

Streptomycin Breakpoints

	Antimicrobial	Cut-off value (mg/L)
		R>
<i>Salmonella</i>	Cefotaxime	0.5
	Nalidixic acid	16
	Ciprofloxacin	0.06
	Ampicillin	4
	Tetracycline	8
	Chloramphenicol	16
	Gentamicin	2
	Streptomycin	32
	Trimethoprim	2
	Sulphonamides	256

	Antimicrobial	Cut-off value (mg/L)	Optimum concentration range to be tested (mg/L)
<i>Escherichia coli</i>	Cefotaxime	0.25	0.016 - 2
	Nalidixic acid	16	1 - 128
	Ciprofloxacin	0.03	0.004 - 4
	Ampicillin	8	1 - 128
	Tetracycline	8	1 - 128
	Chloramphenicol	16	2 - 256
	Gentamicin	2	0.12 - 16
	Streptomycin	16	2 - 256
	Kanamycin	8	0.25-32
	Trimethoprim	2	0.12 - 1
	Sulphonamides	256	8 - 1024

- Breakpoints advised:
 - *Salmonella* > 32 mg/L
 - *E. coli* > 16 mg/L
- Based on EUCAST and NARMS, Glob-SalmSurv etc

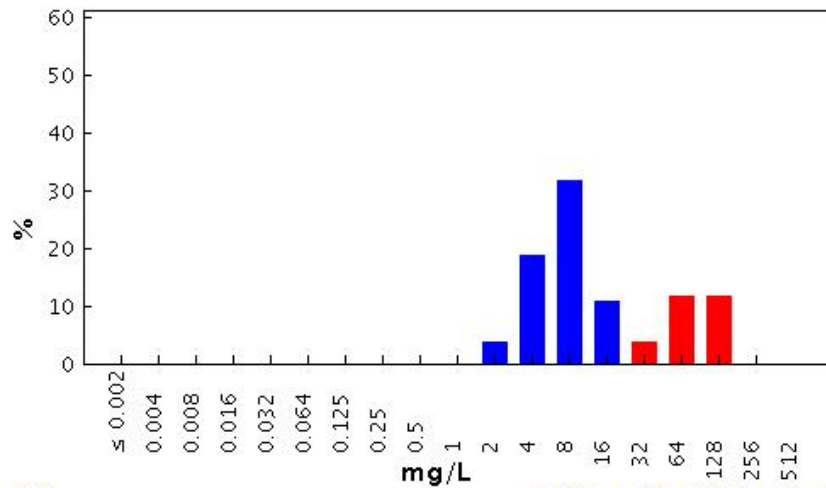
Problems encountered with current breakpoints

- During previous ring trials (without standardised methods except disk diffusion)
 - High level resistant isolates accurately detected by all participants
 - many minor and major deviating results on 'susceptible' isolates
 - Conclusion of previous EQAS Human Salmonella reference labs:
 - Streptomycin results not reliable/accurate
 - Result of using > 32 mg/L:
 - Underestimation of true population with acquired streptomycin R-genes
 - accurate reportage of high level resistance only
 - Example St-5 in this ring trial with MIC 32 mg/L interpreted as S
 - 6 deviations?

WT-distributions

Streptomycin / *Escherichia coli*

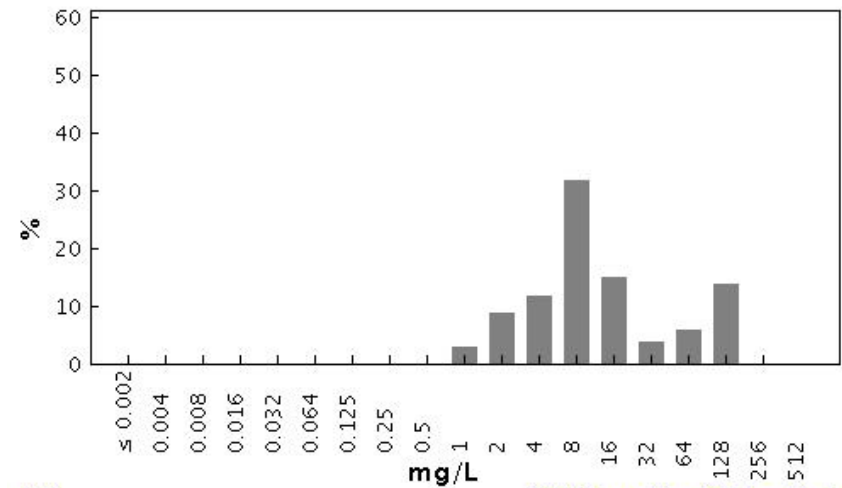
Antimicrobial wild type distributions of microorganisms – reference database
EUCAST



