

What are the rational for the changes in the antimicrobial panels

Changes in MIC plate design

Rene S. Hendriksen, PhD
Research group of Global Capacity Building
National Food Institute,
Technical University of Denmark

21 September 2021
Virtual meeting

Background for update

- Suggestions of **inclusion of additional substances** were based on:
 - discussed in the **EFSA expert group** incl. the EURL
 - through a **specific questionnaire** survey to consider less significance substances for the first panel
 - all were **carefully assessed and addressed**
- Antimicrobials listed in **previous recommendations** should remain in future testing requirements
 - emphasis on **last-resort antimicrobials** in the treatment of certain infections with highly resistant Gram-negative bacteria in humans, such as the **carbapenems** and **colistin**

EFSA (European Food Safety Authority), Aerts M, Battisti A, Hendriksen R, Kempf I, Teale C, Tenhagen B-A, Veldman K, Wasyl D, Guerra B, Liebana E, Thomas-Lopez D and Belœil P-A, 2019. Scientific report on the technical specifications on harmonised monitoring of antimicrobial resistance in zoonotic and indicator bacteria from food-producing animals and food. EFSA Journal 2019;17(6):5709, 122 pp. <https://doi.org/10.2903/j.efsa.2019.5709>

Reasoning behind the new Gram neg panel

- Complement the harmonized panel of substances with amikacin
 - one of the **most commonly used aminoglycosides** in hospitals for the treatment of infections by Gram-negative bacteria in a number of MSs
 - **large differences** in use across the EU, with very high use in some MSs with high levels of resistance in Gram-negatives opposed to not used at all
 - **cross-resistance with other aminoglycosides** - marker in addition to gentamicin
 - **improve the detection of the 16S rRNA methyltransferases** associated with carbapenemases, AmpC or ESBLs and FQ resistance in Gram-negative Enterobacteriaceae
- Allow for inclusion of amikacin by
 - slightly reduce some of the dilution ranges in the upper end of the scales:
 - in particular those for ampicillin, nalidixic acid, tetracycline, gentamicin, trimethoprim, sulfamethoxazole and chloramphenicol

Salmonella / E. coli panel

EUVSEC3 - 2020/1729

EUVSEC2 - 2013/652

	1	2	3	4	5	6	7	8	9	10	11	12
A	AMP 32	AZI 64	AMI 128	GEN 16	TGC 8	TAZ 8	FOT 4	COL 16	NAL 64	TET 32	TMP 16	SMX 512
B	AMP 16	AZI 32	AMI 64	GEN 8	TGC 4	TAZ 4	FOT 2	COL 8	NAL 32	TET 16	TMP 8	SMX 256
C	AMP 8	AZI 16	AMI 32	GEN 4	TGC 2	TAZ 2	FOT 1	COL 4	NAL 16	TET 8	TMP 4	SMX 128
D	AMP 4	AZI 8	AMI 16	GEN 2	TGC 1	TAZ 1	FOT 0.5	COL 2	NAL 8	TET 4	TMP 2	SMX 64
E	AMP 2	AZI 4	AMI 8	GEN 1	TGC 0.5	TAZ 0.5	FOT 0.25	COL 1	NAL 4	TET 2	TMP 1	SMX 32
F	AMP 1	AZI 2	AMI 4	GEN 0.5	TGC 0.25	TAZ 0.25	CHL 8	CHL 16	CHL 32	CHL 64	TMP 0.5	SMX 16
G	MERO 0.03	MERO 0.06	MERO 0.12	MERO 0.25	MERO 0.5	MERO 1	MERO 2	MERO 4	MERO 8	MERO 16	TMP 0.25	SMX 8
H	CIP 0.015	CIP 0.03	CIP 0.06	CIP 0.12	CIP 0.25	CIP 0.5	CIP 1	CIP 2	CIP 4	CIP 8	POS CON	POS CON

