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# Antimicrobial susceptibility of *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Streptococcus suis*, and *Bordetella bronchiseptica* isolated from pigs in the United States and Canada, 2011 to 2015

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## Summary

**Objective**: To report the susceptibility to veterinary antimicrobial agents of *Actinobacillus pleuropneumoniae, Pasteurella multocida, Streptococcus suis,* and *Bordetella bronchiseptica* isolated from pigs in the United States and Canada from 2011 to 2015.

**Materials and methods**: In vitro broth microdilution susceptibility testing for minimal inhibitory concentration values were performed using 10 antimicrobial agents (ampicillin, ceftiofur, danofloxacin, enrofloxacin, florfenicol, penicillin, tetracycline, tilmicosin, trimethoprim-sulfamethoxazole, and tulathromycin) with *Actinobacillu pleuropneumoniae* (n = 312), *P multocida* (n = 855), *S suis* (n = 1201), and *B bronchiseptica* (n = 572) following methods and susceptibility breakpoints approved by the Clinical and Laboratory Standards Institute.

**Results**: *Actinobacillu pleuropneumoniae* isolates were 100% susceptible to ceftiofur and florfenicol, and *P multocida* isolates were 100% susceptible to ceftiofur, enrofloxacin, and florfenicol. High rates of susceptibility (90% to > 99% susceptible) were observed for *A pleuropneumoniae* to enrofloxacin and tulathromycin, for *P multocida* to ampicillin, penicillin, tilmicosin, and tulathromycin, for *S suis* to ampicillin, ceftiofur, and florfenicol, and for *B bronchiseptica* to tulathromycin. Tetracycline exhibited low susceptibility rates against *A pleuropneumoniae* (0% to 6% susceptibility), *P multocida* (22.3% to 35.3%), and *S suis* (0% to 1.3%). No susceptibility of *B bronchiseptica* to ampicillin (0%) and low rates of susceptibility to florfenicol (5.4% to 23.5%) were also observed.

**Implications**: Under the conditions of this study, high rates of susceptibility to most veterinary antimicrobial agents continue to be seen for *A pleuropneumoniae, P multocida, S suis,* and *B bronchiseptica*, the predominant pathogens associated with swine respiratory disease in the United States and Canada.

**Keywords**: swine, surveillance, antimicrobial susceptibility, respiratory disease

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**Resumen - Susceptibilidad antimicrobiana del *Actinobacillus pleuropneumoniae*, la *Pasteurella multocida*, el *Streptococcus suis*, y la *Bordetella bronchiseptica* aislados de cerdos en los Estados Unidos y Canadá, 2011 a 2015**

**Objetivo:** Reportar la susceptibilidad contra agentes antimicrobianos veterinarios del *Actinobacillus pleuropneumoniae*, la *Pasteurella multocida*, el *Streptococcus suis*, y la *Bordetella bronchiseptica* aislados de cerdos en los Estados Unidos y Canadá del 2011 al 2015.

**Materiales y métodos:** Se realizaron pruebas de susceptibilidad in vitro de microdilución en caldo para encontrar valores de concentración inhibitorios mínimos utilizando 10 agentes antimicrobianos (ampicilina, ceftiofur, danofloxacina, enrofloxacina, florfenicol, penicilina, tetraciclina, tilmicosina, trimetoprim-sulfametoxazol, y tulatromcina) con *A pleuropneumoniae* (n = 312), *P multocida* (n = 855), *S suis* (n = 1201), y *B bronchiseptica* (n = 572) siguiendo los métodos y los puntos de rompimiento de la susceptibilidad aprobados por el Instituto de Estándares Clínicos y de Laboratorio.

**Resultados:** Los aislamientos del *A pleuropneumoniae* fueron 100% susceptibles al ceftiofur y al florfenicol, y los aislados del *P multocida* fueron 100% susceptibles al ceftiofur, enrofloxacina, y al florfenicol. Se observaron altos índices de susceptibilidad (90% a > 99% susceptibles) del *A pleuropneumoniae* a la enrofloxacina y la tulatromicina, de la *P multocida* a la ampicilina, la penicilina, la tilmicosina, y la tulatromicina, del *S suis* a la ampicilina, el ceftiofur, y el florfenicol, y de la *B bronchiseptica* a la tulatromicina. La tetraciclina exhibió índices bajos de susceptibilidad contra el *A pleuropneumoniae* (0% a 6% de susceptibilidad), la *P multocida* (22.3% a 35.3%), y el *S suis* (0% a 1.3%). No hubo susceptibilidad de la *B bronchiseptica* a la ampicilina (0%) y además se observaron índices bajos de susceptibilidad al florfenicol (5.4% a 23.5%).

**Implicaciones:** Bajo las condiciones de este estudio, continúan observándose índices altos

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de susceptibilidad a la mayoría de los agentes antimicrobianos veterinarios contra el *A pleuropneumoniae*, la *P multocida*, el *S suis*, y la *B bronchiseptica*, los patógenos predominantes asociados con las enfermedades respiratorias porcinas en los Estados Unidos y Canadá.

**Resumé - Sensibilité antimicrobienne d'isolats porcins *d'Actinobacillus pleuropneumoniae*, de *Pasteurella multocida*, de *Streptococcus suis* et de *Bordetella bronchiseptica* provenant des États-Unis et du Canada, 2011 à 2015**

**Objectif:** Faire rapport de la sensibilité à des antimicrobiens vétérinaires d'isolats porcins *d'Actinobacillus pleuropneumoniae*, de *Pasteurella multocida*, de *Streptococcus suis*, et de *Bordetella bronchiseptica* provenant des États-Unis et du Canada de 2011 à 2015.

**Matériels et méthodes:** Les valeurs de concentration minimale inhibitrice furent déterminées in vitro par la méthode de microdilution en bouillon pour 10 agents antimicrobiens (ampicilline, ceftiofur, danofloxacine, enrofloxacine, florfénicol, pénicilline, tétracycline, tilmicosin, trimethoprime-sulfamethoxazole, et tulathromycine) pour *A pleuropneumoniae* (n = 312), *P multocida* (n = 855), *S suis* (n = 1201) et *B bronchiseptica* (n = 572) en suivant les directives et les valeurs seuils de sensibilité approuvées par le Clinical and Laboratory Standards Institute.

**Résultats:** Les isolats d*'A pleuropneumoniae* étaient sensibles à 100% au ceftiofur et au florfénicol, et les isolats de *P multocida* sensibles à 100% au ceftiofur, à l'enrofloxacine et au florfénicol. Des taux élevés de sensibilité (90% à > 99% de sensibilité) ont été notés pour *A pleuropneumoniae* envers l'enrofloxacine et la tulathromycine, pour *P multocida* envers l'ampicilline, la pénicilline, le tilmicosin et la tulathromycine, pour *S suis* envers l'ampicilline, le ceftiofur et le florfénicol, et pour *B bronchiseptica* envers la tulathromycine. La tétracycline présentait des taux faibles de sensibilité contre *A pleuropneumoniae* (0% à 6%), *P multocida* (22,3% à 35,3%), et *S suis* (0% à 1,3%). Aucune sensibilité de *B bronchiseptica* envers l'ampicilline (0%) et de faibles taux de sensibilité envers le florfénicol (5,4% à 23,5%) furent également observés.

**Implications:** Dans les conditions de la présente étude, de hauts taux de sensibilité à la plupart des agents antimicrobiens vétérinaires continuent d'être observés pour *A pleuropneumoniae*, *P multocida*, *S suis*, et *B bronchiseptica*, les principaux agents pathogènes associés avec les maladies respiratoires porcines aux États-Unis et au Canada.

Antimicrobial agents are important for the humane and efficient production of swine and other food animals in order to meet the challenges of a sustainable food supply for a growing world population.[1] According to the National Animal Health Monitoring System, swine respiratory disease (SRD) is a prevalent cause of nursery pig and grower-finisher deaths in swine in which multiple infectious agents are often involved.[2] Primary pathogens for SRD include *Mycoplasma hyopneumoniae, Actinobacillus pleuropneumoniae,* and *Bordetella bronchiseptica,* as well as viral agents. Common secondary pathogens include *Pasteurella multocida, Streptococcus suis, Hemophilus parasuis, Actinobacillus suis,* and *Salmonella* Choleraesuis.[3] These primary and secondary pathogens act together to increase the severity and duration of SRD.

Antimicrobial surveillance among veterinary bacterial pathogens obtained from clinical specimens provides a platform from which to detect emergence of resistance in animal populations. While veterinary diagnostic laboratories throughout North America provide important antimicrobial susceptibility information for clinical isolates submitted by the attending veterinarian or animal caretaker, the susceptibility results are not typically examined or summarized nationally or regionally. Few surveillance programs monitor susceptibility in swine pathogens nationally.[4,5] Portis et al[4] reported minimal inhibitory concentration (MIC) values for seven antimicrobial agents against *A pleuropneumoniae, P multocida,* and *S suis* isolated from diseased swine in the United States and Canada over a 10-year period (2001 to 2010) and concluded that most isolates showed high rates of susceptibility to all antimicrobial agents tested except tetracycline. Continuing this surveillance program, we report herein the percentages of *A pleuropneumoniae, P multocida, S suis,* and *B bronchiseptica* pathogens isolated from swine in the United States and Canada from 2011 to 2015 that were susceptible to the veterinary antimicrobial agents ampicillin, ceftiofur, danofloxacin, enrofloxacin, florfenicol, penicillin, tetracycline, tilmicosin, trimethoprim-sulfamethoxazole (TMP-SMX), and tulathromycin. This paper presents the findings of that second surveillance period (2011-2015).

