Initial Quality Control Ranges for CEM-102 (Fusidic Acid) Using the CLSI Multi-Laboratory M23-A3 Study Design

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Abstract

Background: The increasing prevalence of resistances in staphylococci, especially CA-MRSA, has brought renewed interest in fusidic acid (FA). A promising feature of FA is the effect on bacterial protein synthesis at the translation stage. This results in the unique mode of action that works by inhibiting bacterial protein synthesis at the translation stage.

Materials and Methods: A total of eight laboratories were recruited to provide data for this study. For the disk diffusion study, four-colonized Mueller-Hinton (MH) broth media lots (A, B, C, D) were provided by Oxoid (lot #459655) and Mast Group International (lot #110850) were used. Four sterilized MH broth lots supplemented with 2-5% lysed horse blood were also supplied by Oxoid. Fusidic acid was provided by Fungias, Paris, France. Geometric mean analysis was performed using a statistical software program.

Results: • Colony counts were performed on the BMD panels with the average colony counts among the participating centers ranging from 1.4 ± 0.01 CFU/ml to 4.4 ± 0.01 CFU/ml for 5.0 µg/ml of S. aureus ATCC 29213 and 1.0 ± 0.00 CFU/ml to 4.4 ± 0.01 CFU/ml for S. pneumoniae ATCC 49619.

Conclusions: • The proposed QC ranges for disk diffusion and BMD methods have been well validated for good inter- and intra-laboratory reproducibility for the commonly utilized control isolates. S. aureus ATCC 29213 and S. pneumoniae ATCC 49619.

Table 2. Inter- and intra-laboratory comparisons of the fusidic acid zone diameter results versus proposed QC ranges. Table 1. Fusidic Acid MIC and DD Results versus Proposed QC Ranges.

Table 1. Fusidic Acid MIC and DD Results versus Proposed QC Ranges.

<table>
<thead>
<tr>
<th>MIC (µg/ml)</th>
<th>ATCC 49619</th>
<th>ATCC 29213</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.06</td>
<td>100.0%</td>
<td>92.1%</td>
</tr>
<tr>
<td>0.12</td>
<td>100.0%</td>
<td>92.1%</td>
</tr>
<tr>
<td>0.5</td>
<td>97.8%</td>
<td>97.8%</td>
</tr>
<tr>
<td>2.0</td>
<td>97.8%</td>
<td>97.8%</td>
</tr>
<tr>
<td>8.0</td>
<td>97.8%</td>
<td>97.8%</td>
</tr>
</tbody>
</table>

References


Acknowledgments

The CLSI study and primary investigators were: Cleveland Clinic Foundation, Cleveland, OH (H. Hal, Ph.D., P. CLSI); JMI Laboratories, North Liberty, IA, (H. S. Sader, M.D., Ph.D.); Robert Wood Johnson Medical School, New Brunswick, N.J.; Weinstein, M.D., TIBS; Diagnosis, Cleveland, OH; C. Kruglyak, M.D.; University of Minnesota, Minneapolis, MN; S. dusty, R. M.D., Duke University Medical Center, Durham, NC; S. Y. D. M.D. University of Texas Southwestern Medical Center, Dallas, TX; B. W. M.D., Washington Medical Center, Seattle, WA; S. E, M.D. M.T. (ASP).

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ICAA 2009
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Introduction

The increasing prevalence of resistances in staphylococci organisms has brought renewed interest in fusidic acid (fusidic acid). A promising feature of fusidic acid is the effect on bacterial protein synthesis at the translation stage. This results in the unique mode of action that works by inhibiting bacterial protein synthesis at the translation stage.

These broth microdilution and disk diffusion quality control studies of fusidic acid were performed following the Clinical and Laboratory Standards Institute (CLSI) M07-A8 (2009) guideline document using eight laboratories; different manufacturers of media and two antimicrobial control agents. The results are presented as proposed quality control MIC and DD ranges for two American Type Culture Collection (ATCC) strains: (S. aureus ATCC 29213 [SA] and S. pneumoniae ATCC 49619 [SPN]).

Methods: CLSI BMD and DD methods were utilized in an eight laboratory study design compliant with M23-A3 specifications. For BMD, four media lots (three manufacturers) of cation-adjusted Mueller-Hinton (MH) broth with 2.0%, 4.0%, 8.0%, and 16.0% of broth used for testing SPN were evaluated and three agar lots for the DD method. Ten replicates tests were performed for each QC organisms grown alone and together using 120 BMD values per strain (960 total) and 480 DD zones (lots of FA tested: 960). Replicates, Lysis blood, and a Blood were used and controlled as controls.

Results: • Colony counts were performed on the BMD panels with the average colony counts among the participating centers ranging from 1.4 ± 0.01 CFU/ml to 4.4 ± 0.01 CFU/ml for 5.0 µg/ml of S. aureus ATCC 29213 and 1.0 ± 0.00 CFU/ml to 4.4 ± 0.01 CFU/ml for S. pneumoniae ATCC 49619.

Conclusions: Proposed MIC and DD QC ranges for FA will guide clinical or reference laboratories involved in the testing of clinical trial isolates and facilitate the regulatory review process.

References


The QC study sites and primary investigators were: Cleveland Clinic Foundation, Cleveland, OH (H. Hal, Ph.D., P. CLSI); JMI Laboratories, North Liberty, IA, (H. S. Sader, M.D., Ph.D.); Robert Wood Johnson Medical School, New Brunswick, N.J.; Weinstein, M.D., TIBS; Diagnosis, Cleveland, OH; C. Kruglyak, M.D.; University of Minnesota, Minneapolis, MN; S. dusty, R. M.D., Duke University Medical Center, Durham, NC; S. Y. D. M.D. University of Texas Southwestern Medical Center, Dallas, TX; B. W. M.D. Washington Medical Center, Seattle, WA; S. E, M.D. M.T. (ASP).