Sample ES-02 (2015) was a simulated sputum culture (probable pneumonia in an elderly male patient). Participants were instructed to identify the organism and perform antimicrobial susceptibility testing\(^1\)\(^{-4}\) by the laboratories’ routinely utilized method/commercial system. The sample was a *Streptococcus pneumoniae* strain in pure culture that has an unusually resistant antibiogram including a reduced potency among β-lactams, fluoroquinolones, tetracyclines, macrolides, lincosamines and folic acid inhibitors (Table 1). This specific strain was distributed as an educational challenge to assess the contemporary accuracy of identification methods for pneumococci and the current breakpoints (CLSI M100-S25 or EUCAST 2015) for all listed classes of antimicrobials that could be applied for serious non-meningitis streptococcal disease presenting in the emergency department.

Table 1. Listing of expected susceptibility testing categorical results for the *S. pneumoniae* strain (sputum sample from elderly pneumonia patient) sent as specimen ES-02 (2015).

| Antimicrobials listed by CLSI category criteria (Reference MIC in µg/ml): |
|---------------------------------|-----------------|-----------------|-----------------|
| **Susceptible** | **Intermediate** | **Resistant** | **No criteria\(^b\)** |
| Ceftaroline (0.5) | Amoxicillin/clavulanate (4) | Azithromycin (>32) | Ampicillin (8)\(^c\) |
| Chloramphenicol (2) | Imapenem (0.5) | Cefepime (4) | Ceftazidime (>32) |
| Linezolid (1) | Meropenem (0.5) | Ceftriaxone (8) | Ciprofloxacin (>4) |
| Tigecycline (0.06) | Moxifloxacin (2) | Clindamycin (>2) | Dalbavancin (0.015) |
| Vancomycin (0.5) | | Doxycycline (>8) | Oritavancin (0.008)\(^d\) |
| | | Erythromycin (>16) | Oxacillin (>2)\(^c\) |
| | | Levofoxacin (>4) | Piperacillin/tazobactam (8)\(^c\) |
| | | Penicillin (8) | Tedizolid (0.25)\(^d\) |
| | | Tetracycline (>8) | Telavancin (<0.015)\(^d\) |
| | | Trimethoprim/sulfamethoxazole (>4) | |

\(^a\) Criteria from CLSI M100-S25 (2015) tables\(^3\) or as indicated.
\(^b\) Shows those drugs without CLSI published criteria.
\(^c\) Susceptibility (but not resistance) can be predicted by oxacillin or penicillin susceptibility criteria/results.\(^3\)
\(^d\) Recently USA-FDA approved agents with potent anti-streptococcal activity.

An identification of *S. pneumoniae* (94.5% of 817 responses); Streptococcus, alpha-hemolytic (2.5%); or Gram-positive organism and eight other responses (2.3%) was considered acceptable performance, for an overall accuracy of 99.3%. The most frequent error was the identification of another species (0.7%). The overall accuracy of the identification to the species level by the various methods was: BD Phoenix (100.0%) > Vitek 2 (96.5%) > manual methods (94.7%) > MicroScan (92.5%). Prior to shipment, this organism was identified as *S. pneumoniae* by reference 16S sequencing, MALDI-TOF (with very high confidence), and manual biochemical procedures.
Organism Identification

When cultured on routine isolation media, tryptic soy blood agar or chocolate agar, the colony morphology of *S. pneumoniae* is usually medium- to large-sized colonies with a zone of alpha hemolysis. Due to the production of capsular polysaccharide, colonies often appear as glistening or moist. Nearly 80% of *S. pneumoniae* also demonstrate the unique feature of a central depression of the colony which is caused by the production of a pneumococcal autolysin. *S. pneumoniae* are facultative anaerobic bacteria with complex nutritional requirements which are provided by the addition of blood or serum to the medium. The optimum growth temperature is 36-37°C with up to 10% of strains requiring an atmosphere of 5% CO2 for growth, and all strains demonstrating some enhanced growth in the presence of 5% CO2. When stained, *S. pneumoniae* is a Gram-positive coccus. In a Gram’s stain of a primary specimen it is most often described as diplococci with an elongated appearance, and on a stain of isolated colonies as diplococci and chains of varying lengths.

