Determination of Tier I Quality Control Ranges for WCK 771

M. Hackel¹, S. Bhagwat², J. Satav², K. Umkar², A. Kulkarni², A. Udaykar², M. Patel², D. Sahm¹; ¹IHMA, Inc., Schaumburg, IL, ²Wockhardt Res. Ctr., Aurangabad, India

Background: WCK 771 is a new broad spectrum anti-MRSA benzoquinolizine quinolone under development by Wockhardt. As part of this drug’s development it is important to establish quality control ranges for disk diffusion and minimal inhibitory concentration to ensure a precision in in vitro testing of the product. This Tier 1 study was done to establish initial quality control ranges for the commonly used CLSI control strains for both disk diffusion and broth microdilution testing. Methods: The strains tested included S. aureus ATCC 25923 (disk only) S. aureus ATCC 29213 (broth dilution testing only), H. influenzae ATCC 49247 (broth dilution and disks diffusion testing), S. pneumoniae ATCC 49619 (broth dilution and disks diffusion testing), E. coli ATCC 25922 (broth dilution and disks diffusion testing), and P. aeruginosa ATCC 27853 (broth dilution and disks diffusion testing). WCK 771 disk masses included WCK 771 5µg, 7.5µg, 10 µg, and 15 µg and MIC dilution range was 0.004 - 8 µg/ml. Levofloxacin disk and broth testing served as the control. Each strain was tested over 20 replicates according to CLSI guidelines for disk diffusion and broth microdilution testing. Results: The recommended Tier 1 disk (10 µg only) and broth microdilution ranges are provided in the following table:

Recommended Tier 1 QC Ranges

<table>
<thead>
<tr>
<th>ATCC Strain</th>
<th>10 µg Disk (mm)</th>
<th>Broth (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus ATCC 25923</td>
<td>35 - 38</td>
<td>NA</td>
</tr>
<tr>
<td>S. aureus ATCC 29213</td>
<td>NA</td>
<td>0.015 - 0.12</td>
</tr>
<tr>
<td>E. coli ATCC 25922</td>
<td>29 - 33</td>
<td>0.06 - 0.25</td>
</tr>
<tr>
<td>P. aeruginosa ATCC 27853</td>
<td>17 - 21</td>
<td>1 - 4</td>
</tr>
<tr>
<td>H. influenzae ATCC 49247</td>
<td>34 - 39</td>
<td>0.015 - 0.06</td>
</tr>
<tr>
<td>S. pneumoniae ATCC 49619</td>
<td>25 - 30</td>
<td>0.12 -0.5</td>
</tr>
</tbody>
</table>

Conclusions: Based on the replicate testing results the Tier 1 QC ranges for disk diffusion and broth microdilution testing have been established. All disk masses gave comparable results (data not shown). A 10 µg mass was chosen since this disk mass consistently provides a zones of ≥15 mm for the susceptible target pathogens including Pseudomonas and provides a good correlation with proposed PK-PD MIC breakpoints based on its high clinical exposures at the selected doses. These ranges provide reliable QC guidelines until such time as a CLSI M23 Tier 2 study is completed.

This material is copyrighted to Wockhardt.
M. Hackel, 
IHMA, Inc. Role(s): Independent Contractor.
S. Bhagwat, 
Wockhardt Research Center Role(s): Employee.
J. Satav, 
Wockhardt Research Center Role(s): Employee.
K. Umarkar, 
Wockhardt Research Center Role(s): Employee.
A. Kulkarni, 
Wockhardt Research Center Role(s): Employee.
A. Udaykar, 
Wockhardt Research Center Role(s): Employee.
M. Patel, 
Wockhardt Research Center Role(s): Employee.
D. Sahm, 
IHMA, Inc. Role(s): Independent Contractor.