## Materials and methods

### Laboratory participants and isolate characterization

Veterinary laboratories from the United States and Canada participated in this surveillance study. The regions from which isolates were obtained are shown in Table 1. All *A pleuropneumoniae, P multocida, S suis,* and *B bronchiseptica* isolates were recovered from diseased or dead pigs. Laboratories selected isolates on the basis of their own protocols and were requested not to use antimicrobial susceptibility as a criterion for selection. Laboratories were also requested to submit no more than eight isolates per quarter year in order to prevent over-representation from any one geographic area. Each participating laboratory was also requested to send no more than one isolate of each bacterial species from a herd each quarter year in order to prevent the over-representation of bacterial clones from one region.

Bacterial isolates were identified to the species level by each participating laboratory before shipment to a central laboratory for susceptibility testing. Any further identification or characterization of bacterial species were performed at Zoetis (Kalamazoo, Michigan) using standard biochemical tests, commercially available identification systems (such as API Microbial Identification Kits, bioMerieux, Durham, North Carolina; and Biolog Microbial Identification Systems, Hayward, California), or Matrix Assisted Laser Desorption Ionization Time-of-Flight Mass Spectrometry (MALDI-ToF MS, Bruker, Billerica, Massachusetts). All isolates were stored in approximately 1.0 mL trypticase soy broth (BD Biosciences, Sparks, Maryland) supplemented with 10% glycerol and stored at approximately -70°C until tested.

### Determination of minimal inhibitory concentration values

In vitro susceptibility data were generated annually by performing MIC tests at two laboratories (Microbial Research Inc, Fort Collins, Colorado; and Zoetis) to minimize testing bias.[6,7] Both laboratories followed Clinical and Laboratory Standards Institute (CLSI) standardized methods and quality-control guidelines during susceptibility testing.[8]The MIC values for all isolates were determined using a dehydrated broth microdilution system (Sensititre System; Thermo Fisher Scientific, Waltham, Massachusetts)

**Table 1:** Origin and number of bacterial isolates per year by region for a 5-year study of antimicrobial susceptibility of *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Streptococcus suis*, and *Bordetella bronchiseptica* from pigs in the United States and Canada*

| Region | 2011 | 2012 | 2013 | 2014 | 2015 | Total |
|---|---|---|---|---|---|---|
| ***Actinobacillus pleuropneumoniae*** | | | | | | |
| Canada | 12 | 13 | 14 | 14 | 16 | 69 |
| Northeast | 0 | 0 | 4 | 2 | 1 | 7 |
| Midwest | 40 | 31 | 46 | 32 | 35 | 184 |
| South | 7 | 11 | 4 | 7 | 3 | 32 |
| West | 8 | 5 | 1 | 6 | 0 | 20 |
| Total | 67 | 60 | 69 | 61 | 55 | 312 |
| ***Pasteurella multocida*** | | | | | | |
| Canada | 43 | 47 | 39 | 36 | 57 | 222 |
| Northeast | 1 | 6 | 0 | 8 | 6 | 21 |
| Midwest | 103 | 91 | 101 | 107 | 143 | 545 |
| South | 4 | 5 | 3 | 2 | 6 | 20 |
| West | 6 | 10 | 10 | 10 | 11 | 47 |
| Total | 157 | 159 | 153 | 163 | 223 | 855 |
| ***Streptococcus suis*** | | | | | | |
| Canada | 60 | 54 | 62 | 62 | 100 | 338 |
| Northeast | 3 | 9 | 0 | 6 | 8 | 26 |
| Midwest | 143 | 129 | 147 | 146 | 162 | 727 |
| South | 7 | 5 | 15 | 8 | 15 | 50 |
| West | 13 | 8 | 11 | 12 | 16 | 60 |
| Total | 226 | 205 | 235 | 234 | 301 | 1201 |
| ***Bordetella bronchiseptica*** | | | | | | |
| Canada | 24 | 17 | 21 | 17 | 32 | 111 |
| Northeast | 1 | 6 | 4 | 1 | 2 | 14 |
| Midwest | 72 | 67 | 75 | 84 | 92 | 390 |
| South | 2 | 8 | 9 | 7 | 7 | 33 |
| West | 3 | 5 | 3 | 7 | 6 | 24 |
| Total | 102 | 103 | 112 | 116 | 139 | 572 |

* Provinces and states that submitted isolates originating from within the regions included Canada: Alberta, British Columbia, Manitoba, Nova Scotia, Ontario, Quebec, Saskatchewan; Northeast: Maryland, New Jersey, New York, Pennsylvania, Vermont; Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin; South: Arkansas, Kentucky, Louisiana, Mississippi, North Carolina, Oklahoma, Texas, Virginia; West: Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, Oregon, Utah, Washington.

which conforms to CLSI standards for testing of veterinary pathogens.[8] Direct colony suspensions were used and prepared at a final bacterial concentration of approximately $5 \times 10^5$ colony forming units per mL. Custom-made 96-well microtitre panels included serial doubling dilutions of the antimicrobial agents ampicillin, ceftiofur, danofloxacin, enrofloxacin, florfenicol, penicillin, tetracycline, tilmicosin, TMP-SMX, and tulathromycin. All concentration ranges for antimicrobials were chosen to encompass appropriate quality-control ranges and published clinical breakpoints, and appropriate quality-control organisms were included with each testing date.[9] Ampicillin was added to the surveillance program starting in 2012, and no susceptibility data were available for 2011 alone.

# Results

## Quality control

Although not shown for this study, MIC values for all appropriate quality-control organisms were acceptable when all study isolates were tested against antimicrobial agents on each date of testing.

### *Actinobacillus pleuropneumoniae*

The MIC distributions, $MIC_{50}$ values, and $MIC_{90}$ values for 10 antimicrobial agents tested against *A pleuropneumoniae* (n = 312) are reported in Table 2. The CLSI has established clinical breakpoints for *A pleuropneumoniae* against ampicillin, ceftiofur, enrofloxacin, florfenicol, tetracycline, tilmicosin, and tulathromycin. *Actinobacillus pleuropneumoniae* susceptibility to ampicillin increased from 85% in 2012 (susceptible breakpoint ≤ 0.5 µg per mL) to 91.3% in 2013, but decreased to 85.4% in 2015. The percentage of isolates susceptible to ceftiofur over the 5-year study period was 100% (susceptible breakpoint ≤ 2 µg per mL) and the $MIC_{90}$ values were ≤ 0.03 µg per mL. The highest ceftiofur MIC value against *A pleuropneumoniae* was 1 µg per mL (2.9% of the isolates) in 2013. The percentage of susceptibility to enrofloxacin was very high (95.7% to 100%; breakpoint ≤ 0.25 µg per mL), and the $MIC_{90}$ values over the study period were 0.06 to 0.12 µg per mL; florfenicol was 100% susceptible (breakpoint ≤ 2 µg per mL), with $MIC_{90}$ values at 0.5 µg per mL. *Actinobacillus pleuropneumoniae* susceptibility to tetracycline (breakpoint ≤ 0.5 µg per mL) was very low, with 6.0% susceptibility in 2011 and 0% susceptibility in 2012, 2013, and 2015, while tilmicosin susceptibility (breakpoint ≤ 16 µg per mL) ranged from 83.6% in 2011 to 100% in 2015. There was 100% percent susceptibility of *A pleuropneumoniae* to tulathromycin (breakpoint ≤ 64 µg per mL) from 2012 to 2015, and $MIC_{90}$ values ranged from 32 to 64 µg per mL. Clinical and Laboratory Standards Institute-approved susceptible breakpoints have not been established for danofloxacin, penicillin, or TMP-SMX, but the $MIC_{90}$ values were determined as 0.12 to 0.25 µg per mL, 2 to ≥ 32 µg per mL, and ≤ 0.06 to 0.12 µg per mL, respectively, from 2011 to 2015.

