21-22 September 2021
15th EURL-AR Workshop 2021

Applied ECOFFs for reporting of surveillance data to the EFSA database

Presenter

Trusted science for safe food

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

efsa European Food Safety Authority

1. Monitoring AMR: Legal Bases

Published on
14 November 2013

Published on
17 November 2020

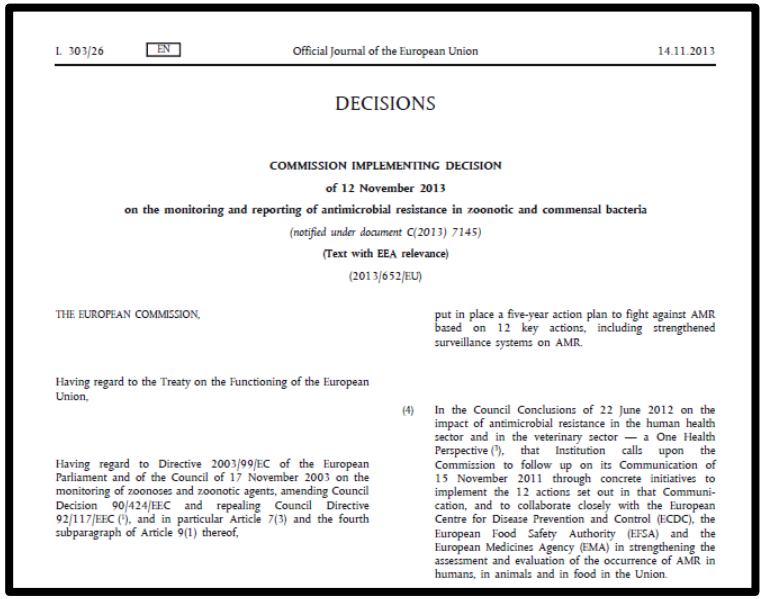
2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022

Commission
Implementing Decision 2013/652/EU

Lays down rules
2014 - 2020

Commission
Implementing Decision 2020/1729/EU

Lays down specific tech. requirements **2021 - 2027**



L 303/26 EN Official Journal of the European Union 14.11.2013

DECISIONS

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)

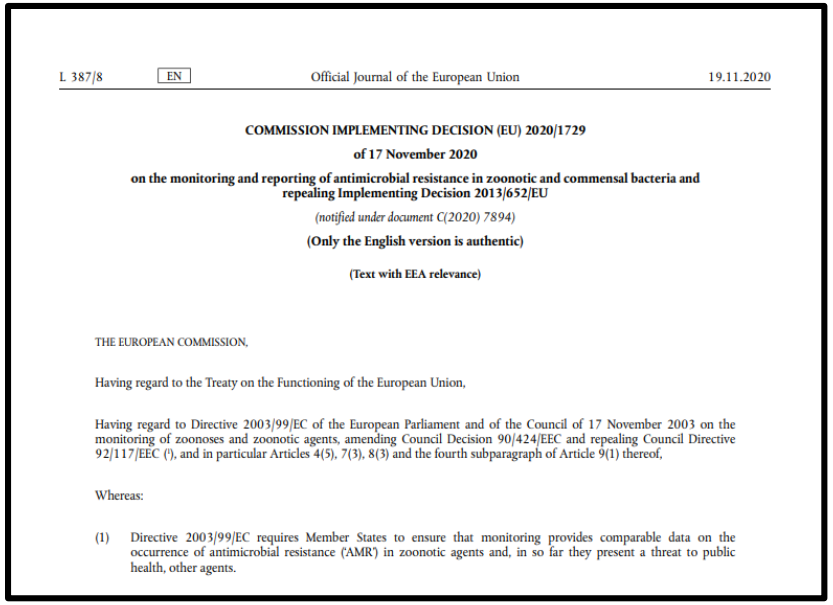
THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Directive 2003/99/EC of the European Parliament and of the Council of 17 November 2003 on the monitoring of zoonoses and zoonotic agents, amending Council Decision 90/424/EEC and repealing Council Directive 92/117/EEC (1), and in particular Article 7(3) and the fourth subparagraph of Article 9(1) thereof,

put in place a five-year action plan to fight against AMR based on 12 key actions, including strengthened surveillance systems on AMR.

