microbiology laboratories*. (2014)

Whenever a clear answer can't be found in other documents,
solution can be frequently found following the link:

- *Frequently Asked Questions* (2015-03-23)

Whenever this option failed, we sent an E-mail to Erika Matuschek,
Clinical Scientist, responsible for the EUCAST Development Laboratory, Växjö, Sweden.
Answers were extremely fast and helpful. Thanks!

Implementation of EUCAST – laboratory work



EUCAST

Version 1.0
2010-05-28

Check list to facilitate implementation of antimicrobial susceptibility testing with EUCAST breakpoints

Before implementing EUCAST breakpoints and antimicrobial susceptibility testing (AST) methods in the laboratory, consider the following:

1. Liaise with the National Antibiotic (or Antimicrobial Susceptibility Testing) Committee (NAC).
2. Identify all AST methods used in the laboratory (disk diffusion, automatic device, gradient tests and others). Ensure that all methods are ready for implementation with EUCAST breakpoints.
3. Identify support systems that may be affected (laboratory accreditation, manuals, laboratory information system and mandatory reporting systems).
4. Identify a "champion" among laboratory staff. The champion will take responsibility for and be the lead person during the whole implementation process.
5. Liaise with a laboratory which has already implemented EUCAST susceptibility testing breakpoints and methods. Arrange for staff to visit.
6. Identify and inform all stakeholders (laboratory staff, customers/users, antimicrobial resistance surveillance programmes and distributors of materials and devices for antimicrobial susceptibility testing).
7. Make sure that necessary "AST materials" will be available. Check EUCAST web page table on preparedness of manufacturers of AST materials.
8. Set up a 3–6 month educational programme within the laboratory with a pre-determined date for implementation.
9. Inform external quality assessment programme organisers.
10. Consult when necessary with EUCAST (contact information available at www.eucast.org).

- **Basic guide: EUCAST "check list".**
- "General issues" were discussed by SKUOPZ
- Practical work was done in each laboratory
- SKUOPZ member was responsible for the process in each laboratory
- About 6 months of work was necessary before Quality Control results were fully compliant and EUCAST implemented.

Laboratory methods - training.

A lot of practice and “fine tuning” of procedures and staff was needed, most difficult parts were:

- searching for suitable MHF agar (home made or ready to use)
- proper inoculum procedure and reading of MHF plates.

Practical advice (provided by E. Matuschek):

- When inoculating haemophilus, procedure part “remove the excess fluid by turning the swab against the inside of the container” must be thorough, **swabs before inoculation extremely dry.**

Procedures on Mueller Hinton were technically relatively simple, **EUCAST disk diffusion reading guide and slide show very useful,** however, considerable amount of time still needed for details.

Laboratory methods - materials

Some new **quality control strains**.

Disk-diffusion method

- Some **disks** have different contents in CLSI and EUCAST.
- New **agar**: Mueller Hinton Fastidious agar.

MIC determination

Note:

- **SKUOPZ policy: use of commercial methods (including gradient diffusion) is the responsibility of each laboratory.**

Essential requirement – MIC materials (machines and consumables must be according to EUCAST).

Laboratory methods – materials, MICs

For EUCAST susceptibility testing purposes, the concentration of beta-lactamase inhibitors is fixed.
(sulbactam is fixed at 4 mg/L, of clavulanic acid at 2 mg/L, of tazobactam at 4 mg/L.)

Optimally, range of MIC values should be suitable for different purposes.
Example: ***Enterobacteriaceae,* meropenem**

Purpose	Lower MIC	Higher MIC
Clinical breakpoints	S ≤ 2 mg/L	R > 8 mg/L
Screening for carbapenemase	Negative screen ≤ 0.12 mg/L	Positive screen > 0.12 mg/L
EUCAST quality control range *Escherichia coli* ATCC 25922	Minimum 0.008	Maximum 0.06

Detailed Slovenian guidelines for *Enterobacteriaceae* – ESBL, AmpC and carbapenemases.

Guideline 001: Carbapenem resistance, *Enterobacteriaceae*.

