



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<sup>[1]</sup>; Le Page et al., 2017<sup>[2]</sup>). The PNEC-Minimum Inhibitory Concentration (PNEC-MIC) values are based on the approach published in Bengtsson-Palme and Larsson (2016)<sup>[3]</sup> 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.

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.

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<sup>[1]</sup> Brandt, et al., 2015. Ecotoxicological assessment of antibiotics: A call for improved consideration of microorganisms. *Environment International*, 85: 189-205.

<sup>[2]</sup> 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.

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

## AMR Alliance Science-Based PNEC Targets for Risk Assessments

| Active Pharmaceutical Ingredient | PNEC <sub>ENV</sub> (µg/L) | PNEC <sub>MIC</sub> (µg/L) | Lowest Value (µg/L) |
|----------------------------------|----------------------------|----------------------------|---------------------|
| Amikacin                         | N/A                        | 16.00                      | 16.00               |
| Amoxicillin                      | 0.57                       | 0.25                       | 0.25                |
| Amphotericin B                   | N/A                        | 0.02                       | 0.02                |
| Ampicillin                       | 0.60                       | 0.25                       | 0.25                |
| Anidulafungin                    | N/A                        | 0.02                       | 0.02                |
| Avilamycin                       | 125.00                     | 8.00                       | 8.00                |
| Azithromycin                     | 0.03                       | 0.25                       | 0.03                |
| Aztreonam                        | N/A                        | 0.50                       | 0.50                |
| Bacitracin                       | 114.59                     | 8.00                       | 8.00                |
| Bedaquiline                      | 0.08                       | N/A                        | 0.08                |
| Capreomycin                      | N/A                        | 2.00                       | 2.00                |
| Cefaclor                         | N/A                        | 0.50                       | 0.50                |
| Cefadroxil                       | 0.14                       | 2.00                       | 0.14                |
| Cefalonium                       | 21.10                      | N/A                        | 21.10               |
| Cefaloridine                     | N/A                        | 4.00                       | 4.00                |
| Cefalothin                       | N/A                        | 2.00                       | 2.00                |
| Cefazolin                        | N/A                        | 1.00                       | 1.00                |
| Cefdinir                         | N/A                        | 0.25                       | 0.25                |
| Cefepime                         | N/A                        | 0.50                       | 0.50                |
| Cefixime                         | 0.60                       | 0.06                       | 0.06                |
| Cefoperazone                     | N/A                        | 0.50                       | 0.50                |
| Cefotaxime                       | 0.12                       | 0.13                       | 0.12                |
| Cefoxitin                        | N/A                        | 8.00                       | 8.00                |
| Cefpirome                        | N/A                        | 0.06                       | 0.06                |
| Cefpodoxime proxetil             | 1.76                       | 0.25                       | 0.25                |
| Cefquinome                       | 1.60                       | N/A                        | 1.60                |
| Ceftaroline                      | 0.12                       | 0.06                       | 0.06                |
| Ceftazidime                      | 1.30                       | 0.50                       | 0.50                |
| Ceftibuten                       | N/A                        | 0.25                       | 0.25                |
| Ceftiofur                        | N/A                        | 0.06                       | 0.06                |
| Ceftobiprole                     | 0.23                       | 0.25                       | 0.23                |
| Ceftolozane                      | 1.90                       | N/A                        | 1.90                |
| Ceftriaxone                      | 29.40                      | 0.03                       | 0.03                |
| Cefuroxime                       | 1.70                       | 0.50                       | 0.50                |
| Cephalexin                       | 0.21                       | 4.00                       | 0.21                |

| Active Pharmaceutical Ingredient | PNEC <sub>ENV</sub> (µg/L) | PNEC <sub>MIC</sub> (µg/L) | Lowest Value (µg/L) |
|----------------------------------|----------------------------|----------------------------|---------------------|
| Cephradine                       | 0.19                       | N/A                        | 0.19                |
| Chloramphenicol                  | N/A                        | 8.00                       | 8.00                |
| Chlortetracycline                | 5.00                       | N/A                        | 5.00                |
| Ciprofloxacin                    | 0.45                       | 0.06                       | 0.06                |
| Clarithromycin                   | 0.26                       | 0.25                       | 0.25                |
| Clinafloxacin                    | N/A                        | 0.50                       | 0.50                |
| Clindamycin                      | 0.10                       | 1.00                       | 0.10                |
| Cloxacillin                      | 20.00                      | 0.13                       | 0.13                |
| Colistin (Polymyxin E)           | 9.00                       | 2.00                       | 2.00                |
| Daptomycin                       | 510.00                     | 1.00                       | 1.00                |
| Delamanid                        | 0.03                       | N/A                        | 0.03                |
| Doripenem                        | 0.46                       | 0.13                       | 0.13                |
| Doxycycline                      | 25.10                      | 2.00                       | 2.00                |
| Enramycin                        | 4.80                       | N/A                        | 4.80                |
| Enrofloxacin                     | 1.91                       | 0.06                       | 0.06                |
| Ertapenem                        | 14.00                      | 0.13                       | 0.13                |
| Erythromycin                     | 0.50                       | 1.00                       | 0.50                |
| Ethambutol                       | N/A                        | 2.00                       | 2.00                |
| Faropenem                        | N/A                        | 0.02                       | 0.02                |
| Fidaxomicin                      | 891.00                     | 0.02                       | 0.02                |
| Florfenicol                      | 38.00                      | 2.00                       | 2.00                |
| Flucloxacillin                   | 26.80                      | N/A                        | 26.80               |
| Fluconazole                      | N/A                        | 0.25                       | 0.25                |
| Flumequine                       | N/A                        | 0.25                       | 0.25                |
| Fosfomicin                       | N/A                        | 2.00                       | 2.00                |
| Fusidic acid                     | N/A                        | 0.50                       | 0.50                |
| Framycetine                      | Testing on-going           | 0.06                       | 0.06                |
| Gatifloxacin                     | N/A                        | 0.13                       | 0.13                |
| Gemifloxacin                     | N/A                        | 0.06                       | 0.06                |
| Gentamicin                       | 0.15                       | 1.00                       | 0.15                |
| Imipenem                         | 0.41                       | 0.13                       | 0.13                |
| Isoniazid                        | N/A                        | 0.13                       | 0.13                |
| Kanamycin                        | 1.05                       | 2.00                       | 1.05                |
| Levofloxacin                     | 0.52                       | 0.25                       | 0.25                |
| Lincomycin                       | 0.81                       | 2.00                       | 0.81                |
| Linezolid                        | 3.50                       | 8.00                       | 3.50                |