(4) In the Council Conclusions of 22 June 2012 on the impact of antimicrobial resistance in the human health sector and in the veterinary sector — a One Health Perspective (2), that Institution calls upon the Commission to follow up on its Communication of 15 November 2011 through concrete initiatives to implement the 12 actions set out in that Communication, and to collaborate closely with the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA) in strengthening the assessment and evaluation of the occurrence of AMR in humans, in animals and in food in the Union.



L 387/8 EN Official Journal of the European Union 19.11.2020

COMMISSION IMPLEMENTING DECISION (EU) 2020/1729

of 17 November 2020

on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria and repealing Implementing Decision 2013/652/EU

(notified under document C(2020) 7894)

(Only the English version is authentic)

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Directive 2003/99/EC of the European Parliament and of the Council of 17 November 2003 on the monitoring of zoonoses and zoonotic agents, amending Council Decision 90/424/EEC and repealing Council Directive 92/117/EEC (1), and in particular Articles 4(5), 7(3), 8(3) and the fourth subparagraph of Article 9(1) thereof,

Whereas:

(1) Directive 2003/99/EC requires Member States to ensure that monitoring provides comparable data on the occurrence of antimicrobial resistance ('AMR') in zoonotic agents and, in so far they present a threat to public health, other agents.

1. Changes on the ECOFFS and CBPs:
1.1 *Salmonella* spp.— First panel

Table 1: Panel of antimicrobial substances to be included in AMR monitoring, interpretative thresholds for interpreting resistance and concentration ranges to be tested in *Salmonella* **spp. (First panel)**

Antimicrobial	Class of Antimicrobial	*Interpretative thresholds of AMR (mg/L) according to* Commission Implementing Decision 2013/652/EU			*Interpretative thresholds of AMR (mg/L) according to* Commission Implementing Decision 2020/1729/EU		
		ECOFF[a]	Clinical breakpoint [b]	Concentration range, mg/L (no of wells)	ECOFF[a]	Clinical breakpoint [b]	Concentration range, mg/L (no of wells)
Amikacin[c]	Aminoglycoside				>4 (**)	>16	4-128 (6)
Ampicillin	Penicillin	>8	>8	1-64 (7)	>8 [>4]	>8	1-32 (6)
Azithromycin	Macrolide	NA	NA	2-64 (6)	NA [>16]	NA	2-64 (6)
Cefotaxime	Cephalosporin	>0,5	>2	0,25-4 (5)	>0,5	>2	0,25-4 (5)
Ceftazidime	Cephalosporin	>2	>4	0,5-8 (5)	>2	>4	0,25-8 (5)
Chloramphenicol	Phenicol	>16	>8	8-128 (5)	>16	>8	8-64 (4)
Ciprofloxacin	Fluoroquinolone	>0,064	>1	0,015-8 (10)	>0,06	>0,06	0,015-8 (10)
Colistin	Polymyxin	>2	>2	1-16 (5)	NA [>2]	>2	1-16 (5)
Gentamicin	Aminoglycoside	>2	>4	0,5-32 (7)	>2	>4	0,5-16 (6)
Meropenem	Carbapenem	>0,125	>8	0,03-16 (10)	>0,125 [0,06]	>8	0,03-16 (10)
Nalidixic acid	Quinolone	>16	NA	4-128 (6)	>8	NA	4-64 (5)
Sulfamethoxazole	Folate pathway antagonist	NA	NA	8-1024 (8)	NA [>256]	NA [>4]	8-512 (7)
Tetracycline	Tetracycline	>8	NA	2-64 (6)	>8	NA	2-32 (5)
Tigecycline	Glycylcycline	>1 (*)	>2 (*)	0,25-8 (6)	NA [>0,5]	NA	0,25-8 (6)
Trimethoprim	Folate pathway antagonist	>2	>4	0,25-32 (8)	>2	>4	0,25-16 (7)

[a] EUCAST epidemiological cut-off values.
[b] EUCAST clinical resistance breakpoints.
[c] EUCAST epidemiological cut-off (ECOFF) value is tentative.
NA: not available.
(*) Data from EUCAST available for *Salmonella* Enteriditis, Typhimurium, Typhi and Paratyphi.
(**) tentative EUCAST threshold

