CIPARS-FNC: Interpretive Criteria

Details of the antimicrobial susceptibility interpretive criteria used by CIPARS are available for:

1) *Salmonella* and *Escherichia coli* breakpoints
2) *Campylobacter* breakpoints
3) AMR prediction from whole genome sequencing data

Table 1. Antimicrobial susceptibility breakpoints for *Salmonella* and *Escherichia coli*

	Antimicrobial	Antimicrobial Class	Years Tested[1]	Range tested[2] (μg/mL)	Breakpoints[3] (μg/mL)		
					S[4]	I[5]	R[6]
I[7]	Amoxicillin-clavulanic acid	Beta-lactams	2001-present	1.0/0.5–32/16	≤ 8/4	16/8	≥ 32/16
	Ceftriaxone	Beta-lactams	2001-present	0.25–64	≤ 1	2	≥ 4
	Ceftiofur	Beta-lactams	2001-2015	0.12-8	≤ 2	4	≥ 8
	Ciprofloxacin	Quinolones	2001-present	0.015–4	≤ 0.06	0.12–0.5	≥ 1
	Colistin	Polymixins	2020-present	0.25–8	N/A[8]	N/A	N/A *mcr*[9]
	Meropenem	Beta-lactams	2016-present	0.06–4	≤ 1	2	≥ 4
II	Amikacin	Aminoglycosides	2001-2010	0.5-64	≤ 4	8	≥ 16
	Ampicillin	Beta-lactams	2001-present	1–32	≤ 8	16	≥ 32
	Azithromycin[10]	Macrolides	2011-present	0.25–64	≤ 16	N/A	≥ 32
	Cefoxitin	Beta-lactams	2001-present	1–32	≤ 8	16	≥ 32
	Cephalothin[11]	Beta-lactams	2001-2004	2-32	≤ 8	16	≥ 32
	Gentamicin	Aminoglycosides	2001-present	0.25–16	≤ 2	4	≥ 8
	Kanamycin	Aminoglycosides	2001-2013	8-64	≤ 16	32	≥ 64
	Nalidixic acid	Quinolones	2001-present	0.5–32	≤ 16	N/A	≥ 32
	Streptomycin[12]	Aminoglycosides	2014-2019	2-64	≤ 16	N/A	≥ 32
	Trimethoprim-sulfamethoxazole	Folate pathway inhibitors	2001-present	0.12/2.38–4/76	≤ 2/38	N/A	≥ 4/76
III	Chloramphenicol	Phenicols	2001-present	2-32	≤ 8	16	≥ 32
	Sulfamethoxazole[13]	Folate pathway inhibitors	2001-2004	16–512	≤ 256	N/A	≥ 512
	Sulfisoxazole	Folate pathway inhibitors	2004-present	16–256	≤ 256	N/A	≥ 512
	Tetracycline	Tetracyclines	2001-present	4–32	≤ 4	8	≥ 16

Footnotes

[1] National Antimicrobial Resistance Monitoring System (NARMS) susceptibility panels (Sensititre™) used by the Public Health Agency of Canada (PHAC) with year ranges: CMV6CNCD (2001), CMV7CNCD (2002-2004), CMV1AGNF (2005-2010), CMV2AGNF (2011-2013), CMV3AGNF (2014-2015), CMV4AGNF (2016-2019) and CMV5AGNF (2020 – present). Isolates tested external to PHAC may have different year ranges for susceptibility plates and antimicrobials tested.

[2] Range tested is for the most recent plate used for testing the antimicrobial.

[3] Breakpoints are from Clinical & Laboratory Standards Institute (CLSI) M100-33 unless otherwise noted.

[4] S = susceptible.

[5] I = intermediate susceptibility.

[6] R = resistant.

[7] Roman numerals I to IV indicate categories of importance to human medicine as outlined by Health Canada's Veterinary Drugs Directorate. Health Canada's categorization of antimicrobials of importance to human medicine (https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/categorization-antimicrobial-drugs-based-importance-human-medicine.html) and list A antimicrobials (https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/lists-incorporated-by-reference/about-list-a.html).

[8] N/A = not applicable.

[9] Resistance to colistin was defined as detecting an *mcr* gene from whole genome sequencing data (excluding *mcr*-9).

[10] No CLSI breakpoints for Enterobacterales were available for this antimicrobial. Breakpoints were based on those used by NARMS.

[11] Cephalothin AMR results are not presented in the CIPARS visualizations due to cephalothin only being tested for four years at the beginning of the program.

[12] Streptomycin AMR results are not presented prior to 2014 due to the range tested not being compatible with the current antimicrobial susceptibility breakpoint.

[13] Since sulfamethoxazole is similar to sulfisoxazole with the same testing range and breakpoints, the AMR results are combined and reported as sulfisoxazole.