	1	2	3	4	5	6	7	8	9	10	11	12
A	SMX 1024	TMP 32	CIP 8	TET 64	MERO 16	AZI 64	NAL 128	CHL 128	TGC 8	COL 16	AMP 64	GEN 32
B	SMX 512	TMP 16	CIP 4	TET 32	MERO 8	AZI 32	NAL 64	CHL 64	TGC 4	COL 8	AMP 32	GEN 16
C	SMX 256	TMP 8	CIP 2	TET 16	MERO 4	AZI 16	NAL 32	CHL 32	TGC 2	COL 4	AMP 16	GEN 8
D	SMX 128	TMP 4	CIP 1	TET 8	MERO 2	AZI 8	NAL 16	CHL 16	TGC 1	COL 2	AMP 8	GEN 4
E	SMX 64	TMP 2	CIP 0.5	TET 4	MERO 1	AZI 4	NAL 8	CHL 8	TGC 0.5	COL 1	AMP 4	GEN 2
F	SMX 32	TMP 1	CIP 0.25	TET 2	MERO 0.5	AZI 2	NAL 4	FOT 1	TGC 0.25	TAZ 2	AMP 2	GEN 1
G	SMX 16	TMP 0.5	CIP 0.12	CIP 0.03	MERO 0.25	MERO 0.06	FOT 4	FOT 0.5	TAZ 8	TAZ 1	AMP 1	GEN 0.5
H	SMX 8	TMP 0.25	CIP 0.06	CIP 0.015	MERO 0.12	MERO 0.03	FOT 2	FOT 0.25	TAZ 4	TAZ 0.5	POS CON	POS CON

ECOFF Salmonella EU surveillance 2021

Red boxes indicate those that have been removed in the new plate

ECOFF E. coli EU surveillance 2021

Reasoning behind the panel for the Spec. monit.

- **Continuation of the current panel** which includes:
 - cefoxitin, cefepime and clavulanate in combination with cefotaxime and ceftazidime for the detection of presumptive ESBL and AmpC producers
 - imipenem, meropenem and ertapenem to phenotypically identify presumptive carbapenemase producers

Panel for the Spec. Monitoring

EUVSEC3 - 2020/1729

EUVSEC2 - 2013/652

	1	2	3	4	5	6	7	8	9	10	11	12
A	FOX 0.5	FOX 1	FOX 2	FOX 4	FOX 8	FOX 16	FOX 32	FOX 64	FOT 0.25	FOT 0.5	FOT 1	TRM 128
B	ETP 0.015	ETP 0.03	ETP 0.06	ETP 0.12	ETP 0.25	ETP 0.5	ETP 1	ETP 2	FOT 2	FOT 4	FOT 8	TRM 64
C	IMI 0.12	IMI 0.25	IMI 0.5	IMI 1	IMI 2	IMI 4	IMI 8	IMI 16	FOT 16	FOT 32	FOT 64	TRM 32
D	MERO 0.03	MERO 0.06	MERO 0.12	MERO 0.25	MERO 0.5	MERO 1	MERO 2	MERO 4	MERO 8	MERO 16	TRM 2	TRM 16
E	TAZ 0.25	TAZ 0.5	TAZ 1	TAZ 2	TAZ 4	TAZ 8	TAZ 16	TAZ 32	TAZ 64	TAZ 128	TRM 1	TRM 8
F	FEP 0.06	FEP 0.12	FEP 0.25	FEP 0.5	FEP 1	FEP 2	FEP 4	FEP 8	FEP 16	FEP 32	TRM 0.5	TRM 4
G	F/C 0.06/4	F/C 0.12/4	F/C 0.25/4	F/C 0.5/ 1/4	F/C 1/4	F/C 2/4	F/C 4/4	F/C 8/4	F/C 16/4	F/C 32/4	F/C 64/4	POS KON
H	T/C 0.12/4	T/C 0.25/4	T/C 0.5/4	T/C 1/4	T/C 2/4	T/C 4/4	T/C 8/4	T/C 16/4	T/C 32/4	T/C 64/4	T/C 128/4	POS KON