### *Pasteurella multocida*

The MIC distributions, $MIC_{50}$ values, and $MIC_{90}$ values for 10 antimicrobial agents tested against *P multocida* (n = 855) are reported in Table 3. The CLSI has established clinical breakpoints for *P multocida* against ampicillin, ceftiofur, enrofloxacin, florfenicol, penicillin, tetracycline, tilmicosin, and tulathromycin. *Pasteurella multocida* susceptibility to ampicillin was very high (97.6% to 98.7%; susceptible breakpoint ≤ 0.5 µg per mL) from 2012 to 2015, while the percentage of susceptibility to ceftiofur was 100% (breakpoint ≤ 2 µg per mL), with $MIC_{90}$ values at ≤ 0.03 µg per mL. *Pasteurella multocida* was 100% susceptible to enrofloxacin (breakpoint ≤ 0.25 µg per mL) with $MIC_{90}$ values at 0.016 to 0.03 µg per mL, and also 100% susceptible to florfenicol (breakpoint ≤ 2 µg per mL) with $MIC_{90}$ values at 0.5 µg per mL. *Pasteurella multocida* isolates were highly susceptible to penicillin (97.6% to 99.4%; breakpoint ≤ 0.25 µg per mL), tilmicosin (97.5% to100%; breakpoint ≤ 16 µg per mL), and tulathromycin (98.8% to 100%; breakpoint ≤ 16 µg per mL) in which the tulathromycin $MIC_{90}$ value ranged from 2 to 4 µg per mL. Clinical and Laboratory Standards Institute-approved susceptible clinical breakpoints have not been established for danofloxacin or TMP-SMX, but $MIC_{90}$ values were determined as 0.03 to 0.06 µg per mL and 0.12 to 0.25 µg per mL, respectively.

### *Streptococcus suis*

The MIC distributions, $MIC_{50}$ values, and $MIC_{90}$ values for 10 antimicrobial agents tested against *S suis* (n = 1201) are reported in Table 4. The CLSI has established clinical breakpoints for *S suis* against ampicillin, ceftiofur, enrofloxacin, florfenicol, penicillin, and tetracycline. *Streptococcus suis* susceptibility to ampicillin was very high (susceptible breakpoint ≤ 0.5 µg per mL) and ranged from 98.0% to 99.2%, while the percentage of susceptibility to ceftiofur was also high (93.6% to 96.6%; breakpoint ≤ 2 µg per mL) over the 5-year study period in which $MIC_{90}$ values ranged from 1 to 2 µg per mL. The percentage of *S suis* susceptible to enrofloxacin (breakpoint ≤ 0.5 µg per mL) increased from 82.3% in 2011 to 94% in 2015, in which $MIC_{90}$ values were 0.5 to 1 µg per mL. The percentage of *S suis* susceptibility to florfenicol was very high (breakpoint ≤ 2 µg per mL) and dropped slightly from 100% in 2012 to 97.1% in 2015, in which $MIC_{90}$ values were 2 µg per mL. The percentage of *S suis* susceptibility to penicillin (breakpoint ≤ 0.25 µg per mL) dropped from 84% in 2011 to 73.6% in 2013, but increased to 82.1% in 2014, in which $MIC_{90}$ values ranged from 1 to 2 µg per mL. No *S suis* isolates were susceptible to tetracycline (breakpoint ≤ 1 µg per mL) in 2012 and 2015, with 0.8% susceptibility in 2011 and 1.3% susceptibility in 2013 and 2014. Susceptible breakpoints were not available for danofloxacin, tilmicosin, TMP-SMX, or tulathromycin, but $MIC_{90}$ values were determined as 1 µg per mL, ≥ 64 µg per mL, 0.12 to 0.25 µg per mL, and ≥ 128 µg per mL, respectively.

### *Bordetella bronchiseptica*

The MIC distributions, $MIC_{50}$ values, and $MIC_{90}$ values for 10 antimicrobial agents tested against *B bronchiseptica* (n = 572) are reported in Table 5. The CLSI has established clinical breakpoints for *B bronchiseptica* against ampicillin, florfenicol, and tulathromycin. *Bordetella bronchiseptica* isolates in this study had no in vitro activity to ampicillin (0% susceptibility; susceptible breakpoint ≤ 0.5 µg per mL) in which $MIC_{90}$ values were ≥ 16 µg per mL. *Bordetella bronchiseptica* susceptibility to florfenicol (breakpoint ≤ 2 µg per mL) was low and decreased from 23.5 % in 2011 to 5.4% in 2013, but increased to 11.2% in 2014, in which $MIC_{90}$ values were 4 µg per mL over the 5-year study period. The percentage of *B bronchiseptica* susceptible to tulathromycin was 99% to 100% (breakpoint ≤ 16 µg per mL) and the $MIC_{90}$ value ranged from 8 to 16 µg per mL. Clinical and Laboratory Standards Institute-approved susceptible breakpoints were not available for ceftiofur, danofloxacin, enrofloxacin, penicillin, tetracycline, tilmicosin, or TMP-SMX, but $MIC_{90}$ values were determined as ≥ 8 µg per mL, 1 µg per mL, 0.5 to 1 µg per mL, ≥ 32 µg per mL, 2 to 4 µg per mL, 32 to ≥ 64 µg per mL, and 8 to ≥ 16 µg per mL, respectively.

## Discussion

The availability of antimicrobial agents to combat respiratory disease in veterinary medicine continues to have a beneficial effect on the health and welfare of swine and other livestock, and the use of antimicrobial agents helps support the safe, humane, and economical production of food.[10] The prevalence of *A pleuropneumoniae, P multocida, S suis*, and *B bronchiseptica* pathogens associated with SRD emphasizes the importance of maintaining high levels of susceptibility to antimicrobial agents that are available to veterinarians for treatment of these pathogens.[11] Surveillance and monitoring studies for antimicrobial resistance in pathogenic bacteria of animal origin are necessary to understand any rates of change in the susceptibility of bacteria to antimicrobial agents, thereby serving as one component among many to help guide practitioners to select the most appropriate antimicrobial agent for treatment of disease.[12] A limited number of recent studies have investigated in vitro susceptibilities of specific antimicrobial agents used to treat swine pathogens associated with respiratory disease on a national basis.[4,5,13,14]

**Table 2:** Summary of minimal inhibitory concentration (MIC) values and frequency distributions for 10 antimicrobial agents tested with *Actinobacillus pleuropneumoniae* (n = 312) isolated from swine in the United States and Canada from 2011 to 2015*

| | | | | | Ampicillin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | | | | | | | NT | | | | | | |
| 2012 | 60 | 0.12 | ≥ 16 | 85 | 1.7 | 48.3 | 33.3 | 1.7 | 0 | 0 | 0 | 0 | 15 |
| 2013 | 69 | 0.25 | 0.5 | 91.3 | 2.9 | 23.2 | 56.5 | 8.7 | 0 | 1.4 | 0 | 0 | 7.3 |
| 2014 | 61 | 0.25 | ≥ 16 | 86.9 | 0 | 41 | 45.9 | 0 | 0 | 1.6 | 0 | 0 | 11.5 |
| 2015 | 55 | 0.25 | ≥ 16 | 85.4 | 3.6 | 41.8 | 40 | 0 | 0 | 0 | 1.8 | 0 | 12.8 |

| | | | | | Ceftiofur MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | ≥ 8 |
| 2011 | 67 | ≤ 0.03 | ≤ 0.03 | 100 | 98.5 | 1.5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2012 | 60 | ≤ 0.03 | ≤ 0.03 | 100 | 93.3 | 6.7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2013 | 69 | ≤ 0.03 | ≤ 0.03 | 100 | 95.7 | 1.4 | 0 | 0 | 0 | 2.9 | 0 | 0 | 0 |
| 2014 | 61 | ≤ 0.03 | ≤ 0.03 | 100 | 95.1 | 4.9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2015 | 55 | ≤ 0.03 | ≤ 0.03 | 100 | 98.2 | 1.8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| | | | | | Danofloxacin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | ≥ 4 |
| 2011 | 67 | 0.06 | 0.12 | NA | 0 | 0 | 64.2 | 31.3 | 1.5 | 1.5 | 1.5 | 0 | 0 |
| 2012 | 60 | 0.06 | 0.12 | NA | 0 | 0 | 53.3 | 43.3 | 1.7 | 0 | 1.7 | 0 | 0 |
| 2013 | 69 | 0.12 | 0.25 | NA | 1.5 | 0 | 34.8 | 53.6 | 5.8 | 1.5 | 2.9 | 0 | 0 |
| 2014 | 61 | 0.12 | 0.12 | NA | 0 | 0 | 32.8 | 65.6 | 1.6 | 0 | 0 | 0 | 0 |
| 2015 | 55 | 0.12 | 0.12 | NA | 0 | 1.8 | 36.4 | 60 | 1.8 | 0 | 0 | 0 | 0 |

| | | | | | Enrofloxacin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.008 | 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | ≥ 2 |
| 2011 | 67 | 0.06 | 0.06 | 98.5 | 0 | 0 | 25.4 | 68.6 | 3 | 1.5 | 1.5 | 0 | 0 |
| 2012 | 60 | 0.06 | 0.12 | 98.3 | 0 | 0 | 23.3 | 65 | 10 | 0 | 0 | 1.7 | 0 |
| 2013 | 69 | 0.06 | 0.12 | 95.7 | 1.4 | 0 | 20.3 | 59.5 | 14.5 | 0 | 4.3 | 0 | 0 |
| 2014 | 61 | 0.06 | 0.12 | 100 | 0 | 0 | 21.3 | 67.2 | 11.5 | 0 | 0 | 0 | 0 |
| 2015 | 55 | 0.06 | 0.06 | 100 | 0 | 1.8 | 29.1 | 61.8 | 7.3 | 0 | 0 | 0 | 0 |

