




EFSA EUSR-AMR Workflow and Criteria for ESBL/AmpC/Carbapenemase -Phenotypes

OUTLINE

- 
- Background documents
 - Workflows (WFs)
 - Workflow ESBL and AMPc
 - Workflow NON ESBL
 - Workflow CARBAPENEMASE
 - Criteria
 - Validation
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BACKGROUND USED TO SET CRITERIA



EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance

Version 1.0
December 2013

SCIENTIFIC REPORT OF EFSA

Technical specifications on the harmonised monitoring and reporting of antimicrobial resistance in *Salmonella*, *Campylobacter* and indicator *Escherichia coli* and *Enterococcus* spp. bacteria transmitted through food¹

European Food Safety Authority^{2,3}

COMMISSION IMPLEMENTING DECISION

of 12 November 2013

on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria

(notified under document C(2013) 7145)

(Text with EEA relevance)


(2013/652/EU)

Table 4

Panel of antimicrobial substances, EUCAST epidemiological cut-off values (ECOFFs) and clinical resistance breakpoints and concentrations ranges to be used for testing only *Salmonella* spp. and indicator commensal *E. coli* isolates resistant to cefotaxime or ceftazidime or meropenem — (Second panel)

Antimicrobial	Species	Interpretative thresholds of AMR (mg/L)		Range of concentrations (mg/L) (No of wells in brackets)
		ECOFF (*)	Clinical breakpoint (†)	
Cefoxitin	<i>Salmonella</i>	> 8	NA	0,5-64 (8)
	<i>E. coli</i>	> 8	NA	
Cefepime	<i>Salmonella</i>	NA	NA	0,06-32 (10)
	<i>E. coli</i>	> 0,125	> 4	
Cefotaxime + clavulanic acid (*)	<i>Salmonella</i>	NA (**)	NA (**)	0,06-64 (11)
	<i>E. coli</i>	NA (**)	NA (**)	
Ceftazidime + clavulanic acid (*)	<i>Salmonella</i>	NA (**)	NA (**)	0,125-128 (11)
	<i>E. coli</i>	NA (**)	NA (**)	
Meropenem	<i>Salmonella</i>	> 0,125	> 8	0,03-16 (10)
	<i>E. coli</i>	> 0,125	> 8	
Temocillin	<i>Salmonella</i>	NA	NA	0,5-64 (8)
	<i>E. coli</i>	NA	NA	
Imipenem	<i>Salmonella</i>	> 1	> 8	0,12-16 (8)
	<i>E. coli</i>	> 0,5	> 8	
Ertapenem	<i>Salmonella</i>	> 0,06	> 1	0,015-2 (8)
	<i>E. coli</i>	> 0,06	> 1	
Cefotaxime	<i>Salmonella</i>	> 0,5	> 2	0,25-64 (9)
	<i>E. coli</i>	> 0,25	> 2	
Ceftazidime	<i>Salmonella</i>	> 2	> 4	0,25-128 (10)
	<i>E. coli</i>	> 0,5	> 4	