Guideline 002: ESBL, AmpC, *Enterobacteriaceae*.

Slovenian guidelines for carbapenemase - producing *Enterobacteriaceae* .

Fully compliant with "EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance", Version 1.0, December 2013.
Details were specified, epidemiological definitions for CRE and CRE-CPE were added.

Screening cut –off:

- EUCAST guideline offers two possibilities for meropenem disk screening cut-off.
<25 mm ("best balance of sensitivity and specificity")
<27 mm ("may be used as a screening cut-off in countries where OXA-48 is endemic, but at the expense of lower specificity").
- meropenem cut-off < 27 mm was chosen
(other combinations of carbapenems can be used)

Phenotypic methods for detection of carbapenemases:

Two methods with different mechanisms are used for each "suspicious" isolate:
- **Carbapenem hydrolisis test** (Carba NP test or Blue-Carba).
- **Combined disks (tablets) with carbapenemase inhibitors**
(including "triple " disk + temocillin + cloxacillin)

Information for clinicians.

April 2014. Transition to EUCAST implemented.
When possible, personal contacts with clinicians were used.

One page long information about EUCAST, supplemented with table of major differences between CLSI and EUCAST, was distributed to users when we changed to EUCAST.
This information included link to SKUOPZ web home page, where concise but quite comprehensive information (15 pages) for clinicians were published:
"**Short explanation on transition to EUCAST** "(in Slovene)

http://www.imi.si/strokovna-zdruzenja/skuopz

Every day on each report.
Comments available when needed.

Bakterija	Antibiotik	Novost
Enterobakterije (*Escherichia coli, Klebsiella spp., Proteus spp., Enterobacter spp., Citrobacter spp., Serratia spp., Providencia spp., Morganella spp. idr.*)	amoksicilin s klavulansko kislino	- Dodana je posebna interpretacija za izolate **pri nezapletenih okužbah sečil** (oznaka v antibiogramu **AMCu**), s tem se možnost uporabe pri nezapletenih okužbah sečil poveča
	cefuroksim (iz generacija cefalosporinov)	- **parenteralno obliko cefuroksima** oznaka v antibiogramu **CXMp** pri enterobakterijah testiramo in interpretiramo le pri izolatih *E. coli*, *Klebsiella spp.* in *Proteus mirabilis*; pri drugih enterobakterijah je klinična učinkovitost vprašljiva, zato rezultate v izvidu ni - rezultati za **peroralno obliko cefuroksima** veljajo za enterobakterije **le pri nezapletenih okužbah sečil**
	vsi oralni cefalosporini	- učinkovitost pri sistemskih okužbah, povzročenih z enterobakterijami, ni zadostna, zato oralnih cefalosporinov ne testiramo - testiramo jih lahko pri izolatih iz sečil, njihova učinkovitost je **večinoma omejena le na nezapletene okužbe sečil**
	nitrofurantoin	- pri enterobakterijah rezultati veljajo le **za *E. coli* pri nezapletenih okužbah sečil**
	aminoglikozidi (gentamicin, idr.)	- rezultati veljajo le pri velikih odmerkih aminoglikozida enkrat dnevno
Pseudomonas spp.	cefepim	- rezultati veljajo le pri velikih odmerkih
	piperacilin s tazobaktamom	
	aminoglikozidi (gentamicin, amikacin, idr.)	- rezultati veljajo le pri velikih odmerkih aminoglikozida enkrat dnevno, pogosto se ne reši uporabi betalaktamskih antibiotikov
Acinetobacter spp.	ampicilin s sulbaktamom	- iz interpretacijskih kriterijev zaradi nezadostnih dokazov o klinični učinkovitosti
	piperacilin s tazobaktamom	
Serratia marcescens, Morganella	levofloksacin	- iz interpretacijskih kriterijev
	ciprofloksacin	[interpretacijski kriterij so le za tirosolopirne z sulfametoksazolom]
Haemophilus influenzae	makrolidi in oralni cefalosporini	- rezultat je lahko le intermediaren ali odporen, kategorije občutljiv ni zaradi prenizkih mejnih koncentracij zdravila
	cefiksim	- klinično neučinkovit in zato ne testiramo
Enterococcus faecalis, Staphylococcus saprophyticus, Streptococcus agalactiae	nitrofurantoin	- rezultati veljajo le za navedene vrste pri nezapletenih okužbah sečil, ne veljajo za druge vrste navedenih rodov bakterij, ne za druge okužbe
Streptococcus agalactiae	penicilin	- OPMK občutljiv za penicilin, je občutljiv za vse penicilime, **razen za protistafilokokne penicilne in oralni fenoksimetilpenicilin**