| | | | | | Florfenicol MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | 67 | 0.25 | 0.5 | 100 | 0 | 0 | 52.2 | 47.8 | 0 | 0 | 0 | 0 | 0 |
| 2012 | 60 | 0.5 | 0.5 | 100 | 0 | 1.7 | 36.7 | 61.6 | 0 | 0 | 0 | 0 | 0 |
| 2013 | 69 | 0.5 | 0.5 | 100 | 0 | 0 | 30.4 | 68.1 | 0 | 1.5 | 0 | 0 | 0 |
| 2014 | 61 | 0.5 | 0.5 | 100 | 0 | 0 | 42.6 | 57.4 | 0 | 0 | 0 | 0 | 0 |
| 2015 | 55 | 0.5 | 0.5 | 100 | 0 | 0 | 25.5 | 74.5 | 0 | 0 | 0 | 0 | 0 |

| | | | | | Penicillin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | ≥ 32 |
| 2011 | 67 | 0.5 | ≥ 32 | NA | 7.5 | 19.4 | 47.8 | 7.5 | 1.5 | 0 | 0 | 1.5 | 14.9 |
| 2012 | 60 | 0.5 | ≥ 32 | NA | 5 | 15 | 51.7 | 13.3 | 0 | 0 | 0 | 0 | 15 |
| 2013 | 69 | 0.5 | 2 | NA | 7.2 | 24.6 | 56.5 | 1.5 | 1.5 | 1.5 | 0 | 0 | 7.2 |
| 2014 | 61 | 0.25 | ≥ 32 | NA | 8.2 | 47.5 | 28 | 1.6 | 1.6 | 0 | 1.6 | 0 | 11.5 |
| 2015 | 55 | 0.5 | ≥ 32 | NA | 7.3 | 30.9 | 47.3 | 0 | 0 | 1.8 | 0 | 0 | 12.8 |

**Table 2:** Continued

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tetracycline MIC frequency distribution (% of isolates) ≤ 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | 67 | ≥ 16 | ≥ 16 | 6 | 1.5 | 4.5 | 11.9 | 0 | 3 | 17.9 | 61.2 |
| 2012 | 60 | ≥ 16 | ≥ 16 | 0 | 0 | 0 | 16.7 | 3.3 | 0 | 18.3 | 61.7 |
| 2013 | 69 | ≥ 16 | ≥ 16 | 0 | 0 | 0 | 10.1 | 1.5 | 0 | 17.4 | 71 |
| 2014 | 61 | ≥ 16 | ≥ 16 | 3.3 | 0 | 3.3 | 16.4 | 1.6 | 0 | 24.6 | 51.4 |
| 2015 | 55 | ≥ 16 | ≥ 16 | 0 | 0 | 0 | 9.1 | 0 | 0 | 21.8 | 69.1 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tilmicosin MIC frequency distribution (% of isolates) ≤ 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | ≥ 64 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | 67 | 16 | 32 | 83.6 | 0 | 0 | 0 | 0 | 0 | 10.5 | 73.1 | 16.4 | 0 |
| 2012 | 60 | 8 | 16 | 98.3 | 0 | 0 | 0 | 0 | 3.3 | 73.3 | 21.7 | 1.7 | 0 |
| 2013 | 69 | 16 | 32 | 89.9 | 0 | 0 | 0 | 0 | 1.5 | 36.2 | 52.2 | 10.1 | 0 |
| 2014 | 61 | 16 | 16 | 96.7 | 0 | 0 | 0 | 0 | 0 | 14.7 | 82 | 3.3 | 0 |
| 2015 | 55 | 8 | 16 | 100 | 0 | 0 | 0 | 0 | 1.8 | 56.4 | 41.8 | 0 | 0 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | TMP-SMX MIC frequency distribution (% of isolates) ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | 67 | ≤ 0.06 | ≤ 0.06 | NA | 92.5 | 7.5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2012 | 60 | ≤ 0.06 | ≤ 0.06 | NA | 98.3 | 1.7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2013 | 69 | ≤ 0.06 | ≤ 0.06 | NA | 92.8 | 7.2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2014 | 61 | ≤ 0.06 | 0.12 | NA | 83.6 | 16.4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2015 | 55 | ≤ 0.06 | 0.12 | NA | 67.3 | 30.9 | 1.8 | 0 | 0 | 0 | 0 | 0 | 0 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tulathromycin MIC frequency distribution (% of isolates) ≤ 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | ≥ 128 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | 67 | 64 | 64 | 98.5 | 0 | 0 | 0 | 0 | 0 | 0 | 11.9 | 86.6 | 1.5 |
| 2012 | 60 | 16 | 32 | 100 | 0 | 0 | 0 | 0 | 1.7 | 48.3 | 50 | 0 | 0 |
| 2013 | 69 | 32 | 64 | 100 | 0 | 0 | 0 | 0 | 0 | 7.2 | 66.7 | 26.1 | 0 |
| 2014 | 61 | 64 | 64 | 100 | 0 | 0 | 0 | 0 | 0 | 4.9 | 37.7 | 57.4 | 0 |
| 2015 | 55 | 32 | 64 | 100 | 0 | 0 | 0 | 0 | 1.8 | 9.1 | 78.2 | 12.7 | 0 |

* No. = the number of isolates tested per year; $MIC_{50}$ = antibacterial drug concentration that inhibits 50% of the bacterial population; $MIC_{90}$ = antibacterial drug concentration that inhibits 90% of the bacterial population; %S = the percentage of isolates that are susceptible to the antibacterial drug using Clinical and Laboratory Standards Institute (CLSI) criteria; NA = not applicable since there are no CLSI-approved clinical breakpoints for susceptibility in that swine respiratory disease pathogen; NT = not tested; vertical bold lines indicate the CLSI-approved breakpoint for susceptible, intermediate, and resistant in that swine respiratory disease pathogen; TMP-SMX = trimethoprim-sulfamethoxazole; numbers in the lowest concentration of the tested antibacterial drug range represents the percentage of isolates that had MICs less than or equal to the lowest drug concentration tested per year, while numbers above the highest antibacterial drug concentration represent the percentage of isolates that had MICs greater than the highest drug concentration tested that year. Percent MIC frequency rows may not add to 100% due to rounding.

The SRD surveillance program reported herein has continuously obtained swine pathogens for over 15 years from veterinary diagnostic laboratories in North America, that have then been tested for antimicrobial susceptibility. The purpose for this ongoing surveillance study was to summarize the antimicrobial susceptibility profiles of 2940 isolates of four different pathogenic bacterial species associated with SRD collected from laboratories in the United States and Canada over a 5-year period from 2011 to 2015.

To our knowledge, when coupled with our published SRD surveillance data from 2001 to 2010,[4] this is the only surveillance program that has collected and published 15 years of SRD susceptibility data against a total of 9043 isolates from the United States and Canada. Susceptibility data from this ongoing surveillance study may be used as an indicator for the emergence of bacterial resistance, a feature which is found in other antimicrobial susceptibility surveillance programs.[5,13,15] In addition to presenting summarized values such as $MIC_{50}$, $MIC_{90}$, and range values for the antimicrobial drugs, this report also includes the MIC frequencies for all available years in order to provide evidence of potential antimicrobial susceptibility changes among the SRD pathogens collected from 2011 to 2015. The presentation of MIC frequencies allows for the observation of any MIC shifts that may not be reflected with $MIC_{50}$, $MIC_{90}$, or percent susceptibility values.