[] value to be used proposed by EFSA + EURL-AR for data reporting purposes
[] value to be used is the new value established by EUCAST
[] value recently changed in EUCAST

1. Changes in the ECOFFS and CBPs

1.2. Indicator *E. coli* — First panel

Table 2: Panel of antimicrobial substances to be included in AMR monitoring, interpretative thresholds for interpreting resistance and concentration ranges to be tested in indicator *E. coli* **(First panel)**

Antimicrobial	Class of Antimicrobial	*Interpretative thresholds of AMR (mg/L) according to* Commission Implementing Decision 2013/652/EU			*Interpretative thresholds of AMR (mg/L) according to* Commission Implementing Decision 2020/1729/EU		
		ECOFF[a]	Clinical breakpoint [b]	Concentration range, mg/L (no of wells)	ECOFF[a]	Clinical breakpoint [b]	Concentration range, mg/L (no of wells)
Amikacin[c]	Aminoglycoside				>8	>16	4-128 (6)
Ampicillin	Penicillin	>8	>8	1-64 (7)	>8	>8	1-32 (6)
Azithromycin	Macrolide	NA	NA	2-64 (6)	NA [>16] [>8]	NA	2-64 (6)
Cefotaxime	Cephalosporin	>0,25	>2	0,25-4 (5)	>0,25	>2	0,25-4 (5)
Ceftazidime	Cephalosporin	>0,5	>4	0,5-8 (5)	>0,5	>4	0,25-8 (5)
Chloramphenicol	Phenicol	>16	>8	8-128 (5)	>16	>8	8-64 (4)
Ciprofloxacin	Fluoroquinolone	>0,064	>1	0,015-8 (10)	>0,06	>0,5	0,015-8 (10)
Colistin	Polymyxin	>2	>2	1-16 (5)	>2	>2	1-16 (5)
Gentamicin	Aminoglycoside	>2	>4	0,5-32 (7)	>2	>4	0,5-16 (6)
Meropenem	Carbapenem	>0,125	>8	0,03-16 (10)	>0,125 [>0,06]	>8	0,03-16 (10)
Nalidixic acid	Quinolone	>16	NA	4-128 (6)	>8	NA	4-64 (5)
Sulfamethoxazole	Folate pathway antagonist	>64	NA	8-1.024 (8)	>64	NA [>4]	8-512 (7)
Tetracycline	Tetracycline	>8	NA	2-64 (6)	>8	NA	2-32 (5)
Tigecycline	Glycylcycline	>1	>2	0,25-8 (6)	>0,5	>0,5	0,25-8 (6)
Trimethoprim	Folate pathway antagonist	>2	>4	0,25-32 (8)	>2	>4	0,25-16 (7)

[a] EUCAST epidemiological cut-off values.
[b] EUCAST clinical resistance breakpoints.
NA: not available.

[] value to be used proposed by EFSA + EURL-AR for data reporting purposes
[] value to be used is the new value established by EUCAST
[] value recently changed in EUCAST

1. Changes in the ECOFFS and CBPs

1.3. *C. jejuni* and *C. coli*

Table 3: Panel of antimicrobial substances to be included in AMR monitoring, interpretative thresholds for resistance and concentration ranges to be tested in *C. jejuni* and *C. coli*