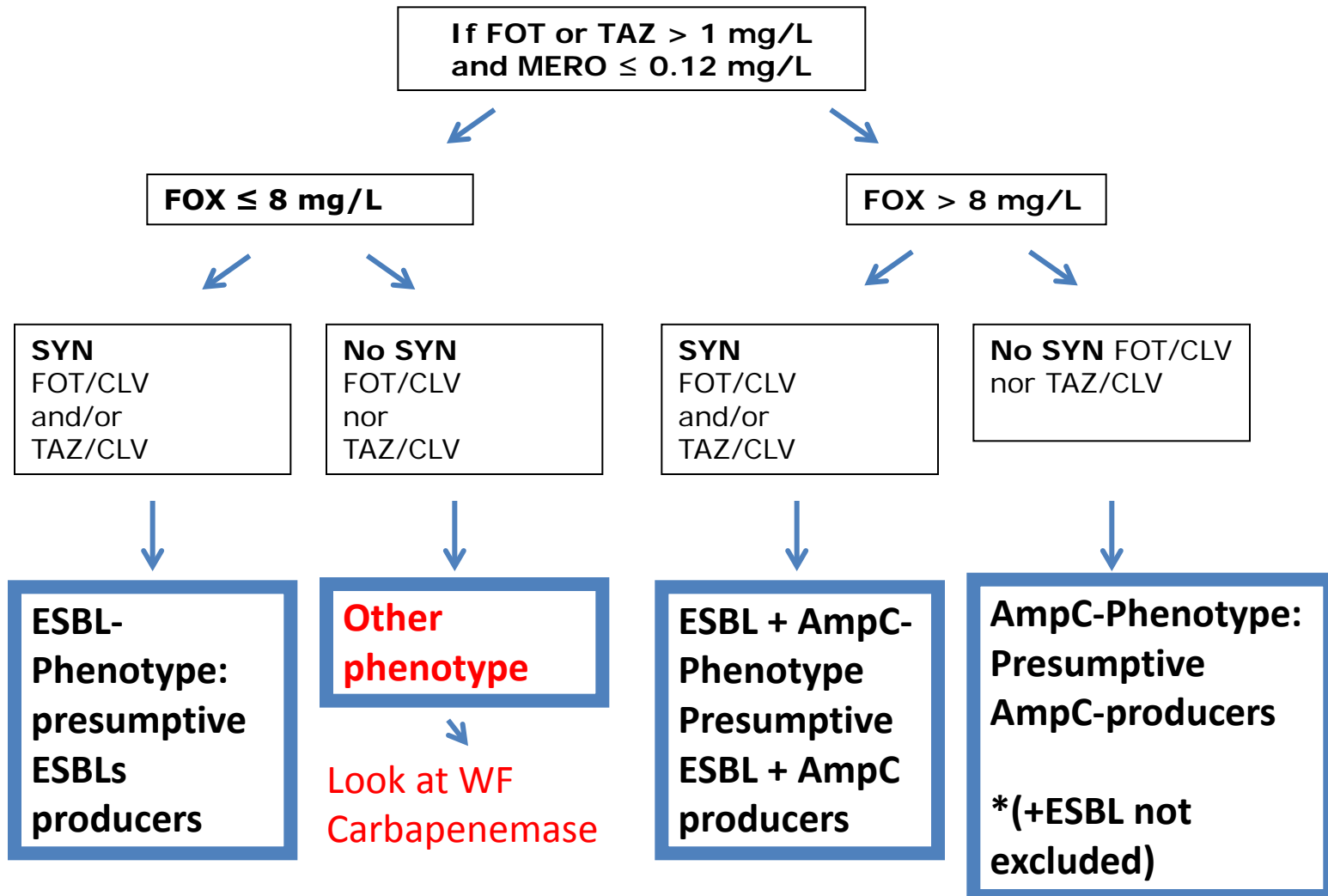
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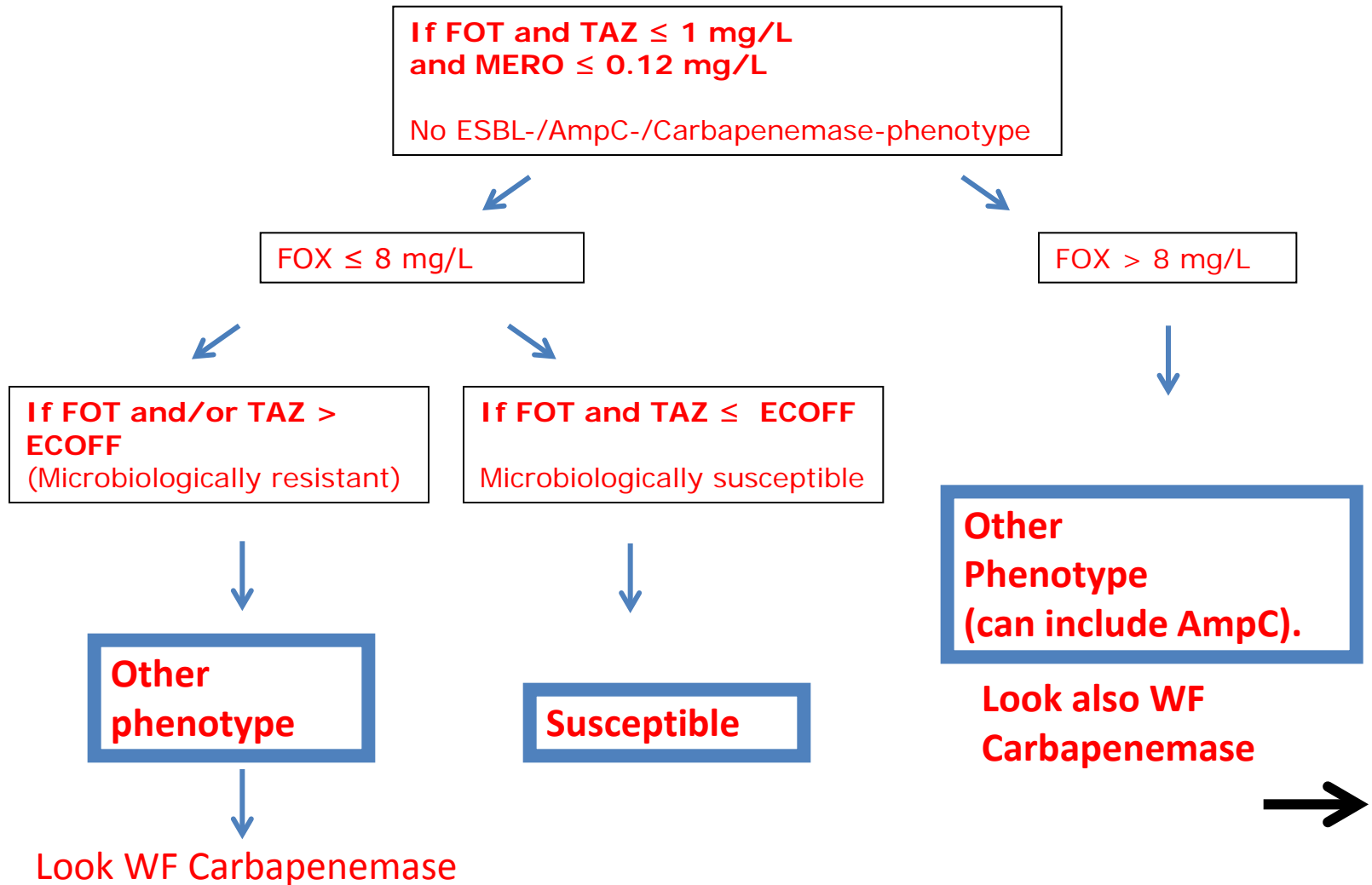
WORKFLOW (WF) ESBL AND AMPC