**Table 3:** Summary of minimal inhibitory concentration (MIC) values and frequency distributions for 10 antimicrobial agents tested with *Pasteurella multocida* (n = 855) isolated from swine in the United States and Canada from 2011 to 2015*

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Ampicillin MIC frequency distribution (% of isolates) ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | | | | | NT | | | | | | | | |
| 2012 | 159 | 0.12 | 0.12 | 98.6 | 32 | 64.2 | 2.5 | 0 | 0 | 0 | 0 | 0 | 1.2 |
| 2013 | 153 | 0.12 | 0.25 | 98 | 19.6 | 67.3 | 11.1 | 0 | 0 | 0 | 0 | 0 | 2 |
| 2014 | 163 | 0.12 | 0.12 | 97.6 | 41.1 | 49.1 | 7.4 | 0 | 0 | 0 | 0.6 | 0 | 1.8 |
| 2015 | 223 | 0.12 | 0.12 | 98.7 | 41.7 | 53.4 | 3.6 | 0 | 0 | 0 | 0 | 0 | 1.3 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Ceftiofur MIC frequency distribution (% of isolates) ≤ 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | ≥ 8 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | 157 | ≤ 0.03 | ≤ 0.03 | 100 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2012 | 159 | ≤ 0.03 | ≤ 0.03 | 100 | 97.4 | 1.3 | 1.3 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2013 | 153 | ≤ 0.03 | ≤ 0.03 | 100 | 90.2 | 3.9 | 5.2 | 0.7 | 0 | 0 | 0 | 0 | 0 |
| 2014 | 163 | ≤ 0.03 | ≤ 0.03 | 100 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2015 | 223 | ≤ 0.03 | ≤ 0.03 | 100 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Danofloxacin MIC frequency distribution (% of isolates) ≤ 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | ≥ 4 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | 157 | ≤ 0.016 | 0.03 | NA | 54.8 | 38.9 | 5.1 | 1.2 | 0 | 0 | 0 | 0 | 0 |
| 2012 | 159 | ≤ 0.016 | 0.03 | NA | 62.9 | 34 | 3.1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2013 | 153 | 0.03 | 0.06 | NA | 42.5 | 46.4 | 11.1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2014 | 163 | ≤ 0.016 | 0.03 | NA | 60.2 | 30.6 | 8 | 0.6 | 0.6 | 0 | 0 | 0 | 0 |
| 2015 | 223 | 0.015 | 0.03 | NA | 53.8 | 42.6 | 3.6 | 0 | 0 | 0 | 0 | 0 | 0 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Enrofloxacin MIC frequency distribution (% of isolates) ≤ 0.008 | 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | ≥ 2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | 157 | 0.016 | 0.03 | 100 | 14.6 | 66.3 | 15.9 | 3.2 | 0 | 0 | 0 | 0 | 0 |
| 2012 | 159 | 0.016 | 0.03 | 100 | 30.2 | 56 | 13.8 | 0 | 0 | 0 | 0 | 0 | 0 |
| 2013 | 153 | 0.016 | 0.03 | 100 | 18.9 | 54.9 | 24.2 | 2 | 0 | 0 | 0 | 0 | 0 |
| 2014 | 163 | ≤ 0.008 | 0.03 | 100 | 57.7 | 31.3 | 7.4 | 3.1 | 0.5 | 0 | 0 | 0 | 0 |
| 2015 | 223 | ≤ 0.008 | 0.016 | 100 | 61.9 | 32.3 | 5.4 | 0.4 | 0 | 0 | 0 | 0 | 0 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Florfenicol MIC frequency distribution (% of isolates) ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | 157 | 0.5 | 0.5 | 100 | 0 | 0.6 | 7.6 | 89.8 | 2 | 0 | 0 | 0 | 0 |
| 2012 | 159 | 0.5 | 0.5 | 100 | 1.3 | 0 | 13.2 | 84.3 | 1.3 | 0 | 0 | 0 | 0 |
| 2013 | 153 | 0.5 | 0.5 | 100 | 0 | 0 | 6.5 | 93.5 | 0 | 0 | 0 | 0 | 0 |
| 2014 | 163 | 0.5 | 0.5 | 100 | 0.6 | 0 | 6.8 | 86.5 | 6.1 | 0 | 0 | 0 | 0 |
| 2015 | 223 | 0.5 | 0.5 | 100 | 0.9 | 0 | 2.2 | 90.6 | 5.8 | 0.5 | 0 | 0 | 0 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Penicillin MIC frequency distribution (% of isolates) ≤ 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | ≥ 32 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2011 | 157 | ≤ 0.12 | ≤ 0.12 | 99.4 | 91.8 | 7.6 | 0 | 0 | 0 | 0.6 | 0 | 0 | 0 |
| 2012 | 159 | ≤ 0.12 | ≤ 0.12 | 98.8 | 98.2 | 0.6 | 0 | 0 | 0 | 0 | 0 | 0.6 | 0.6 |
| 2013 | 153 | ≤ 0.12 | ≤ 0.12 | 98.1 | 93.5 | 4.6 | 0 | 0 | 0 | 0 | 0 | 0 | 1.9 |
| 2014 | 163 | ≤ 0.12 | ≤ 0.12 | 97.6 | 95.8 | 1.8 | 0 | 0 | 0 | 0 | 0.6 | 0 | 1.8 |
| 2015 | 223 | ≤ 0.12 | ≤ 0.12 | 98.6 | 98.6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1.4 |

**Table 3:** Continued

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tetracycline MIC frequency distribution (% of isolates) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≤ 16 |
| 2011 | 157 | 2 | ≤ 16 | 28.7 | 1.9 | 26.8 | 15.3 | 33.1 | 6.4 | 1.2 | 15.3 |
| 2012 | 159 | 2 | ≥ 16 | 35.3 | 5.7 | 29.6 | 12 | 27 | 2.5 | 3.1 | 20.1 |
| 2013 | 153 | 2 | ≥ 16 | 22.3 | 0.7 | 21.6 | 10.5 | 42.4 | 2.6 | 2 | 20.2 |
| 2014 | 163 | 2 | ≥ 16 | 27.6 | 5.5 | 22.1 | 13.5 | 35.6 | 4.3 | 3.7 | 15.3 |
| 2015 | 223 | 2 | ≥ 16 | 31.4 | 1.4 | 30 | 5.4 | 39 | 3.6 | 2.2 | 18.4 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tilmicosin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | ≥ 64 |
| 2011 | 157 | 4 | 16 | 100 | 0 | 0 | 3.2 | 19.8 | 38.2 | 24.8 | 14 | 0 | 0 |
| 2012 | 159 | 4 | 8 | 97.5 | 1.3 | 0 | 1.9 | 18.9 | 39.6 | 28.9 | 6.9 | 0.6 | 1.9 |
| 2013 | 153 | 4 | 16 | 99.3 | 0 | 0 | 2.6 | 18.3 | 44.4 | 21.6 | 12.4 | 0 | 0.7 |
| 2014 | 163 | 4 | 16 | 98.2 | 0 | 0 | 5.5 | 9.2 | 36.8 | 24.5 | 22.1 | 0.6 | 1.2 |
| 2015 | 223 | 8 | 16 | 97.8 | 0 | 0.4 | 0.9 | 8.5 | 38.1 | 29.6 | 20.2 | 2.2 | 0 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | TMP-SMX MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | 157 | ≤ 0.06 | 0.12 | NA | 75.8 | 17.2 | 4.5 | 0.6 | 0.6 | 1.3 | 0 | 0 | 0 |
| 2012 | 159 | ≤ 0.06 | 0.12 | NA | 68.6 | 27 | 3.8 | 0.6 | 0 | 0 | 0 | 0 | 0 |
| 2013 | 153 | ≤ 0.06 | 0.25 | NA | 69.3 | 19.6 | 7.8 | 1.3 | 0 | 0 | 0 | 0 | 2 |
| 2014 | 163 | ≤ 0.06 | 0.12 | NA | 73.6 | 20.3 | 4.3 | 1.2 | 0.6 | 0 | 0 | 0 | 0 |
| 2015 | 223 | ≤ 0.06 | 0.12 | NA | 62.3 | 30.9 | 4 | 1.3 | 0 | 0.4 | 0 | 0 | 1 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tulathromycin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | ≥ 128 |
| 2011 | 157 | 2 | 4 | 100 | 6.4 | 24.2 | 44.6 | 15.2 | 9.6 | 0 | 0 | 0 | 0 |
| 2012 | 159 | 1 | 2 | 98.8 | 24.5 | 32.1 | 35.2 | 6.9 | 0 | 0 | 0.6 | 0.6 | 0 |
| 2013 | 153 | 1 | 2 | 100 | 13.7 | 49 | 30.1 | 7.2 | 0 | 0 | 0 | 0 | 0 |
| 2014 | 163 | 2 | 4 | 100 | 11.7 | 31.3 | 30.7 | 22.7 | 3.7 | 0 | 0 | 0 | 0 |
| 2015 | 223 | 2 | 4 | 100 | 6.7 | 22.9 | 38.1 | 28.7 | 3.5 | 0 | 0 | 0 | 0 |

* No. = the number of isolates tested per year; $MIC_{50}$ = antibacterial drug concentration that inhibits 50% of the bacterial population; $MIC_{90}$ = antibacterial drug concentration that inhibits 90% of the bacterial population; %S = the percentage of isolates that are susceptible to the antibacterial drug using Clinical and Laboratory Standards Institute (CLSI) criteria; NA = not applicable since there are no CLSI-approved clinical breakpoints for susceptibility in that swine respiratory disease pathogen; NT = not tested; vertical bold lines indicate the CLSI-approved breakpoint for susceptible, intermediate, and resistant in that swine respiratory disease pathogen; TMP-SMX = trimethoprim-sulfamethoxazole; numbers in the lowest concentration of the tested antibacterial drug range represent the percentage of isolates that had MICs less than or equal to the lowest drug concentration tested per year, while numbers above the highest antibacterial drug concentration represent the percentage of isolates that had MICs greater than the highest drug concentration tested that year. Percent MIC frequency rows may not add to 100% due to rounding.