Antimicrobial	Class of Antimicrobial	Species	*Interpretative thresholds of AMR (mg/L) according to* Commission Implementing Decision 2013/652/EU			*Interpretative thresholds of AMR (mg/L) according to* Commission Implementing Decision 2020/1729/EU		
			ECOFF[(a)]	Clinical breakpoint [(b)]	Concentration range, mg/L (no of wells)	ECOFF[(a)]	Clinical breakpoint [(b)]	Concentration range, mg/L (no of wells)
Chloramphenicol	Phenicol	*C. jejuni*				>16	NA	2-64 (6)
		C. coli				>16	NA	2-64 (6)
Ciprofloxacin	Fluoroquinolone	*C. jejuni*	>0,5	>0,5	0,12-16 (8)	>0,5	>0,5	0,12-32 (9)
		C. coli	>0,5	>0,5	0,12-16 (8)	>0,5	>0,5	0,12-32 (9)
Ertapenem	Carbapenem	*C. jejuni*				NA [>0,5]	NA	0,125-4 (6)
		C. coli				NA [>0,5]	NA	0,125-4 (6)
Erythromycin	Macrolide	*C. jejuni*	>4	>4	1-128 (8)	>4	>4	1-512 (10)
		C. coli	>8	>8	1-128 (8)	>8	>8	1-512 (10)
Gentamicin	Aminoglycoside	*C. jejuni*	>2	NA	0,12-16 (8)	>2 [>1]	NA	0,25-16 (7)
		C. coli	>2	NA	0,12-16 (8)	>2 [>1]	NA	0,25-16 (7)
Tetracycline	Tetracycline	*C. jejuni*	>1	>2	0,5-64 (8)	>1	>2	0,5-64 (8)
		C. coli	>2	>2	0,5-64 (8)	>2	>2	0,5-64 (8)
Nalidixic Acid	Quinolone	*C. jejuni*	>16	NA	1-64 (7)			
		C. coli	>16	NA	1-64 (7)			
Streptomycin[(c)]	Aminoglycoside	*C. jejuni*	>4	NA	0,25–16 (7)			
		C. coli	>4	NA	0,25–16 (7)			

[(a)] EUCAST epidemiological cut-off values.
[(b)] EUCAST clinical resistance breakpoints.
[(c)] At a voluntary basis.
NA: not available.

[] value to be used proposed by EFSA + EURL-AR for data reporting purposes
[] value recently changed in EUCAST

1. Changes on the ECOFFS and CBPs:
1.4 *Salmonella* spp.— Second panel

Table 4: Panel of antimicrobial substances, EUCAST epidemiological cut-off values (ECOFFs) and clinical resistance breakpoints and concentration ranges to be used for testing only ***Salmonella*** **spp.** isolates resistant to cefotaxime or ceftazidime or meropenem (**Second panel**)

Antimicrobial	Class of Antimicrobial	*Interpretative thresholds of AMR (mg/L) according to* Commission Implementing Decision 2013/652/EU			*Interpretative thresholds of AMR (mg/L) according to* Commission Implementing Decision 2020/1729/EU		
		ECOFF[(a)]	Clinical breakpoint [(b)]	Concentration range, mg/L (no of wells)	ECOFF[(a)]	Clinical breakpoint [(b)]	Concentration range, mg/L (no of wells)
Cefoxitin	Cephamycin	>8	NA	0,5-64 (8)	>8	NA	0,5-64 (8)
Cefepime	Cephalosporin	NA	NA	0,06-32 (10)	NA [>0,125]	>4	0,06-32 (10)
Cefotaxime + clavulanic acid(*)	Cephalosporin/ beta-lactamase inhibitor combination	NA (**)	NA (**)	0,06-64 (11)	NA [>0,5]	NA	0,06-64 (11)
Ceftazidime + clavulanic acid (*)	Cephalosporin/ beta-lactamase inhibitor combination	NA (**)	NA (**)	0,125-128 (11)	NA [>2]	NA	0,125-128 (11)
Meropenem	Carbapenem	>0,125	>8	0,03-16 (10)	>0,125	>8	0,03-16 (10)
Imipenem	Carbapenem	>1	>8	0,12-16 (8)	>1	>4	0,12-16 (8)
Ertapenem	Carbapenem	> 0,06	> 1	0,015-2 (8)	NA [>0,06]	>0,5	0,015-2 (8)
Cefotaxime	Cephalosporin	>0,5	> 2	0,25-64 (9)	>0,5	> 2	0,25-64 (9)
Ceftazidime	Cephalosporin	>2	>4	0,25-128 (10)	>2	>4	0,25-128 (10)
Temocillin	Penicillin	NA	NA	0,5-64 (8)	NA [>16]	NA [>16]	0,5-128 (9)

[(a)] EUCAST epidemiological cut-off values.
[(b)] EUCAST clinical resistance breakpoints.
NA: not available.
(*) 4 mg/L clavulanic acid.
(**) The values shall be compared to the values of Cefotaxime and Ceftazidime and interpreted according to CLSI or EUCAST guidelines regarding synergy testing.
[] value to be used proposed by EFSA + EURL-AR for data reporting purposes
[] value to be used is the new value established by EUCAST