Reasoning behind the panel for the Campy. panel

- Recent findings related to **emerging mechanisms of resistance in Campylobacter spp. need to be addressed:**
 - the presence of the **erm(B) gene** in Campylobacter spp. has been reported
 - detection is critical as often present on mobile genetic elements
 - usually responsible for a very high level of macrolide resistance (> 128 mg/L)
 - current harmonised panel does **not allow detection of the precise ciprofloxacin MIC** of isolates not inhibited by 16 mg/L
 - **chloramphenicol** or florfenicol absent but included to allow detection of CmeABC pump
 - **carbapenem-non-susceptible** Campylobacter strains have already been reported and this should be addressed by incl. a carbapenem
- Allow for inclusion of ertapenem and chloramphenicol by
 - **omitting streptomycin** which is optional for testing
 - resistance to ciprofloxacin parallels resistance to **nalidixic acid, thus omitted**

Campylobacter panel

EUVSEC3 - 2020/1729

	1	2	3	4	5	6
A	CHL 64	ERY 512	GEN 16	CIP 32	TET 64	ETP 4
B	CHL 32	ERY 256	GEN 8	CIP 16	TET 32	ETP 2
C	CHL 16	ERY 128	GEN 4	CIP 8	TET 16	ETP 1
D	CHL 8	ERY 64	GEN 2	CIP 4	TET 8	ETP 0.5
E	CHL 4	ERY 32	GEN 1	CIP 2	TET 4	ETP 0.25
F	CHL 2	ERY 16	GEN 0.5	CIP 1	TET 2	ETP 0.12
G	ERY 2	ERY 8	GEN 0.25	CIP 0.5	TET 1	POS CON
H	ERY 1	ERY 4	CIP 0.12	CIP 0.25	TET 0.5	POS CON

EUVSEC2 - 2013/652

	1	2	3	4	5	6
A	ERY 128	CIP 16	TET 64	GEN 16	NAL 64	STR 16
B	ERY 64	CIP 8	TET 32	GEN 8	NAL 32	STR 8
C	ERY 32	CIP 4	TET 16	GEN 4	NAL 16	STR 4
D	ERY 16	CIP 2	TET 8	GEN 2	NAL 8	STR 2
E	ERY 8	CIP 1	TET 4	GEN 1	NAL 4	STR 1
F	ERY 4	CIP 0.5	TET 2	GEN 0.5	NAL 2	STR 0.5
G	ERY 2	CIP 0.25	TET 1	GEN 0.25	NAL 1	STR 0.25
H	ERY 1	CIP 0.12	TET 0.5	GEN 0.12	POS CON	POS CON

Red boxes indicate those that have been removed in the new plate

In summary

- **Gram neg panel for Salmonella and E. coli:**
 - amikacin was included on the basis of a slight reduction of ampicillin, nalidixic acid, tetracycline, gentamicin, trimethoprim, sulfamethoxazole and chloramphenicol
- **Panel for the Spec. Monitoring:**
 - continuation of the current panel
- **Panel for Campylobacter:**
 - extending range for ciprofloxacin and erythromycin
 - including chloramphenicol and ertapenem by omitting streptomycin and nalidixic acid



What are the current experiences from NRLs

- Amikacin-R in Gram- negatives?
- Ertapenem-R in Campylobacter?



Questions and discussion

Prof. Rene S. Hendriksen, PhD

Head of Research Group Global Capacity Building
WHO Collaborating Centre for Antimicrobial Resistance in Food borne
Pathogens and Genomics

European Union Reference Laboratory for Antimicrobial Resistance
FAO Reference Laboratory for Antimicrobial Resistance
National Food Institute, Technical University of Denmark

rshe@food.dtu.dk