"Short explanation on transition to EUCAST"

*Kratka pojasnila ob prehodu na EUCAST, marec 2014, **verzija 1***

Iztok Štrumbelj, Helena Ribič, Mateja Pirš

Kratka pojasnila ob prehodu na evropske smernice za antibiogram - EUCAST

Po sklepu Slovenske komisije za ugotavljanje občutljivosti za protimikrobna zdravila, SKUOPZ, laboratoriji za klinično mikrobiologijo v Sloveniji na področju antibiogramov konec meseca marca 2014 prehajamo iz ameriških standardov (**CLSI**, Clinical and Laboratory Standard Institute) na **evropske smernice (EUCAST, European Committee on Antimicrobial Susceptibility Testing).** Številni dokumenti EUCAST so prosto dostopni na spletni strani EUCAST: http://www.eucast.org/

Te smernice v Evropi močno prevladujejo, temeljijo na rezultatih raziskav farmakokinetike in farmakodinamike posameznega zdravila, mehanizmov odpornosti mikrobov, »*in vitro*« raziskav, kliničnih raziskav glede učinkovitosti in na izkušnjah z uspešnostjo zdravljenja okužb v klinični praksi.

Želimo vas opozoriti **na najpomembnejše in najpogostejše spremembe ob prehodu na EUCAST**. Veljavna verzija tega besedila je objavljena na spletni strani SKUOPZ (www.imi.si/strokovna-zdruzenja/skuopz/). Podrobnejše obrazložitve bomo pripravili v priročniku »Interpretacija antibiograma za zdravnike«, ki bo kasneje objavljen na isti spletni strani. Tudi ta »kratka pojasnila« bomo večkrat posodobili.

Results of the process

April 2014: all but one diagnostic medical microbiology laboratories in Slovenia implemented EUCAST.

Results of external quality assessment (EQA)

All SKUOPZ laboratories that have implemented EUCAST were asked to report all scored results of EQA since April 2014 to the end of 2014.

Cumulative results for 1154 bacteria/antibiotic results:

- Categorical agreement: 1149 (99.6 %)
- Major discrepancy: 4 (0.3%)
- Very major discrepancy: 1 (0.1%)

Conclusions

Introduction of EUCAST was a **demanding national project**:

- coordinated by the national AST committee – SKUOPZ
- activities “at the bench” were performed by each laboratory.

Three key points were:

- Changes in laboratory information system
- Changes in laboratory methods
- Information for clinicians.

System was **well accepted** by both laboratories and clinicians.

Acknowledgments

EUCAST Secretariat, EUCAST Development Laboratory and speakers at EUCAST symposium in Ljubljana

Rafael Cantón, Derek Brown, Gunnar Kahlmeter, Erika Matuschek, Arjana Tambić Andrašević, Iva Butić, Katja Seme

SKUOPZ members

Ingrid Berce, Jerneja Fišer, Andrej Golle, Tatjana Harlander, Martina Kavčič, Jana Kolman, Slavica Lorenčič-Robnik, Tadeja Matos, Verica Mioč, Manica Mueller-Premru, Irena Piltaver-Vajdec, Mateja Pirš, Katja Seme, Helena Ribič, Alenka Štorman, Viktorija Tomič, Barbara Zdolšek, Manca Žolnir Dovč.

Laboratory staff of Slovenian clinical microbiology laboratories

Review of this presentation

Katja Seme, Mateja Pirš, Jernej Štrumbelj