MIC
Epidemiological cut-off: WT ≤ 16 mg/L
8237 observations (24 data sources)
Clinical breakpoints: S ≤ - mg/L, R > - mg/L

Streptomycin / *Salmonella* spp

Antimicrobial wild type distributions of microorganisms – reference database
EUCAST



MIC
Epidemiological cut-off: -
11403 observations (12 data sources)
Clinical breakpoints: S ≤ - mg/L, R > - mg/L

“new” info from literature

Journal of Antimicrobial Chemotherapy (2005) 56, 87–90

doi:10.1093/jac/dki150

Advance Access publication 16 May 2005

JAC

The genetic background for streptomycin resistance in *Escherichia coli* influences the distribution of MICs

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Received 15 February 2005; returned 14 March 2005; revised 31 March 2005; accepted 6 April 2005

- Genes associated with streptomycin resistance in *E. coli*
 - strA-strB
 - aadA-genes

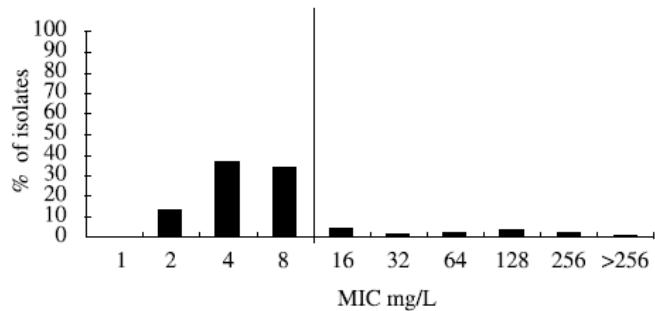


Figure 1. Distribution (%) of MICs of streptomycin for all *E. coli* isolates from meat and meat products investigated in NORM-VET 2000–2003 ($n=944$). The vertical black line indicates a possible choice of an epidemiological cut-off value for streptomycin >8 mg/L.

- streptomycin MICs (mg/L)

- *strA-strB*: 32 - $>$ 256

- *aadA*: 16 - 64

- Combinations 128 - $>$ 256

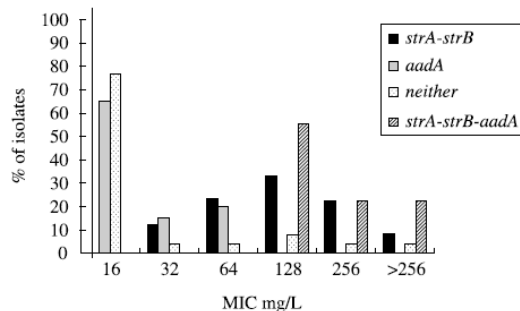
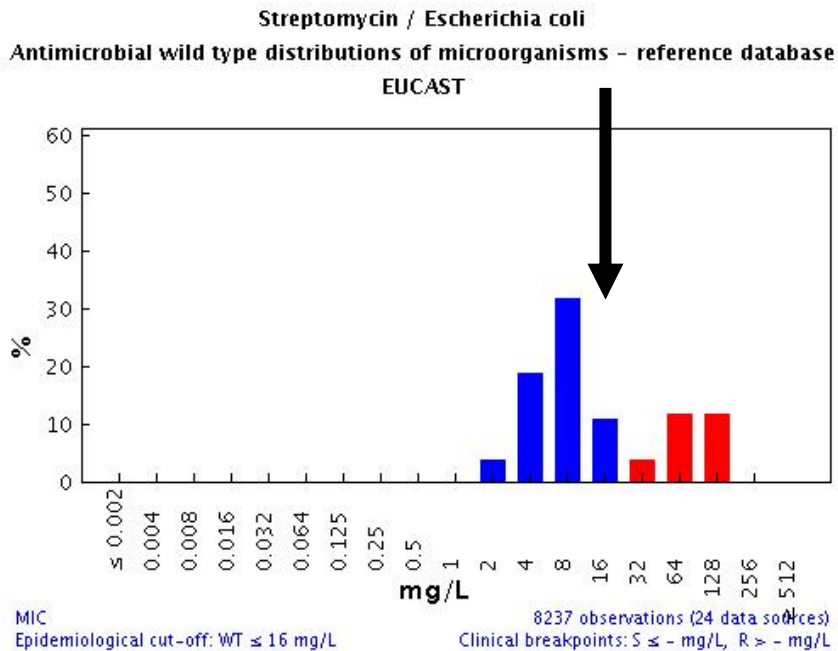


