### Materials and Methods

**Objectives:** To assess the potential and intermethod agreement for doxycycline (DOXY) and tetracycline (TETRA) susceptibility testing methods when evaluated against SENTRY Antimicrobial Surveillance Program isolates of Gram-positive species (13,188 isolates) collected worldwide.

**Methods:** All organisms were cultured in 2010 with S testing by CLSI M07-A9 (2012) methods and results interpreted by CLSI M100-S22 (2012) and EUCAST (2012) (Table 1). A total of 9,012 S. aureus (SA; 44.9% MRSA); 2,325 S. pneumoniae (SPN); and 1,851 beta-haemolytic streptococci (BHS; 42.8% S. pyogenes [SPYO]) were analyzed for susceptibility to TETRA and DOXY using the breakpoint criteria of the CLSI (2012) and EUCAST (2012) documents. Control strains included: S. aureus (9012; 44.9% methicillin-resistant [MRSA]); Streptococcus pneumoniae (2,325), and Streptococcus pyogenes (1,851; 42.8% S. pyogenes [SPYO]).

**Antimicrobial susceptibility tests:** These 13,188 Gram-positive pathogenic organisms were tested against tetracycline and doxycycline by the broth method as described in the CLSI M07-A9 (2012) document in validated panels produced under GMP conditions at ThermoFisher Scientific (formerly TREK Diagnostics). All QC strains were tested with each CLSI/GMRL.

**Results:** Results for DOXY were consistently greater than TETRA for each interpretive method used and for each pathogen analyzed. The CLSI DOXY/TETRA susceptibility test results were as follows: 99.2-94.2% (96.7-88.9%) for SA; 75.3-73.7% (76.3-73.9%) for SPN; 81.2-78.9% (82.6-82.6%) for SPYO and 15.7-14.6% (15.1-14.6%) for BHS. 

**Conclusions:** CLSI and EUCAST interpretive criteria for tetracycline and doxycycline are discordant in percent, but each determines DOXY to have wider spectrum against four Gram-positive pathogen species and that TETRA cannot accurately predict MICS for S. pyogenes (99.9-99.9% across 13,188 isolates). Moreover, molecular test-confirmed resistance to tetracycline on-line or genetically confirmed to overproduce tetracyclines or inactivates tetracycline efflux pumps could be categorized by CLSI as S (MICs < 0.4 mg/L) or more potent than TETRA (MIC > 0.4 mg/L) versus MRS. Use of TETRA-S results to predict DOXY was excellent (99.8-100%) for S. aureus (SA), 96.7-98.6% across 13,188 isolates. Further studies with other tetracyclines (minocycline or doxycycline) and other MIC categories are urgently needed, especially in the EUCAST for strains with MICs > 4 mg/L.

### References