Simple biochemical tests which help to presumptively identify *S. pneumoniae* include catalase, optochin, and bile solubility. Like all streptococci, *S. pneumoniae* are negative for the catalase test when exposed to a 3% peroxide solution; however, false positives can be observed when performed on colonies from blood containing media. The optochin test involves incubating a subculture of the isolate with a 5-µg optochin disk placed on the agar surface overnight in a CO2 atmosphere. *S. pneumoniae* should show a zone of inhibition ≥14 mm around the optochin disk. The bile solubility test can be performed by either direct application of the 10% sodium doxycholate solution to the agar plate, or by the tube method. Clearing of the colonies under the reagent or in the tube exposure demonstrates a positive test. Various commercial systems or products (VITEK, VITEK 2, BD-Phoenix, MicroScan, MALDI-TOF) provide high degrees of accuracy for *S. pneumoniae* identification; however, due to the genetic similarity of *S. pneumoniae* among the other species in the *S. mitis* group (*S. mitis, S. oralis, S. sanguinis, S. parasanguinis, S. gordonii and S. pseudopneumoniae*), molecular method identifications rely on the addition of phenotypic methods for complete identification to the species level.

Antimicrobial Susceptibility Testing

The API Survey participants were asked to perform antimicrobial susceptibility testing on the *S. pneumoniae* isolates; see Tables 1-3. This well-characterized multidrug-resistant (MDR) organism was selected to focus participants on this emerging MDR pathogen, sometimes differing methods/criteria to identify resistances, and the recent release of new agents having potent activity against streptococci, including the pneumococci. This type of organism, when isolated from a compromised patient with symptoms of pneumonia, requires the susceptibility testing of active parenteral agents for therapy of a serious systemic infection. A list of potential treatment options for testing and reporting follows with interpretive criteria for susceptible/resistant published in 2015 by the CLSI and the EUCAST/EMA:
## Antimicrobial Susceptibility – Maximizing Clinical Microbiology Support for Serious Multidrug-Resistant Pneumococcal Infections (cont.)

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>Susceptible/Resistant MIC (µg/ml) breakpoint criteria(^3,4):</th>
<th>CLSI (2015)</th>
<th>EUCAST (2015)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-meningitis, parenteral</td>
<td>$≤ 2 / ≥ 8^a$</td>
<td>$≤ 0.06 / &gt; 2^b$</td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>NC</td>
<td>$≤ 0.5 / &gt; 2^c$</td>
<td></td>
</tr>
<tr>
<td>Cefepime</td>
<td>$≤ 1 / ≥ 4$</td>
<td>$≤ 1 / &gt; 2$</td>
<td></td>
</tr>
<tr>
<td>Cefotaxime, Ceftriaxone</td>
<td>$≤ 1 / ≥ 4$</td>
<td>$≤ 0.5 / &gt; 2$</td>
<td></td>
</tr>
<tr>
<td>Ceftaroline</td>
<td>$≤ 0.5 / --$</td>
<td>$≤ 0.25 / &gt; 0.25$</td>
<td></td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>$≤ 0.5 / ≥ 2$</td>
<td>$≤ 0.5 / &gt; 1$</td>
<td></td>
</tr>
<tr>
<td>Meropenem</td>
<td>$≤ 0.25 / ≥ 1$</td>
<td>$≤ 2 / &gt; 2$</td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>$≤ 4 / ≥ 8$</td>
<td>$≤ 8 / &gt; 8$</td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>$≤ 2 / --$</td>
<td>$≤ 2 / &gt; 4$</td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td>$≤ 1 / --$</td>
<td>$≤ 2 / &gt; 2$</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>$≤ 0.25 / ≥ 1$</td>
<td>$≤ 0.25 / &gt; 0.5$</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>$≤ 0.25 / ≥ 1$</td>
<td>$≤ 0.5 / &gt; 0.5$</td>
<td></td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>$≤ 2 / ≥ 8$</td>
<td>$≤ 2 / &gt; 2$</td>
<td></td>
</tr>
<tr>
<td>Tetracycline</td>
<td>$≤ 1 / ≥ 4$</td>
<td>$≤ 1 / &gt; 2$</td>
<td></td>
</tr>
<tr>
<td>TMP/SMX(^d)</td>
<td>$≤ 0.5 / ≥ 4$</td>
<td>$≤ 1 / &gt; 2$</td>
<td></td>
</tr>
</tbody>
</table>