Figure 2. Distribution (%) of MICs of streptomycin for *E. coli* isolates with an MIC ≥ 16 mg/L and harbouring the *strA-strB* genes (solely) ($n=81$) (black bars), an *aadA1* gene cassette ($n=20$) (grey bars), both the *strA-strB* genes and an *aadA* gene cassette ($n=9$) (striped bars) and neither the *strA-strB* genes nor an *aadA* gene cassette ($n=26$) (dotted bars).

Suggested adjusted WT and ECOFF E. coli



- WT ≤ 8 mg/L
- ECOFF: > 8 mg/L

Recent publication on Salmonella



International Journal of Antimicrobial Agents 27 (2006) 538–540



Interpreting streptomycin susceptibility test results for *Salmonella enterica* serovar Typhimurium

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Received 12 January 2006; accepted 7 March 2006

- Genes associated with streptomycin resistance in *Salmonella*
 - strA-strB
 - aadA1
 - aadA2

- Streptomycin MICs

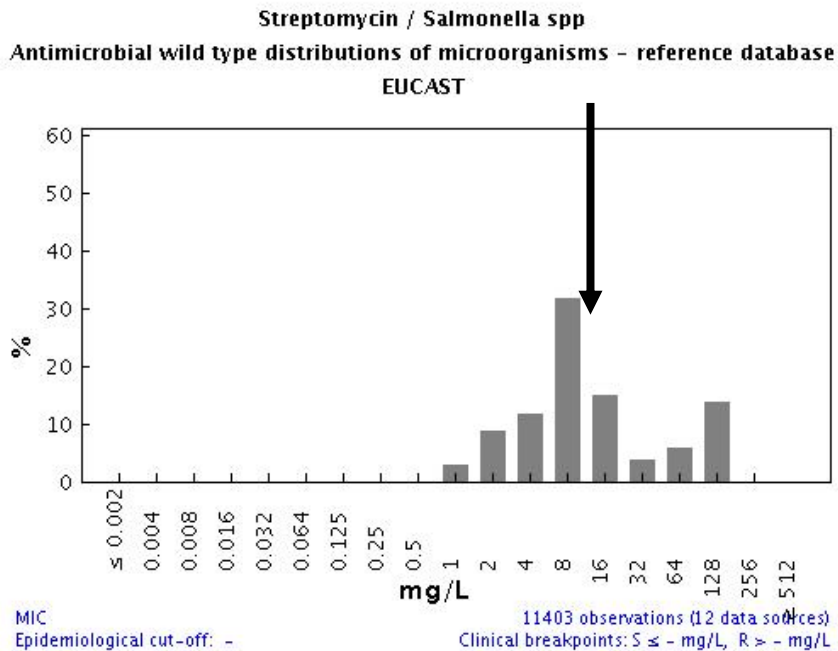
Table 1
Minimum inhibitory concentration (MIC), zone diameter range and streptomycin resistance genotype of 90 isolates of *Salmonella enterica* serovar Typhimurium

MIC (mg/L)	No. of strains	Zone diameter range (mm)	No. gene positive	No. gene negative
2	4	14–17	0	4
4	13	12–17 ^a	0	13
8	34	11–17 ^a	0	34
16	12	7–11 ^a	12	0
32	7	7–12 ^a	7	0
64	17	6–7	17	0
128	1	6	1	0
≥256	2	6	2	0
Total	90	–	39	51

^a A total of five isolates gave a zone diameter of 11 mm (three gene positive, two gene negative) and eight isolates gave a zone diameter of 12 mm (one gene positive and seven gene negative).

- all isolates with MIC \geq 16 mg/L positive for one of the genes
- isolates with MIC \leq 8 mg/L lacking the genes

Suggested adjusted WT and ECOFF Salmonella



- WT ≤ 8 mg/L
- ECOFF: > 8 mg/L