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|----------------------------------|----------------------------|----------------------------|---------------------|
| Loracarbef                       | N/A                        | 2.00                       | 2.00                |
| Mecillinam                       | N/A                        | 1.00                       | 1.00                |
| Meropenem                        | 1.50                       | 0.06                       | 0.06                |
| Metronidazole                    | N/A                        | 0.13                       | 0.13                |
| Minocycline                      | Testing on-going           | 1.00                       | 1.00                |
| Moxifloxacin                     | N/A                        | 0.13                       | 0.13                |
| Mupirocin                        | N/A                        | 0.25                       | 0.25                |
| Nalidixic acid                   | N/A                        | 16.00                      | 16.00               |
| Narasin                          | N/A                        | 0.50                       | 0.50                |
| Natamycin                        | Testing on-going           | N/A                        | N/A                 |
| Neomycin                         | 0.03                       | 2.00                       | 0.03                |
| Netilmicin                       | N/A                        | 0.50                       | 0.50                |
| Nitrofurantoin                   | N/A                        | 64.00                      | 64.00               |
| Norfloxacin                      | 120.00                     | 0.50                       | 0.50                |
| Ofloxacin                        | 10.00                      | 0.50                       | 0.50                |
| Oxacillin                        | N/A                        | 1.00                       | 1.00                |
| Oxytetracycline                  | 47.00                      | 0.50                       | 0.50                |
| Pefloxacin                       | N/A                        | 8.00                       | 8.00                |
| Penicillin G Procaine            | 16.00                      | 0.25                       | 0.25                |
| Phenoxymethylpenicillin          | N/A                        | 0.06                       | 0.06                |
| Piperacillin                     | 4.30                       | 0.50                       | 0.50                |
| Polymixin B                      | 0.06                       | N/A                        | 0.06                |
| Pristinamycin                    | Testing on-going           | N/A                        | N/A                 |
| Puromycin                        | 31.00                      | N/A                        | 31.00               |
| Retapamulin                      | N/A                        | 0.06                       | 0.06                |
| Rifampicin                       | Testing on-going           | 0.06                       | 0.06                |
| Rifamycin                        | N/A                        | N/A                        | N/A                 |
| Rifaximin                        | N/A                        | N/A                        | N/A                 |
| Roxithromycin                    | 6.80                       | 1.00                       | 1.00                |
| Secnidazole                      | N/A                        | 1.00                       | 1.00                |
| Sparfloxacin                     | N/A                        | 0.06                       | 0.06                |
| Spectinomycin                    | N/A                        | 32.00                      | 32.00               |
| Spiramycin                       | 1.09                       | 0.50                       | 0.50                |
| Streptomycin                     | N/A                        | 16.00                      | 16.00               |
| Sulbactam                        | N/A                        | 16.00                      | 16.00               |
| Sulfadiazine                     | 11.21                      | 13.00                      | 11.21               |
| Sulfamethoxazole                 | 0.60                       | 16.00                      | 0.60                |

| Active Pharmaceutical Ingredient | PNEC <sub>ENV</sub> (µg/L) | PNEC <sub>MIC</sub> (µg/L) | Lowest Value (µg/L) |
|----------------------------------|----------------------------|----------------------------|---------------------|
| Tedizolid                        | 3.20                       | N/A                        | 3.20                |
| Teicoplanin                      | 12.90                      | 0.50                       | 0.50                |
| Telithromycin                    | Testing on-going           | 0.06                       | 0.06                |
| Tetracycline                     | 3.20                       | 1.00                       | 1.00                |
| Thiamphenicol                    | N/A                        | 1.00                       | 1.00                |
| Tiamulin                         | N/A                        | 1.00                       | 1.00                |
| Ticarcillin                      | N/A                        | 8.00                       | 8.00                |
| Tigecycline                      | Testing on-going           | 1.00                       | 1.00                |
| Tildipirosin                     | 0.42                       | N/A                        | 0.42                |
| Tilmicosin                       | 0.80                       | 1.00                       | 0.80                |
| Tobramycin                       | 4.30                       | 1.00                       | 1.00                |
| Trimethoprim                     | 312.45                     | 0.50                       | 0.50                |
| Trovafloxacin                    | N/A                        | 0.03                       | 0.03                |
| Tulathromycin                    | Testing on-going           | N/A                        | N/A                 |
| Tylosin                          | 0.98                       | 4.00                       | 0.98                |
| Vancomycin                       | N/A                        | 8.00                       | 8.00                |
| Viomycin                         | N/A                        | 2.00                       | 2.00                |
| Virginiamycin                    | N/A                        | 2.00                       | 2.00                |