

P0361

Poster Session I

Susceptibility testing of multiresistant bacteria

GSK2140944 MIC QUALITY CONTROL RANGES USING A MULTI-LABORATORY STUDY DESIGN

J.E. Ross¹, R.K. Flamm¹, **R.N. Jones¹**

¹Microbiology, JMI Laboratories, North Liberty IA, USA

Objectives: To conduct a study to establish MIC quality control (QC) ranges for GSK2140944, a type II topoisomerase inhibitor, using the reference CLSI broth microdilution (BMD) method. This antimicrobial is being developed for the treatment of conventional and biothreat pathogens including methicillin-resistant *Staphylococcus aureus* (MRSA).

Methods: An eight laboratory study design was compliant with CLSI M23-A3 guidelines. Four QC strains were tested (*S. aureus* ATCC 29213 [SA], *E. coli* ATCC 25922 [EC], *H. influenzae* ATCC 49247 [HI], and *S. pneumoniae* ATCC 49619 [SP]) using three media lots (three manufacturers) of cation-adjusted Mueller-Hinton broth (MHB), Haemophilus Test Medium (HTM) and MHB with 5% lysed horse blood. Ten replicate tests were performed for each QC organism generating 320 BMD values/QC strain (1,280 total). Levofloxacin, linezolid and azithromycin were used as control agents.

Results: The table lists the proposed MIC QC ranges for GSK2140944. A four log₂ dilution range was only required for SA with GSK2140944 due to a dominant 'shoulder' MIC at 0.25 mg/L, which had 61.7% of the MIC values compared to the modal occurrences at 0.5 mg/L. A range was established for GSK2140944 with *E. coli* of 1 – 4 mg/L which included all reported results and a solid mode (255 of 320 results) at 2 mg/L. Only a three doubling dilution range was necessary for both HI and SPN to also include all reported results. No significant differences were noted among media lots for GSK2140944. Only one value of 1,120 generated control results was outside of the CLSI published QC ranges. All GSK2140944 values were within the proposed QC ranges for all processed organisms. The CLSI Subcommittee on Antimicrobial Susceptibility Testing approved these QC ranges in January 2012 for publication after the selection of the compound's chemical name.

Conclusions: Proposed MIC QC ranges for GSK2140944 should accurately guide clinical or reference laboratories participating in the testing of clinical trial isolates, and facilitate the regulatory review process for this investigational antimicrobial combination exhibiting a unique mode of action.

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QC organism (ATCC no.)	Proposed QC ranges for BMD tests (MIC in mg/L; % in proposed range)
	GSK2140944
<i>S. aureus</i> ATCC 29213	0.12 – 1 (100.0)
<i>E. coli</i> ATCC 25922	1 – 4 (100.0)
<i>H. influenzae</i> ATCC 49247	0.25 – 1 (100.0)
<i>S. pneumoniae</i> ATCC 49619	0.06 – 0.25 (100.0)