a. Breakpoint criteria established for high-dose penicillin parenteral therapy (12 million units/day), if intermediate at MIC of 4 µg/ml, then 18-24 million units would be required for treatment.
b. EUCAST criteria are guided by initial penicillin or ampicillin MIC screens and results applied to other β-lactams.\(^4\) Oxacillin disk screens (susceptible at ≥ 20 mm) could also be used.
c. Ampicillin results should be used to guide therapy for other aminopenicillins or combinations (ampicillin-sulbactam, amoxicillin, amoxicillin-clavulanate, piperacillin-tazobactam), not direct susceptibility testing.\(^4\)
d. TMP/SMX = trimethoprim-sulfamethoxazole.

Only 13 of the 30 (43.3%) listed breakpoints (above) from these two organizations are the same. A similar list comparing breakpoints for recently approved (USA-FDA and EUCAST/EMA) agents with high activity against streptococci follows. None have attained an indication for pneumonia caused by *S. pneumoniae*, but clinical trials are pending.

### New antimicrobial agent

<table>
<thead>
<tr>
<th>Streptococcal species</th>
<th>Streptococcal breakpoints (Susceptible/Resistant)(^a):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>USA-FDA</td>
</tr>
<tr>
<td>Dalbavancin</td>
<td>$≤ 0.12 / --$</td>
</tr>
<tr>
<td>Viridans group</td>
<td>$≤ 0.12 / --$</td>
</tr>
<tr>
<td>Oritavancin</td>
<td>$≤ 0.25 / --$</td>
</tr>
<tr>
<td>Viridans group</td>
<td>$≤ 0.25 / --$</td>
</tr>
<tr>
<td>Telavancin</td>
<td>$≤ 0.12 / --$</td>
</tr>
<tr>
<td>Viridans group</td>
<td>$≤ 0.06 / --$</td>
</tr>
<tr>
<td>Tedizolid</td>
<td>$≤ 0.5 / --$</td>
</tr>
<tr>
<td>Viridans group</td>
<td>$≤ 0.25 / --$</td>
</tr>
</tbody>
</table>

a. These criteria are published on the USA-FDA, EUCAST and USCAST websites. No breakpoints have been established / published by CLSI for dalbavancin, oritavancin, telavancin, and tedizolid.
Table 1 illustrates the MDR nature of this ES-02 *S. pneumoniae* challenge organism. Only ceftaroline, chloramphenicol, linezolid, tigecycline and vancomycin had susceptible-level reference MIC values. In fact, ceftaroline would be categorized as not usable (resistant) by EUCAST breakpoints (≤ 0.25 µg/ml), illustrating the broad range of β-lactam resistances demonstrated by this isolate as well as the differing interpretations possible with different breakpoints. Three other β-lactams (amoxicillin-clavulanate, imipenem and meropenem) had intermediate results when applying CLSI breakpoints, but variable assigned categories per EUCAST susceptibility criteria, e.g., imipenem and meropenem were declared susceptible and amoxicillin-clavulanate would be categorized as resistant using penicillin, ampicillin and oxacillin surrogate screening tests methods. The latter finding illustrates a stark and clinically relevant difference between the susceptibility criteria for aminopenicillins in the United States (CLSI) and Europe (EUCAST). In laboratories applying EUCAST criteria, amoxicillin-clavulanate (reference MIC, 4 µg/ml) would have been categorized by the following rules:

1. “Susceptibility inferred from MIC of ampicillin” (8 µg/ml) – resistant; and
2. “For isolates categorized as intermediate to ampicillin, avoid oral treatment with ampicillin, amoxicillin or amoxicillin-clavulanate”.

