**Amended Abstract**

**Objectives:** To establish the disk diffusion (DD) and MIC quality control (QC) ranges for BC-3205 and BC-3781, novel semi-synthetic pleuromutilin derivatives in the early stage clinical development for treatment of skin and skin structure infections (SSSI).

**Methods:** These QC studies for the 20 µg BC-3205 and 20 µg BC-3781 disk and broth microdilution method follow the CLSI M3-A10 (2011), M4-A11 (2003) and M2-A3 (2008) document using eight laboratories, two lots of BC-3205, two lots of BC-3781, and three or four different medium lots. The results are presented as proposed QC ranges in mg concentrations and zone diameters measured in mm for four American Type Culture Collection (ATCC) strains: S. aureus ATCC 29213 (BMD only), S. pneumoniae ATCC 49247, and Streptococcus pyogenes ATCC 49619.

A total of eight laboratories were recruited to provide data for this QC investigation. For the BMD study, four non-automated Mueller-Hinton (MH) media were included (produced by Biorad Laboratories, Detroit, MI; Beckman-Coulter, Fullerton, CA; and Thermo Fisher Scientific, Waltham, MA). For the CLSI study, MIC values for S. pneumoniae ATCC 49619 showed trailing endpoints of at least one dilution range of 0.03–0.12 mg/l was proposed with a three dilution QC range. The BC-3205 range of 1 to 4 mg/l includes only 100.0 % of results (excluding one laboratory). For BC-3781, a proposed range of 0.06–0.5 with 98.6 % results included (excluding one laboratory).

**Materials and Methods**

- **Colonies after MIC testing averaged between 1.8 x 10^8 and 1.0 x 10^9 CFU/ml** for S. aureus ATCC 29213 and 1.0 x 10^8 and 1.0 x 10^9 CFU/ml for S. pneumoniae ATCC 49619 and 1.0 x 10^8 to 1.2 x 10^9 CFU/ml for H. influenzae ATCC 44247.
- **Frequency of colonies**<br>
  - Frequency of colonies for S. aureus ATCC 29213 is 1.0 x 10^8 to 1.0 x 10^9 CFU/ml for S. pneumoniae ATCC 49619 and 1.0 x 10^8 to 1.2 x 10^9 CFU/ml for H. influenzae ATCC 44247.
- **Range of colonies**
  - Frequency of colonies for S. aureus ATCC 29213 is 1.0 x 10^8 to 1.0 x 10^9 CFU/ml for S. pneumoniae ATCC 49619 and 1.0 x 10^8 to 1.2 x 10^9 CFU/ml for H. influenzae ATCC 44247.
  - Frequency of colonies for S. aureus ATCC 29213 is 1.0 x 10^8 to 1.0 x 10^9 CFU/ml for S. pneumoniae ATCC 49619 and 1.0 x 10^8 to 1.2 x 10^9 CFU/ml for H. influenzae ATCC 44247.

**Results**

- **MIC QC range of S. aureus ATCC 29213:** Includes 100.0 % of results.
- **MIC QC range of S. pneumoniae ATCC 49619:** Includes 100.0 % of results.
- **MIC QC range of H. influenzae ATCC 44247:** Includes 100.0 % of results.

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The QC study sites and primary investigators were: The Cleveland Clinic Foundation, Cleveland, OH (G. Hall, Ph.D.); University of Texas Medical Center, Houston, TX (A. Wanger, Ph.D.); Massachusetts General Hospital, Boston, MA (M. Weinstein, M.D.); TREK Diagnostics, Cleveland, OH (C. Knapp, M.S.); University of Alberta, Edmonton, Canada (R. Rennie, Ph.D.); Duke University Medical Center, Durham, NC (L. Berek, M.D.); Wunderlich Francis Laboratory, Wayne, WI (E. Munson, Ph.D.) and the University of Washington Medical Center, Seattle, WA (M. Seely, S.M.); T. J. (Arthur).

**Selected References**