Retrospective studies have been published that investigated the antimicrobial susceptibility of *A pleuropneumoniae* isolates from swine. Archambault et al[16] reported the antimicrobial susceptibilities of 43 isolates of *A pleuropneumoniae* from Canada in which all isolates were 100% susceptible to ceftiofur, florfenicol, enrofloxacin, erythromycin, clindamycin, TMP-SMX, and tilmicosin, but reported a low level of susceptibility to chlortetracycline and oxytetracycline (11.6% and 9.3% susceptibility, respectively). A study by Vanni et al[17] also showed high antimicrobial susceptibility for 992 isolates of *A pleuropneumoniae* to amphenicols, fluoroquinolones, and ceftiofur, while low rates of susceptibility were observed for tetracycline (< 17%) and penicillin (< 15%). El Garch et al[18] reported the susceptibilities of 158 *A pleuropneumoniae* isolates isolated from pigs in 2009 to 2012 that showed 100% susceptibility to amoxicillin-clavulanate, ceftiofur, tiamulin, and tulathromycin with 96% to > 99% susceptibility to enrofloxacin, florfenicol, and tilmicosin, while tetracycline susceptibility was reported at 70%. Finally, Dayao et al[14] reported 100% susceptibility to ceftiofur, florfenicol, and tulathromycin for 71 isolates. Susceptibility data for *A pleuropneumoniae* from our 2001 to 2010 SRD surveillance program reported 100% susceptibility to ceftiofur, florfenicol, and tulathromycin.[4]The high susceptibility rates

**Table 4:** Summary of minimal inhibitory concentration (MIC) values and frequency distributions for 10 antimicrobial agents tested with *Streptococcus suis* (n = 1201) isolated from swine in the United States and Canada from 2011 to 2015*

| Year | No. | $MIC_{50}$ (µ/mL) | $MIC_{90}$ (µg/mL) | %S | Ampicillin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | | | | | | | NT | | | | | | |
| 2012 | 205 | ≤ 0.03 | 0.12 | 98.6 | 86.9 | 7.3 | 4.4 | 0 | 0 | 0.5 | 0.5 | 0.5 | 0 |
| 2013 | 235 | ≤ 0.03 | 0.12 | 98 | 83.4 | 8.1 | 5.5 | 0.9 | 0.9 | 0.8 | 0.4 | 0 | 0 |
| 2014 | 234 | ≤ 0.03 | 0.12 | 99.2 | 88.9 | 6.8 | 3 | 0.4 | 0.9 | 0 | 0 | 0 | 0 |
| 2015 | 301 | ≤ 0.03 | 0.12 | 99.1 | 89.4 | 6 | 3 | 0.6 | 0.3 | 0.3 | 0 | 0.3 | 0 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Ceftiofur MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | ≥ 8 |
| 2011 | 226 | 0.12 | 1 | 96.5 | 15 | 34.5 | 20.4 | 7.1 | 11.1 | 6.2 | 2.2 | 2.2 | 1.3 |
| 2012 | 205 | 0.12 | 1 | 96.6 | 9.3 | 35.1 | 26.3 | 3.9 | 8.8 | 8.8 | 4.4 | 1 | 2.5 |
| 2013 | 235 | 0.12 | 2 | 93.6 | 38.3 | 20.9 | 7.2 | 8.1 | 10.6 | 8.5 | 3 | 1.3 | 2.1 |
| 2014 | 234 | 0.12 | 1 | 96.2 | 5.1 | 37.6 | 32.1 | 5.6 | 4.7 | 6 | 5.1 | 1.3 | 2.5 |
| 2015 | 301 | 0.12 | 1 | 93.9 | 6.3 | 36.2 | 28.9 | 5.3 | 7.6 | 7.3 | 2.3 | 0.7 | 5.4 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Danofloxacin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.015 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | ≥ 4 |
| 2011 | 226 | 0.5 | 1 | NA | 0 | 0 | 1.3 | 3.1 | 21.2 | 52.7 | 18.1 | 2.2 | 1.4 |
| 2012 | 205 | 0.5 | 1 | NA | 0 | 0 | 0.5 | 4.4 | 22.4 | 52.7 | 18 | 2 | 0 |
| 2013 | 235 | 0.5 | 1 | NA | 0 | 0 | 0.9 | 2.1 | 16.2 | 51.9 | 23.8 | 2.6 | 2.6 |
| 2014 | 234 | 0.5 | 1 | NA | 0 | 0 | 0.9 | 3.8 | 13.2 | 62.4 | 16.2 | 2.1 | 1.3 |
| 2015 | 301 | 0.5 | 1 | NA | 0.3 | 0.3 | 0.3 | 2.3 | 10.6 | 59.1 | 25.3 | 0.3 | 1.3 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Enrofloxacin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.008 | 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | ≥ 2 |
| 2011 | 226 | 0.5 | 1 | 82.3 | 0 | 0 | 0 | 1.8 | 6.6 | 23.5 | 50.4 | 15 | 2.7 |
| 2012 | 205 | 0.5 | 1 | 84 | 0 | 0 | 0 | 0.5 | 5.4 | 25.4 | 52.7 | 13.6 | 2.4 |
| 2013 | 235 | 0.5 | 1 | 84.3 | 0 | 0 | 0.4 | 0.4 | 5.5 | 30.6 | 47.2 | 11.2 | 4.7 |
| 2014 | 234 | 0.5 | 0.5 | 95.3 | 0 | 0 | 0.4 | 0.9 | 8.1 | 39.7 | 46.2 | 3.4 | 1.3 |
| 2015 | 301 | 0.5 | 0.5 | 94 | 0 | 0 | 0.3 | 0.7 | 7.3 | 33.2 | 52.5 | 4.7 | 1.3 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Florfenicol MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | 226 | 2 | 2 | 99.1 | 0 | 0.4 | 0 | 6.6 | 42.5 | 49.6 | 0.9 | 0 | 0 |
| 2012 | 205 | 2 | 2 | 100 | 0 | 0 | 0 | 3.9 | 34.6 | 61.5 | 0 | 0 | 0 |
| 2013 | 235 | 2 | 2 | 99.6 | 0 | 0 | 0.4 | 3 | 33.2 | 63 | 0.4 | 0 | 0 |
| 2014 | 234 | 2 | 2 | 97.9 | 0 | 0 | 0.4 | 3.4 | 27.4 | 66.7 | 2.1 | 0 | 0 |
| 2015 | 301 | 2 | 2 | 97.1 | 0 | 0 | 0 | 2.7 | 20.9 | 73.5 | 2.3 | 0 | 0.6 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Penicillin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | ≥ 32 |
| 2011 | 226 | ≤ 0.12 | 1 | 84 | 80.5 | 3.5 | 2.7 | 4 | 4.9 | 4 | 0 | 0.4 | 0 |
| 2012 | 205 | ≤ 0.12 | 1 | 81.5 | 77.6 | 3.9 | 3.9 | 5.4 | 3.4 | 4.4 | 1 | 0.5 | 0 |
| 2013 | 235 | ≤ 0.12 | 2 | 73.6 | 69.8 | 3.8 | 5.1 | 6.8 | 6.8 | 5.5 | 1.3 | 0.9 | 0 |
| 2014 | 234 | ≤ 0.12 | 2 | 82.1 | 79.5 | 2.6 | 3 | 3.8 | 4.8 | 3.8 | 1.7 | 0.4 | 0.4 |
| 2015 | 301 | ≤ 0.12 | 2 | 80.1 | 75.8 | 4.3 | 5.6 | 3.7 | 3 | 5.6 | 1.7 | 0 | 0.3 |

**Table 4:** Continued

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tetracycline MIC frequency distribution (% of isolates) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | 226 | ≥ 16 | ≥ 16 | 0.8 | 0.4 | 0.4 | 0 | 0 | 3.2 | 1.8 | 94.2 |
| 2012 | 205 | ≥ 16 | ≥ 16 | 0 | 0 | 0 | 2 | 0.5 | 1.5 | 1.5 | 94.5 |
| 2013 | 235 | ≥ 16 | ≥ 16 | 1.3 | 1.3 | 0 | 0.9 | 2.1 | 1.7 | 0.9 | 93.1 |
| 2014 | 234 | ≥ 16 | ≥ 16 | 1.3 | 0.4 | 0.9 | 0 | 0.9 | 2.6 | 0.9 | 94.3 |
| 2015 | 301 | ≥ 16 | ≥ 16 | 0 | 0 | 0 | 0.3 | 1 | 2.7 | 1.7 | 94.3 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tilmicosin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | ≥ 64 |
| 2011 | 226 | ≥ 64 | ≥ 64 | NA | 1.8 | 0 | 3.5 | 16.8 | 2.7 | 0.9 | 0 | 0 | 74.3 |
| 2012 | 205 | ≥ 64 | ≥ 64 | NA | 1.5 | 2.4 | 7.8 | 10.7 | 1 | 0.5 | 0 | 0 | 76.1 |
| 2013 | 235 | ≥ 64 | ≥ 64 | NA | 1.3 | 0 | 0 | 0.9 | 10.6 | 13.6 | 0.4 | 0 | 73.2 |
| 2014 | 234 | ≥ 64 | ≥ 64 | NA | 0 | 0 | 0.4 | 0.4 | 14.5 | 6.8 | 0 | 0 | 77.9 |
| 2015 | 301 | ≥ 64 | ≥ 64 | NA | 0 | 0.3 | 0 | 0.7 | 7 | 9.6 | 0.7 | 0 | 81.7 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | TMP-SMX MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | 226 | ≤ 0.06 | 0.12 | NA | 86.7 | 8.4 | 1.3 | 1.3 | 1.8 | 0 | 0 | 0.4 | 0 |
| 2012 | 205 | ≤ 0.06 | 0.12 | NA | 86.8 | 10.2 | 2 | 0.5 | 0 | 0.5 | 0 | 0 | 0 |
| 2013 | 235 | ≤ 0.06 | 0.25 | NA | 63 | 25.1 | 3 | 2.1 | 2.6 | 0.9 | 0.9 | 0.4 | 2.1 |
| 2014 | 234 | ≤ 0.06 | 0.12 | NA | 83 | 9.4 | 1.3 | 0.9 | 1.7 | 0.9 | 0.4 | 0.4 | 2 |
| 2015 | 301 | ≤ 0.06 | 0.12 | NA | 73.8 | 17.6 | 3.3 | 0 | 1 | 0 | 1.3 | 0.3 | 2.7 |