In contrast, CLSI recommendations for amoxicillin-clavulanate follow:

1. “For non-meningitis isolates, a penicillin MIC of ≤ 0.06 µg/ml (or oxacillin zone ≥ 20mm) can predict susceptibility to the following β-lactams: ampicillin (oral or parenteral), amoxicillin-clavulanate” and 19 other tested β-lactams i.e., resistant; and
2. Separate, unqualified non-meningitis breakpoints are offered in the published tables for amoxicillin with or without clavulanic acid at ≤ 2 µg/ml for susceptible and ≥ 8 µg/ml as resistant i.e., intermediate by reference method, but dominantly susceptible by participant responses (Table 3).

These contradictory recommendations result in possible susceptible or intermediate or resistant interpretations for amoxicillin-clavulanate. One commercial product (the only system with adequate sample size) routinely categorized this ES-02 challenge strain as susceptible (97.0%). This is for an orally administered antimicrobial, where broad-spectrum parenteral β-lactams used in high-dose (third- and-fourth-generation cephalosporins) would be determined to be non-usable, regardless of method or applied commercial system.

Other variations among commercial system results were noted (Table 3) for this strain having many non-susceptible MIC or disk diffusion responses from participants (Table 2). It must be emphasized that NO disk diffusion breakpoints are published for the β-lactams when tested against *S. pneumoniae*, except for the 1 - µg oxacillin screening test. The MIC methods generally performed with high accuracy (95.0-100.0%) in recognizing the appropriate categories for the nine non-β-lactam drugs listed in Table 2.
Lower acceptable performance rates were observed for cefotaxime and ceftriaxone (58.0-74.1% resistant). The resistances among the macrolides (98.2-100.0% accurate), lincosamines (98.9-100.0%), fluoroquinolones (98.1-100.0%) and tetracyclines (98.1-100.0%) were efficiently recognized by both disk diffusion and MIC methods (Table 2). Susceptibility testing experience for the recently approved agents (lipoglycopeptides and the oxazolidinone) awaits future API challenges and releases of validated commercial susceptibility testing devices. Applications of surrogate susceptibility testing with commonly tested drugs in the same antimicrobial class (vancomycin or linezolid) have been suggested by recent publications. In conclusion, from these summarized results, greater harmonization of susceptible breakpoints for \textit{S. pneumoniae} are needed between the CLSI and EUCAST organizations, updated by the contemporary application of pharmacokinetic/pharmacodynamic principles, particularly addressing the orally delivered β-lactams such as amoxicillin ± clavulanic acid.\textsuperscript{3,4}

Table 2. Participant performance for selected agents (≥ 100 responses by one or both tests) listed by disk agar diffusion (DD) and quantitative MIC methods for ES-02 (2015); a \textit{S. pneumoniae} clinical pneumonia isolate in an elderly patient.

