AMR Alliance Science-Based PNEC Targets for Risk Assessments

The members of the AMR Industry Alliance have developed a unified approach to establishing discharge targets for antibiotic manufacturing, based on Predicted No-Effect Concentrations (PNECs) for use in environmental risk assessments of antibiotics. The discharge target can be derived using these PNECs and site-specific parameters. The publication of the PNEC table fulfills the commitment of the AMR Industry Alliance to publish science-driven, risk-based targets for discharge concentrations of antibiotics. For the first time, the pharmaceutical industry, as member companies of the Alliance, have collated, shared, analyzed, and published existing antibiotic data with respect to antimicrobial resistance and eco-toxicity.

The PNEC table contains two values. PNEC-Environment (PNEC-ENV) values are based on eco-toxicology data generated by Alliance member companies and relevant peer reviewed literature. These values are intended to be protective of ecological species and incorporate assessment factors consistent with standard environmental risk methodologies (Brandt et al., 2015[1]; Le Page et al., 2017[2]). The PNEC-Minimum Inhibitory Concentration (PNEC-MIC) values are based on the approach published in Bengtsson-Palme and Larsson (2016)[3] and are intended to be protective of resistance promotion. This table will be updated periodically as new reliable and robust data become available.

The release of this table is an important step in the journey of evaluating antibiotic discharge concentrations using science-driven, risk-based targets, allowing Alliance member companies to work toward achieving these target values at the receiving water body. The AMR Industry Alliance recommendation is that companies target the lower of these two values (when available) for assessing manufacturing site discharges under a risk-based framework.

If an antibiotic is not listed in the table, read-across to a similar antibiotic based on chemical structure or mode of action can be made.[4] Alternatively, based on a statistical assessment of all available data, a default PNEC in the absence of both a PNEC-ENV and PNEC-MIC of 0.05 µg/L can be leveraged as a target.[5] When available, a compound specific PNEC-ENV, PNEC-MIC or the lowest of both values should be used. If no data are available, a default PNEC of 0.05 µg/L should be used.

The AMR Industry Alliance believes working toward achieving these antibiotic discharge concentration targets will be both protective of ecological resources and also lower the potential for the evolution and selection of AMR in the environment. It is important to note that these values are recommended based on currently available information, thus, may change as new reliable and relevant information generated to recognized protocols comes to light.

[1] Brandt, et al., 2015. Ecotoxicological assessment of antibiotics: A call for improved consideration of microorganisms. Environment International, 85: 189–205.

[2] Le Page, et al., 2017. Integrating human and environmental health in antibiotic risk assessment: A critical analysis of protection goals, species sensitivity and antimicrobial resistance. Environment International, 109: 155–169.

[3] Bengtsson-Palme & Larsson, 2016. Concentrations of antibiotics predicted to select for resistant bacteria: Proposed limits for environmental regulation, Environment International 86: 140–149.

[4] Grouping of substances and read-across - ECHA (europa.eu)

[5] Vestel, et al., 2022. Default Predicted No Effect Target Concentrations for Antibiotics in the Absence of Data for the Protection Against Antibiotic Resistance and Environmental Toxicity, IEAM 10.1002/ieam.4560

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Active Pharmaceutical Ingredient	PNEC-ENV (µg/L)	PNEC-MIC (µg/L)	Lowest Value (µg/L)
Amikacin	Testing On-Going	16	16
Amoxicillin	0.57	0.25	0.25
Ampicillin	0.6	0.25	0.25
Avilamycin	125	8	8
Azithromycin	0.03	0.25	0.03
Aztreonam	N/A	0.5	0.5
Bacitracin	115	8.0	8.0
Bedaquiline	0.08	N/A	0.08
Benzylpenicillin (Penicillin G) [1]	1	0.25	0.25
Capreomycin	N/A	2	2
Cefaclor	N/A	0.5	0.5
Cefadroxil	0.14	2	0.14
Cefalonium	21	N/A	21
Cefaloridine	N/A	4	4
Cefalothin	N/A	2	2
Cefazolin	Testing On-Going	1	1
Cefdinir	N/A	0.25	0.25
Cefepime	1.3	0.5	0.5
Cefixime	0.6	0.06	0.06
Cefoperazone	N/A	0.5	0.5
Cefotaxime	0.12	0.13	0.12
Cefoxitin	N/A	8	8
Cefpirome	N/A	0.06	0.06
Cefpodoxime proxetil	1.8	0.25	0.25
Cefquinome	1.6	N/A	1.6
Ceftaroline	0.12	0.06	0.06
Ceftazidime	1.3	0.5	0.5
Ceftibuten	N/A	0.25	0.25
Ceftiofur	0.4	0.06	0.06
Ceftobiprole	0.23	0.25	0.23
Ceftolozane	1.9	N/A	1.90
Ceftriaxone	0.33	0.03	0.03

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[1] Corrected 25-May-2023: Benzylpenicillin and Penicillin G were incorrectly displayed as different entries.