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tulathromycin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | ≥ 128 |
| 2011 | 226 | ≥ 128 | ≥ 128 | NA | 15.5 | 6.2 | 3.1 | 0.4 | 0.9 | 0.9 | 1.8 | 5.7 | 65.5 |
| 2012 | 205 | ≥ 128 | ≥ 128 | NA | 18.5 | 4.9 | 0.5 | 0 | 2 | 2 | 3.9 | 12.7 | 55.6 |
| 2013 | 235 | ≥ 128 | ≥ 128 | NA | 1.7 | 3 | 8.9 | 13.2 | 0.9 | 0 | 0.4 | 1.3 | 70.6 |
| 2014 | 234 | ≥ 128 | ≥ 128 | NA | 1.3 | 3 | 9.8 | 8.6 | 0 | 0 | 1.3 | 3.4 | 72.6 |
| 2015 | 301 | ≥ 128 | ≥ 128 | NA | 0.6 | 1.3 | 5.3 | 10.3 | 0.7 | 0.3 | 0.3 | 2.7 | 78.4 |

* No. = the number of isolates tested per year; $MIC_{50}$ = antibacterial drug concentration that inhibits 50% of the bacterial population; $MIC_{90}$ = antibacterial drug concentration that inhibits 90% of the bacterial population; %S = the percentage of isolates that are susceptible to the antibacterial drug using Clinical and Laboratory Standards Institute (CLSI) criteria; NA = not applicable since there are no CLSI-approved clinical breakpoints for susceptibility in that swine respiratory disease pathogen; NT = not tested; vertical bold lines indicate the CLSI-approved breakpoint for susceptible, intermediate, and resistant in that swine respiratory disease pathogen; TMP-SMX = trimethoprim-sulfamethoxazole; numbers in the lowest concentration of the tested antibacterial drug range represents the percentage of isolates that had MICs less than or equal to the lowest drug concentration tested per year, while numbers above the highest antibacterial drug concentration represent the percentage of isolates that had MICs greater than the highest drug concentration tested that year. Percent MIC frequency rows may not add to 100% due to rounding.

from these reports are consistent with observations reported herein in which 100% susceptibility to ceftiofur and florfenicol, high levels of susceptibility (> 90% to 100%) to enrofloxacin and tulathromycin, and low levels of susceptibility (0% to 6%) to tetracycline were observed for 312 isolates of *A pleuropneumoniae* from 2011 to 2015. Additionally, the $MIC_{90}$ values for ceftiofur (≤ 0.06 µg per mL) and florfenicol (0.5 µg per mL) with *A pleuropneumoniae* have remained well below the susceptible breakpoints since 2001.[4]

For *P multocida* isolated from swine, Glass-Kaastra et al[19] published results on 1464 isolates collected from 1998 to 2010 in which susceptibility to ampicillin remained high from 1998 to 2007, with slightly decreased susceptibility from 2007 to 2010, while tetracycline susceptibility ranged from 60% to 90%. Dayao et al[14] reported 100% susceptibility to ceftiofur, tilmicosin, and tulathromycin for 51 isolates, and El Garch et al[18] reported 100% susceptibility for 152 *P multocida* isolates from pigs to amoxicillin-clavulanate, ceftiofur, enrofloxacin, and tulathromycin and 65.8% susceptibility to tetracycline. Susceptibility data for 2001 to 2010[4] from our SRD surveillance program reported 100% susceptibility to ceftiofur with high rates of susceptibility (> 90% to 100%) to enrofloxacin, florfenicol, tilmicosin, and tulathromycin. This current report shows 100% susceptibility

**Table 5:** Summary of minimal inhibitory concentration (MIC) values and frequency distributions for 10 antimicrobial agents tested with *Bordetella bronchiseptica* (n = 572) isolated from swine in the United States and Canada from 2011 to 2015*

| | | | | | Ampicillin MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | | | | | | | NT | | | | | | |
| 2012 | 103 | ≥ 16 | ≥ 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2.9 | 96.1 |
| 2013 | 112 | ≥ 16 | ≥ 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6.3 | 93.7 |
| 2014 | 116 | ≥ 16 | ≥ 16 | 0 | 0 | 0 | 0 | 0 | 0 | 1.7 | 0.9 | 3.5 | 93.9 |
| 2015 | 139 | ≥ 16 | ≥ 16 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2.2 | 4.3 | 93.6 |
| | | | | | Ceftiofur MIC frequency distribution (% of isolates) | | | | | | | | |
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | ≥ 8 |
| 2011 | 102 | ≥ 8 | ≥ 8 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 |
| 2012 | 103 | ≥ 8 | ≥ 8 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 |
| 2013 | 112 | ≥ 8 | ≥ 8 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 |
| 2014 | 116 | ≥ 8 | ≥ 8 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 |
| 2015 | 139 | ≥ 8 | ≥ 8 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 |
| | | | | | Danofloxacin MIC frequency distribution (% of isolates) | | | | | | | | |
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.015 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | ≥ 4 |
| 2011 | 102 | 1 | 1 | NA | 0 | 0 | 0 | 0 | 2 | 20.6 | 77.4 | 0 | 0 |
| 2012 | 103 | 1 | 1 | NA | 0 | 0 | 0 | 0 | 2 | 18.4 | 79.6 | 0 | 0 |
| 2013 | 112 | 1 | 1 | NA | 0 | 0 | 0 | 0 | 4.5 | 7.1 | 87.5 | 0.9 | 0 |
| 2014 | 116 | 1 | 1 | NA | 0.9 | 0 | 0.9 | 0 | 2.6 | 17.2 | 78.5 | 0 | 0 |
| 2015 | 139 | 1 | 1 | NA | 0 | 0 | 0 | 0 | 5.8 | 7.2 | 87 | 0 | 0 |
| | | | | | Enrofloxacin MIC frequency distribution (% of isolates) | | | | | | | | |
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.008 | 0.016 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | ≥ 2 |
| 2011 | 102 | 0.5 | 1 | NA | 0 | 0 | 0 | 0 | 0 | 2.9 | 56.9 | 40.2 | 0 |
| 2012 | 103 | 0.5 | 0.5 | NA | 0 | 0 | 0 | 0 | 0 | 2.9 | 87.4 | 9.7 | 0 |
| 2013 | 112 | 0.5 | 1 | NA | 0 | 0 | 0 | 0 | 0.9 | 5.4 | 63.4 | 30.3 | 0 |
| 2014 | 116 | 0.5 | 1 | NA | 0.9 | 0 | 0 | 0.9 | 4.3 | 1.7 | 82 | 10.3 | 0 |
| 2015 | 139 | 0.5 | 1 | NA | 0 | 0 | 0 | 0 | 4.3 | 5 | 77.7 | 13 | 0 |
| | | | | | Florfenicol MIC frequency distribution (% of isolates) | | | | | | | | |
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | 102 | 4 | 4 | 23.5 | 0 | 0 | 0 | 0 | 4.9 | 18.6 | 74.5 | 2 | 0 |
| 2012 | 103 | 4 | 4 | 14.5 | 0 | 0 | 0 | 0 | 1.9 | 12.6 | 83.5 | 2 | 0 |
| 2013 | 112 | 4 | 4 | 5.4 | 0 | 0 | 0 | 0 | 0 | 5.4 | 94.6 | 0 | 0 |
| 2014 | 116 | 4 | 4 | 11.2 | 0 | 0 | 0 | 0 | 0 | 11.2 | 88.8 | 0 | 0 |
| 2015 | 139 | 4 | 4 | 7.9 | 0 | 0 | 0 | 0 | 0 | 7.9 | 84.2 | 7.2 | 0 |
| | | | | | Penicillin MIC frequency distribution (% of isolates) | | | | | | | | |
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | ≤ 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | ≥ 32 |
| 2011 | 102 | ≥ 32 | ≥ 32 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 |
| 2012 | 103 | ≥ 32 | ≥ 32 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 |
| 2013 | 112 | ≥ 32 | ≥ 32 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 |
| 2014 | 116 | ≥ 32 | ≥ 32 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1.7 | 98.3 |
| 2015 | 139 | ≥ 32 | ≥ 32 | NA | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.7 | 99.3 |