Table 2. Antimicrobial susceptibility breakpoints for *Campylobacter*

	Antimicrobial	Antimicrobial Class	Years Tested[1]	Range tested[2] (μg/mL)	Breakpoints[3](μg/mL)		
					S[4]	I[5]	R[6]
I[7]	Ciprofloxacin	Quinolones	2003-present	0.015–64	≤ 1	2	≥ 4
	Meropenem[8]	Beta-lactams	2020-present	0.004–16	≤ 1	2	≥ 4
	Telithromycin	Ketolides	2006-2019	0.015-8	≤ 4	N/A[9]	≥ 8
II	Azithromycin[8]	Macrolides	2003-present	0.015–64	≤ 2	4	≥ 8
	Clindamycin[8]	Lincosamides	2003-present	0.03–16	≤ 2	4	≥ 8
	Erythromycin	Macrolides	2003-present	0.03–64	≤ 8	16	≥ 32
	Gentamicin[8]	Aminoglycosides	2003-present	0.12–32	≤ 2	4	≥ 8
	Nalidixic acid[8]	Quinolones	2003-present	4–64	≤ 16	32	≥ 64
III	Chloramphenicol[10]	Phenicols	2003-2005	0.016-256	≤ 16	N/A	≥ 32
	Florfenicol[8]	Phenicols	2006-present	0.12–64	≤ 4	N/A	≥ 8
	Tetracycline	Tetracyclines	2003-present	0.12–64	≤ 4	8	≥ 16

Footnotes

[1] Antimicrobial susceptibility testing methodology used by PHAC with year ranges: ETest® (2003-05), and NARMS susceptibility panels (Sensititre™) CAMPY (2006-19) and CMVCAMPY (2020-present). Isolates tested external to PHAC may have different year ranges for susceptibility plates and antimicrobials tested.

[2] Range tested is for the most recent plate used for testing the antimicrobial.

[3] Breakpoints are from CLSI M45-ED-3 unless otherwise noted.

[4] S = susceptible.

[5] I = intermediate susceptibility.

[6] R = resistant.

[7] Roman numerals I to IV indicate categories of importance to human medicine as outlined by Health Canada's Veterinary Drugs Directorate. Health Canada's categorization of antimicrobials of importance to human medicine (https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/categorization-antimicrobial-drugs-based-importance-human-medicine.html) and list A antimicrobials (https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/lists-incorporated-by-reference/about-list-a.html).

[8] No CLSI breakpoints available. The breakpoints used by CIPARS are based on NARMS breakpoints.

[9] N/A = not applicable.

[10] Chloramphenicol AMR results are not presented in the CIPARS visualizations due to chloramphenicol only being tested for three years at the beginning of the program.

Antimicrobial resistance prediction from whole genome sequencing data

The prediction of antimicrobial resistance (AMR) from whole genome sequencing (WGS) data is performed using PHAC's Staramr program[1] (available at https://github.com/phac-nml/staramr). Staramr incorporates the Centre for Genomic Epidemiology's databases for ResFinder (resistance genes), PointFinder (resistance mutations), PlasmidFinder, and PubMLST and the gene-drug key developed by the United States Centers for Disease Control (US CDC) for prediction of AMR profiles. It also checks quality metrics for the genome assembly.

- Validation tests performed by PHAC's National Microbiology Laboratory found that the prediction of AMR from WGS data for *Salmonella* is accurate and reliable.[1] Staramr was validated for prediction of resistance to the antimicrobials on the CMV4AGNF and CMV5AGNF National Antimicrobial Resistance Monitoring System (NARMS) susceptibility panels (15 antimicrobials).

The Staramr program is periodically updated. Staramr versions 0.7.0 or 0.7.1, which were based on the same gene/mutation-drug key, were used for WGS data from 2017 to 2021. Staramr versions 0.8.0 or 0.9.1, which were based on the same gene/mutation-drug key, were used for WGS data from 2022 to 2024.

Comparison of the two gene/mutation-drug keys outlined above was performed to identify relevant differences and where possible interpretations were updated to align with the current Staramr version (0.9.1). When new genes/mutations are added to new versions of the gene/mutation-drug key, interpretations are unable to be applied retrospectively, as the new gene/mutation was not screened for in the previous version. For genes of higher interest (ESBL, *mcr*, carbapenemases), if sequences are identified that are not perfect matches to the gene/mutation in the database, an alignment is performed to identify if it is a new resistance variant or mutation, which minimizes missing newly identified genes and mutations.

Footnotes

[1] Bharat A, Petkau A, Avery BP, Chen JC, Folster JP, Carson CA, Kearney A, Nadon C, Mabon P, Thiessen J, Alexander DC, Allen V, El Bailey S, Bekal S, German GJ, Haldane D, Hoang L, Chui L, Minion J, Zahariadis G, Domselaar GV, Reid-Smith RJ, Mulvey MR. Correlation between phenotypic and In Silico detection of antimicrobial resistance in *Salmonella enterica* in Canada using Staramr. Microorganisms. 2022;10(2):292 doi:10.3390/microorganisms10020292.