Active Pharmaceutical Ingredient	PNEC-ENV (µg/L)	PNEC-MIC (µg/L)	Lowest Value (µg/L)
Cefuroxime	1.7	0.5	0.5
Cephalexin	0.21	4	0.21
Cephradine	0.19	N/A	0.19
Chloramphenicol	N/A	8	8
Chlortetracycline	5	N/A	5
Ciprofloxacin	0.45	0.06	0.06
Clarithromycin	0.25	0.25	0.25
Clinafloxacin	N/A	0.5	0.5
Clindamycin	0.1	1	0.1
Cloxacillin	20	0.13	0.13
Colistin (Polymyxin E)	9	2	2
Daptomycin	510	1	1
Delamanid	0.03	N/A	0.03
Doripenem	0.46	0.13	0.13
Doxycycline	25	2	2
Enramycin	4.8	N/A	4.8
Enrofloxacin	1.9	0.06	0.06
Ertapenem	14	0.13	0.13
Erythromycin	0.5	1	0.5
Ethambutol	Testing On-Going	2	2
Faropenem	N/A	0.02	0.02
Fidaxomicin	891	0.02	0.02
Florfenicol	38	2	2
Flucloxacillin	27	N/A	27
Flumequine	N/A	0.25	0.25
Fosfomycin	52	2	2
Fusidic acid	N/A	0.5	0.5
Framycetine	Testing On-Going	0.06	0.06
Gamithromycin	0.24	N/A	0.24
Gatifloxacin	N/A	0.13	0.13
Gemifloxacin	N/A	0.06	0.06
Gentamicin	0.15	1	0.15
Imipenem	0.41	0.13	0.13
Isoniazid	1290	0.13	0.13
Kanamycin	1.1	2	1.1
Levofloxacin	1.5	0.25	0.25

Active Pharmaceutical Ingredient	PNEC-ENV (µg/L)	PNEC-MIC (µg/L)	Lowest Value (µg/L)
Lincomycin	0.81	2	0.81
Linezolid	3.5	8	3.5
Loracarbef	N/A	2	2
Mecillinam	N/A	1	1
Meropenem	1.5	0.06	0.06
Metronidazole	N/A	0.13	0.13
Minocycline	1.1	1	1
Moxifloxacin	N/A	0.13	0.13
Mupirocin	N/A	0.25	0.25
Nalidixic acid	N/A	16	16
Narasin	N/A	0.5	0.5
Natamycin	210	N/A	210
Neomycin	0.03	2	0.03
Netilmicin	N/A	0.5	0.5
Nitrofurantoin	N/A	64	64
Norfloxacin	120	0.5	0.5
Novobiocin	20	N/A	20
Ofloxacin	10	0.5	0.5
Oxacillin	N/A	1	1
Oxytetracycline	47	0.5	0.5
Pefloxacin	N/A	8	8
Penicillin G Procaine	16	N/A	16
Penicillin V (phenoxymethylpenicillin)[2]	3	0.06	0.06
Piperacillin	4.3	0.5	0.5
Polymyxin B	0.06	N/A	0.06
Pristinamycin	71	N/A	71
Puromycin	31	N/A	31
Retapamulin	N/A	0.06	0.06
Rifampicin	4	0.06	0.06
Rifamycin	1	N/A	1
Rifaximin	0.11	N/A	0.11
Roxithromycin	6.8	1	1
Secnidazole	N/A	1	1
Sparfloxacin	N/A	0.06	0.06

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[2] Corrected 25-May-2023: Phenoxymethylpenicillin and Penicillin V were incorrectly displayed as different entries.

Active Pharmaceutical Ingredient	PNEC-ENV (µg/L)	PNEC-MIC (µg/L)	Lowest Value (µg/L)
Spectinomycin	N/A	32	32
Spiramycin	1.1	0.5	0.5
Streptomycin	N/A	16	16
Sulfadiazine	11	N/A	11
Sulfamethoxazole	6.6	16	6.6
Sulfanilamide	230	N/A	230
Tedizolid	3.2	N/A	3.2
Teicoplanin	13	0.5	0.5
Telithromycin	Testing On-Going	0.06	0.06
Tetracycline	3.2	1	1
Thiamphenicol	N/A	1	1
Tiamulin	N/A	1	1
Ticarcillin	N/A	8	8
Tigecycline	0.1	1	0.1
Tildipirosin	0.42	N/A	0.42
Tilmicosin	0.8	1	0.8
Tobramycin	4	1	1
Trimethoprim	928	0.5	0.5
Trovafloxacin	N/A	0.03	0.03
Tulathromycin	0.04	N/A	0.04
Tylosin	1	4	1
Vancomycin	14	8	8
Viomycin	N/A	2	2
Virginiamycin	N/A	2	2