1. Changes in the ECOFFS and CBPs

1.2. Indicator *E. coli* — Second panel

Table 5: Panel of antimicrobial substances, EUCAST epidemiological cut-off values (ECOFFs) and clinical resistance breakpoints and concentration ranges to be used for testing only *E. coli* isolates resistant to cefotaxime or ceftazidime or meropenem (**Second panel**)

Antimicrobial	Class of Antimicrobial	Interpretative thresholds of AMR (mg/L) according to Commission Implementing Decision 2013/652/EU			Interpretative thresholds of AMR (mg/L) according to Commission Implementing Decision 2020/1729/EU		
		ECOFF[a]	Clinical breakpoint [b]	Concentration range, mg/L (no of wells)	ECOFF[a]	Clinical breakpoint [b]	Concentration range, mg/L (no of wells)
Cefoxitin	Cephamycin	>8	NA	0,5-64 (8)	>8	NA	0,5-64 (8)
Cefepime	Cephalosporin	>0,125	>4	0,06-32 (10)	>0,125 [>0,25]	>4	0,06-32 (10)
Cefotaxime + clavulanic acid(*)	Cephalosporin/ beta-lactamase inhibitor combination	NA (**)	NA (**)	0,06-64 (11)	>0,25	NA	0,06-64 (11)
Ceftazidime + clavulanic acid (*)	Cephalosporin/ beta-lactamase inhibitor combination	NA (**)	NA (**)	0,125-128 (11)	>0,5	NA	0,125-128 (11)
Meropenem	Carbapenem	>0,125	>8	0,03-16 (10)	>0,125 [>0,06]	>8	0,03-16 (10)
Imipenem	Carbapenem	>0,5	>8	0,12-16 (8)	>0,5	>4	0,12-16 (8)
Ertapenem	Carbapenem	> 0,06	> 1	0,015-2 (8)	NA [>0,06] [0,03]	>0,5	0,015-2 (8)
Cefotaxime	Cephalosporin	>0,25	> 2	0,25-64 (9)	>0,25	> 2	0,25-64 (9)
Ceftazidime	Cephalosporin	>0,5	>4	0,25-128 (10)	>0,5	>4	0,25-128 (10)
Temocillin	Penicillin	NA	NA	0,5-64 (8)	>16	NA [>16]	0,5-128 (9)

[a] EUCAST epidemiological cut-off values.
[b] EUCAST clinical resistance breakpoints.
NA: not available.
(*) 4 mg/L clavulanic acid.
(**) The values shall be compared to the values of Cefotaxime and Ceftazidime and interpreted according to CLSI or EUCAST guidelines regarding synergy testing.

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Possible Approaches

- 2020 Decision should remain a binding reference – slight alterations of the Decision **?**
- Most changes are not large (+/- 1 dilution) and may have limited/minor effect on the outputs.
- Possible Options:

- Adopt the new ECOFFs forwards and do not recalculate the old data.
- Adopt the new ECOFFs and also apply that change to the historical data.

- Re-calculating the old “core” data is quite possible but amending all the subsequent analyses of the data (comparisons with medical results, trend analysis, MDR analysis etc.) may be more problematic in practical and communication terms => re-analysis of historical data.
- EFSA and ECDC also generally tried to use the same harmonised ECOFF/CBP for the human, animal and meat isolates. If the animal and meat outputs are retrospectively changed, it should really mean that the human ones should be re-calculated too (where necessary/ appropriate). -> further coordination with ECDC.
- The most practical option is to keep a timeline of what breakpoints/ECOFFs were applied and when/over what period. A breakpoint/ECOFF change should be noted in the methods section of the report for that year and subsequent years stating how it changed and what year it changed and also state that a change can affect the prevalence of resistance. If we think resistance occurrence/prevalence has changed only because of the breakpoint change, this should be discussed in the output section.
- Investigations of the impact of ECOFF changes on resistance occurrence/prevalence (by interpreting the 2021 prevalence data by both the old and new ECOFFs) and include a short one-off text box section in the 2021.

Thank you for your attention!

KEEPING ANTIBIOTICS WORKING!

EUROPEAN ANTIBIOTIC AWARENESS DAY

A EUROPEAN HEALTH INITIATIVE