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>Acceptable category\textsuperscript{a}</th>
<th>DD No.</th>
<th>% correct</th>
<th>MIC No.</th>
<th>% correct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin/clavulanate</td>
<td>Intermediate</td>
<td>2</td>
<td>50.0\textsuperscript{b}</td>
<td>175</td>
<td>4.0</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Resistant</td>
<td>1</td>
<td>100.0</td>
<td>113</td>
<td>98.2</td>
</tr>
<tr>
<td>Cefepime</td>
<td>Resistant</td>
<td>0</td>
<td>--\textsuperscript{b}</td>
<td>151</td>
<td>20.5</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>Resistant</td>
<td>2</td>
<td>50.0\textsuperscript{b}</td>
<td>274</td>
<td>74.1</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Resistant</td>
<td>13</td>
<td>61.5\textsuperscript{b}</td>
<td>350</td>
<td>58.0</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>Resistant</td>
<td>1</td>
<td>100.0\textsuperscript{b}</td>
<td>143</td>
<td>96.5</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Susceptible</td>
<td>7</td>
<td>100.0</td>
<td>139</td>
<td>95.0</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Resistant</td>
<td>17</td>
<td>100.0</td>
<td>268</td>
<td>98.9</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Resistant</td>
<td>29</td>
<td>100.0</td>
<td>373</td>
<td>98.9</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Resistant</td>
<td>25</td>
<td>100.0</td>
<td>371</td>
<td>98.1</td>
</tr>
<tr>
<td>Linezolid</td>
<td>Susceptible</td>
<td>1</td>
<td>100.0</td>
<td>109</td>
<td>99.1</td>
</tr>
<tr>
<td>Meropenem</td>
<td>Intermediate or Resistant</td>
<td>0</td>
<td>--\textsuperscript{b}</td>
<td>186</td>
<td>31.2\textsuperscript{c}</td>
</tr>
<tr>
<td>Penicillin</td>
<td>Resistant</td>
<td>50</td>
<td>92.0\textsuperscript{d}</td>
<td>356</td>
<td>77.5</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Resistant</td>
<td>16</td>
<td>100.0</td>
<td>324</td>
<td>98.1</td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole</td>
<td>Resistant</td>
<td>27</td>
<td>96.3</td>
<td>350</td>
<td>98.3</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Susceptible</td>
<td>26</td>
<td>100.0</td>
<td>384</td>
<td>100.0</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Correct categorical interpretation was determined by the reference MIC result using the M07-A10, M100-S25 and USA-FDA breakpoint criteria or participant consensus (e.g., chloramphenicol).
\textsuperscript{b} No DD criteria. Oxacillin disk screen and penicillin MIC results should be applied.
\textsuperscript{c} Intermediate MIC by reference method,\textsuperscript{b} but resistant by the screening tests. The cited “correct” percentage is the total of both categories.
\textsuperscript{d} Accuracy using combined oxacillin screen and reported penicillin results reported by participants.
Table 3. Comparisons of β-lactam drug susceptibility categorizations by four commercial MIC systems/methods.

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>Susceptibility categories by method (% S/I/R)(^a):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E-test</td>
</tr>
<tr>
<td>Penicillin</td>
<td>5.9 / 8.8 / 85.3 (^a)</td>
</tr>
<tr>
<td>Amoxicillin/clavulanate</td>
<td>NT(^b)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>NT</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>4.2 / 8.3 / 87.5</td>
</tr>
<tr>
<td>Meropenem</td>
<td>NT</td>
</tr>
</tbody>
</table>

\(^a\) Underlined percentages are the reference MIC derived acceptable results; see Table 2.  
\(^b\) NT = not tabulated, <10 reported results. Sensititre and Vitek had limited numbers of responses.

Emerging Resistance Patterns Among \textit{S. pneumoniae}

The modification of penicillin binding proteins (PBPs), enzymes involved in the final steps of bacterial cell wall synthesis, constitutes the classical mechanism of resistance to penicillins and other β-lactam agents.\(^{14}\) β-lactam resistance develops from the presence of mosaic PBP, which shows reduced affinity to the antimicrobial agent. The PBPs 1a, 1b, 2x, 2a and 2b (high molecular weight) and PBP3 (low molecular weight) have been described in \textit{S. pneumoniae}. However, resistance often arises from mutations in just three of these sites. Resistant isolates express highly variable PBPs containing sequence blocks that differ approximately 20% and 10% at the nucleotide and amino acid levels, respectively, when compared with a susceptible representative.\(^{15}\)

Fluoroquinolone resistance in pneumococci primarily originates from the alteration of the fluoroquinolone binding site due to the gradual accumulation of spontaneous mutations in the quinolone resistance determinant region (QRDR) in gyrA and/ or parC.\(^{16}\) Most high-level fluoroquinolone resistance phenotypes (MIC, ≥16 µg/ml) originate from mutations in both \textit{parC} and \textit{gyrA}, and will confer resistance to newer fluoroquinolones, such as levofloxacin, moxifloxacin and gatifloxacin.\(^{17}\) Mutations in \textit{gyrB} and \textit{parE} can also occur, but generally confer a lesser degree of MIC elevation.