ESBL/AmpC/ESBL+AmPC Phenotypes



WORKFLOW NON ESBL

Non ESBL Phenotypes





WORKFLOW CARBAPENEMASE

Carbapenemase-Phenotype

If MERO > 0.12 mg/L



**Carbapenemase-Phenotype:
presumptive CP
producers*
(+ ESBL and/or AmpC
is possible)****

***Confirmation by
molecular/biochemical tests
needed.**

****i.e. if SYN CLAV, suggest +ESBL**

If MERO ≤ 0.12 mg/L
But ETP > 0.06 mg/L
and/or
IMI > 0.5 mg/L EC, > 1 mg/L Salmonella



**Other
Phenotype?***



Look at the other Workflows

*** Some CP-producers could be
found here. Confirmation by
molecular/biochemical tests
needed.**

CRITERIA

ESBL-Phenotype

- FOT or TAZ > 1 mg/L AND
- MERO ≤ 0.12 mg/L AND
- FOX ≤ 8 mg/L AND
- SYN FOT/CLV and/or TAZ/CLV

AmpC-Phenotype

- FOT or TAZ > 1 mg/L AND
- MERO ≤ 0.12 mg/L AND
- FOX > 8 mg/L AND
- No SYN FOT/CLV nor TAZ/CLV
- (Not excluded presence of ESBLs)

ESBL + AmpC-Phenotype

- FOT or TAZ > 1 mg/L AND
- MERO ≤ 0.12 mg/L AND
- FOX > 8 mg/L AND
- SYN FOT/CLV and/or TAZ/CLV

Carbapenemase-Phenotype

- MEROM > 0.12 mg/L
- Needs confirmation
- (Not excluded presence of ESBLs or AmpC)

Susceptible

FOT-TAZ-FOX-MEM
≤ ECOFF

Other phenotypes

- 1) If FOT or TAZ > 1 mg/ml AND
 - MEM ≤ 0.12 mg/L AND
 - FOX ≤ 8 mg/L AND
 - NO SYN FOT/CLV nor TAZ/CLV
 - Not excluded CPs (consult EURL)
- 2) If FOT and/or TAZ ≤ 1 mg/L AND > ECOFF AND
 - MERO ≤ 0.12 mg/L
 - FOX ≤ 8 mg/L
- 3) If FOT and/or TAZ ≤ 1 mg/L
 - MERO ≤ 0.12 mg/L
 - FOX > 8 mg/L.
 - *cAmpCs could be included here
- 4) If MERO ≤ 0.12 mg/L BUT
 - ETP > ECOFF AND/OR
 - IMI > ECOFF
 - Not excluded CPs, needs confirmation (consult EURL)

5) Any other combinations not described in previous boxes (contact EURL)

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VALIDATION

- MSs provided genotypic data: BE, SE, ES, CZ, IT
- Comparisson of results with MSs that provided both Panel 2 phenotypical data and genetic data:
 - All excepting 6 out of 151 isolates correctly classified
- Differences for classification:
 - “Presumptive ESBL + AmpC-producers” with reported low MIC values for FOX:
 - Could be related, at least in *E. coli*, with putative expression of intrinsic AmpC genes (not reported to us).
 - Could be related to reporting 1 step MIC over the ECOFF
 - 1 isolate no synergy reported and no FOX, but SHV-positive
 - Wrong reporting? Other mechanisms not detected?
- To analyse results from last PTs applying the criteria (to be done)

CONCLUSSIONS

- **As we only have phenotypic data...**
- ...and different combinations of genes exist
- ...and „wrong“ reporting is possible
- ...and „wrong“ interpretation is possible
- ...and strange results can appear
- **Overseing mechanisms /missclassification can happens but most of the results can be inferred in the right way!!!**
- For CPs, molecular/biochemical confirmation is needed. In other cases, is recommended.
- In case of problems when interpreting results, please contact EURL-AR or EFSA

THANK YOU FOR YOUR ATTENTION !

Thanks to:

EFSA AMR Team (P-A, Anca, Ernesto)

EURL-AR Team (Lina, Valeria)

Other experts: H. Hasman, S. Granier, C. Teale

MSs, specially for providing genetic data

- 2014 EU Summary Report on AMR
 - www.efsa.europa.eu

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