

# Solothromycin MIC and Disk Diffusion Quality Control Ranges, a CLSI Multi-Laboratory M23-A3 Study Design

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**Authors:** JE ROSS, DJ FARRELL, RK FLAMM, RN JONES  
JMI Laboratories, North Liberty, Iowa, USA

**Background:** Solithromycin is a fluoroketolide with potent activity against most macrolide-resistant pathogens, including *S. pneumoniae*, *N. gonorrhoeae* and other organisms that cause genitourinary tract infections. We conducted two studies to establish MIC quality control (QC) ranges for solithromycin using CLSI reference disk diffusion method and agar dilution methods

**Methods:** *N. gonorrhoeae* ATCC 49226 was tested against solithromycin using disk diffusion and agar dilution methods with ciprofloxacin as an internal control. Eight laboratories participated in each study (7 laboratories were the same in both studies). Study designs were compliant with CLSI M23-A3 guidelines with both studies using three media lots of GC agar base. Ten replicates were performed for *N. gonorrhoeae* ATCC 49226 (480 values/disk diffusion; 240 values/agar dilution) against solithromycin.

**Results:** Proposed QC ranges for *N. gonorrhoeae* ATCC 49226 were established for disk diffusion at 34 –42mm. This included 95.8% of all reported zone diameters. The Range Finder (RF) statistical program calculated an alternative range of 33 –43mm which included 98.5% of all zones and was approved by the CLSI subcommittee on Antimicrobial Susceptibility Testing in January 2015. There was no significant difference between the two lots of 15- $\mu$ g solithromycin disks. The agar dilution study proposed a QC range of 0.03 –0.25  $\mu$ g/mL which included all of the solithromycin MIC results. A bimodal “shoulder” ( $\geq 60\%$  of data points than the mode) occurs at 0.06  $\mu$ g/mL creating the need for a four log<sub>2</sub>dilution range. The RF statistical program agreed with this range and found no outlier laboratories. No significant differences were noted among GC agar media lots for solithromycin. All MIC results (80/80; 100.0%) and nearly all disk zones (239/240; 99.6%) of the control agent ciprofloxacin were within CLSI published ranges.

**Conclusion:** The proposed MIC (0.03 –0.25  $\mu$ g/mL) and disk diffusion (33 –43 mm) QC ranges for solithromycin should guide clinical or reference laboratories participating in the testing of clinical trial isolates and facilitate the regulatory review process for this investigational antimicrobial agents.