Overall, there are two main mechanisms of macrolide (erythromycin, clarithromycin, azithromycin) resistance. These mechanisms are modification of the target site, and efflux of the antimicrobial from the bacterial cell via acquisition of the \textit{erm} or \textit{mef} genes, respectively.\(^{18}\) Acquisition of \textit{erm}(B) encoding a 23S RNA methylase (target site alteration) represents the major resistant determinant in pneumococci, and causes the so-called macrolides, lincosamides and streptogramins B (MLS\(_B\)) resistance phenotype. \textit{erm}(B) is carried by members of the Tn916 family of transposons, which often harbor the \textit{tet}(M) gene conferring tetracycline resistance. As a result there is a high incidence of tetracycline co-resistance among isolates displaying a MLS\(_B\) resistance phenotype.\(^{19}\) Pneumococci exhibiting resistance to linezolid remains very rare. However, a few reports have shown the detection of such isolates\(^{20}\) and resistances in other streptococcal species.
The prevalence of drug resistance in *S. pneumoniae* has increased globally, and the overall pattern of changes in antimicrobial susceptibility varies among serotypes and geographic regions. Prevalence of resistant serotypes may be influenced by several factors, including overuse of antimicrobial agents, which is a major driving force behind the evolution of antimicrobial resistance, attendance in overcrowded institutions (e.g. daycare centers), and low rates of patient vaccination. In the United States, 19A remains the most common serotype causing pneumococcal disease (IPD) in adults, IPD and non-IPD in all age groups, and children ≤5-years old. These trends occur despite the decrease of 13-valent pneumococcal conjugate vaccine (PCV13) serotypes across all age groups after implementation of PCV13 use in the USA. Moreover, serotype 19A isolates usually display a resistant MDR phenotype, such as that observed in this sample.

**Clinical *S. pneumoniae* Infections and Evolving Treatment Options**

The presence of MDR *S. pneumoniae* is a growing concern in both the hospital and community settings. These antimicrobial-resistant organisms have been associated with increased morbidity and mortality. The CDC lists MDR *S. pneumoniae* in their list of organisms which exist at a serious public health threat level. Vaccines have been beneficial in lowering the occurrence of IPD; however, drug resistance is still common as over time pneumococcal strains with serotypes not included in the vaccines have appeared. Drug-resistant *S. pneumoniae* are frequently MDR such that in addition to resistance to β-lactams, resistance to macrolides, tetracyclines and fluoroquinolones may occur, as in this specimen. *S. pneumoniae* from patients at USA medical centers from 2009-2012 were shown to exhibit 89.2% susceptibility to penicillin (parenteral non-meningitis susceptibility breakpoint; only 57.3% susceptible at oral penicillin V breakpoint) and 56.8, 75.0, and 98.9% were susceptible to erythromycin, tetracycline, or levofloxacin, respectively.

Penicillin-susceptible *S. pneumoniae* are usually susceptible to many other agents and recommended treatments include penicillin and vancomycin. Levofloxacin, ceftriaxone, and linezolid are also commonly recommended if the isolate is penicillin-resistant (MIC, ≥2 µg/mL). Ceftaroline, approved for commercial use in 2010 for use in community-acquired pneumonia and acute bacterial skin and skin structure infections, is highly active against *S. pneumoniae* including MDR strains. *S. pneumoniae* in vitro susceptibility to ceftaroline in a USA national surveillance program conducted over a five year period (2009-2013, AWARE) was demonstrated to be at 100.0% with the highest MIC value occurring at 0.5 µg/mL, which is the CLSI and USA-FDA susceptible breakpoint. The new lipoglycopeptides (dalbavancin and oritavancin) as well as the recently approved oxazolidinone, tedezolid, are very active in vitro against *S. pneumoniae*; however, they are currently only approved for use in the treatment of acute bacterial skin and skin structure infections. Further studies will be required to assess if their potent in vitro activity against pneumococci will prove useful in other clinical indications.
References