**Table 5:** Continued

| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tetracycline MIC frequency distribution (% of isolates) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | ≤ 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | ≥ 64 |
| 2011 | 102 | 1 | 2 | NA | 4.9 | 42.2 | 38.2 | 8.8 | 4.9 | 0 | 1 | 0 | 0 |
| 2012 | 103 | 0.5 | 2 | NA | 7.8 | 51.5 | 29.1 | 4.8 | 4.8 | 0 | 1.9 | 0 | 0 |
| 2013 | 112 | 1 | 4 | NA | 0 | 6.3 | 75 | 8 | 8 | 0 | 2.7 | 0 | 0 |
| 2014 | 116 | 0.5 | 2 | NA | 0 | 59.5 | 25 | 12.1 | 2.6 | 0 | 0.9 | 0 | 0 |
| 2015 | 139 | 1 | 2 | NA | 0 | 45.3 | 44.6 | 7.9 | 1.4 | 0 | 0.7 | 0 | 0 |
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tilmicosin MIC frequency distribution (% of isolates) | | | | | | | | |
| | | | | | ≤ 0.25 | 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | ≥ 64 |
| 2011 | 102 | 32 | ≥ 64 | NA | 0 | 0 | 0 | 0 | 0 | 2 | 14.7 | 68.6 | 14.7 |
| 2012 | 103 | 32 | 32 | NA | 0 | 0 | 0 | 0 | 1 | 1 | 13.6 | 77.6 | 6.8 |
| 2013 | 112 | 32 | ≥ 64 | NA | 0 | 0 | 0 | 0 | 0 | 4.5 | 9.8 | 63.4 | 22.3 |
| 2014 | 116 | 32 | ≥ 64 | NA | 0 | 0 | 0 | 0 | 0.9 | 6.9 | 8.6 | 56 | 27.6 |
| 2015 | 139 | 32 | ≥ 64 | NA | 0 | 0 | 0 | 0 | 0.7 | 5 | 2.9 | 48.2 | 43.2 |
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | TMP-SMX MIC frequency distribution (% of isolates) | | | | | | | | |
| | | | | | ≤ 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | 8 | ≥ 16 |
| 2011 | 102 | 8 | 8 | NA | 6.9 | 1.9 | 3.9 | 0 | 0 | 12.7 | 21.6 | 48 | 4.9 |
| 2012 | 103 | 8 | 8 | NA | 10.7 | 0 | 1 | 0 | 1.9 | 4.8 | 24.3 | 47.6 | 9.7 |
| 2013 | 112 | 8 | ≥ 16 | NA | 7.1 | 1.8 | 0 | 0 | 0 | 3.6 | 6.3 | 43.8 | 37.4 |
| 2014 | 116 | 8 | ≥ 16 | NA | 7.8 | 0 | 0.9 | 0 | 0.9 | 4.3 | 21.6 | 47.4 | 17.1 |
| 2015 | 139 | 8 | ≥ 16 | NA | 5 | 0 | 0 | 0 | 0.7 | 4.3 | 8.6 | 71.9 | 9.4 |
| Year | No. | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) | %S | Tulathromycin MIC frequency distribution (% of isolates) | | | | | | | | |
| | | | | | ≤ 0.5 | 1 | 2 | 4 | 8 | 16 | 32 | 64 | ≥ 128 |
| 2011 | 102 | 8 | 16 | 100 | 0 | 0 | 2 | 2.9 | 54.9 | 40.2 | 0 | 0 | 0 |
| 2012 | 103 | 8 | 8 | 99 | 0 | 0 | 2.9 | 22.3 | 70.9 | 2.9 | 1 | 0 | 0 |
| 2013 | 112 | 8 | 8 | 99.1 | 0 | 0.9 | 4.5 | 19.6 | 71.4 | 2.7 | 0.9 | 0 | 0 |
| 2014 | 116 | 8 | 8 | 100 | 0 | 0.9 | 12.1 | 6.9 | 73.3 | 6.9 | 0 | 0 | 0 |
| 2015 | 139 | 8 | 16 | 100 | 1.4 | 2.2 | 2.9 | 3.6 | 71.2 | 18.7 | 0 | 0 | 0 |

* No. = the number of isolates tested per year; $MIC_{50}$ = antibacterial drug concentration that inhibits 50% of the bacterial population; $MIC_{90}$ = antibacterial drug concentration that inhibits 90% of the bacterial population; %S = the percentage of isolates that are susceptible to the antibacterial drug using Clinical and Laboratory Standards Institute (CLSI) criteria; NA = not applicable since there are no CLSI-approved clinical breakpoints for susceptibility in that swine respiratory disease pathogen; NT = not tested; vertical bold lines indicate the CLSI-approved breakpoint for susceptible, intermediate, and resistant in that swine respiratory disease pathogen; TMP-SMX = trimethoprim-sulfamethoxazole; numbers in the lowest concentration of the tested antibacterial drug range represent the percentage of isolates that had MICs less than or equal to the lowest drug concentration tested per year, while numbers above the highest antibacterial drug concentration represent the percentage of isolates that had MICs greater than the highest drug concentration tested that year. Percent MIC frequency rows may not add to 100% due to rounding.

to ceftiofur, enrofloxacin, and florfenicol, and high levels of susceptibility (> 90% to 100%) to ampicillin, penicillin, tilmicosin, and tulathromycin, with low levels of susceptibility (22.3% to 35.3%) to tetracycline for 855 *P multocida* isolates from 2011 to 2015. The $MIC_{90}$ values for ceftiofur (≤ 0.03 µg per mL), enrofloxacin (≤ 0.03 µg per mL), and florfenicol (0.5 µg per mL) have also remained well below the susceptible breakpoints since 2001.[4]

Numerous studies have been published on the susceptibility of *S suis* to antimicrobial agents.[19-21] Additionally, Callens et al[22] reported on the antimicrobial susceptibility to nine antimicrobial agents for *S suis* isolated from healthy pigs in which low rates of susceptibility (5%) were reported for tetracycline, and high rates of susceptibility were reported for florfenicol (99.7%) and enrofloxacin (99.7% ). El Garch et al[18] reported high susceptibility (96% to100%) to amoxicillin-clavulanate, ceftiofur, enrofloxacin, and florfenicol and 4% susceptibility to tetracycline when tested against 151 isolates of *S suis*. Susceptibility data from our 2001-2010 SRD surveillance program reported high rates of susceptibility (> 90% to 100%) to ceftiofur and florfenicol,[4] and this current report shows high levels of susceptibility (> 90% to 100%) to ampicillin, ceftiofur, and florfenicol, with low levels of susceptibility (0% to 1.3%) to tetracycline against 1201 *S suis* isolates from 2011 to 2015.

For *B bronchiseptica*, Dayao et al[14] reported 100% susceptibility to tulathromycin for 18 isolates, while El Garch et al[18] reported high susceptibility to amoxicillin-clavulanate (95.8%) and tulathromycin (99.2%) and lower susceptibility to florfenicol (52.5%) for 118 isolates. The inclusion of *B bronchiseptica* into this surveillance program did not occur until 2009. Three antimicrobial drugs used in this study have established CLSI clinical breakpoints for *B bronchiseptica* including ampicillin, florfenicol, and tulathromycin. For this study, 99% to 100% susceptibility to tulathromycin was observed, while no susceptibility (0%) to ampicillin and low susceptibility (5.4% to 23.5%) to florfenicol were observed against 572 *B bronchiseptica* isolates from 2011 to 2015.

A number of authors have highlighted the challenges of surveillance programs and the potential biases that may be encountered.[6,23,24] While there is no "gold standard" for evaluating the antimicrobial surveillance of animal pathogens, a report is available that offers guidance on areas in which harmonization can be achieved in veterinary antimicrobial surveillance programs with the intent of facilitating comparison of data among surveillance programs.[25] All surveillance studies still have certain biases and limitations to consider when interpreting susceptibility data. For this current study, 2940 clinical isolates were collected from 2011 to 2015 and analyzed, but this number of clinical isolates is still small when considering the number of cases of SRD in North America over the last 5 years. As the isolates in this current study originated from many veterinary diagnostic laboratories, the methods of sample selection, collection, and submission varied among laboratories. To help decrease regional sampling bias in this study, the number of isolates of a target species from any herd was restricted to one isolate during any quarter year period.[4] However, the number of isolates submitted by each participating laboratory was different per year, and not all enrolled laboratories may have actually submitted isolates for susceptibility testing. The design of the survey, including limits on the number of isolates collected within a given time period from a single herd and from a single diagnostic laboratory, can help reduce but not eliminate selection bias. The use of just two laboratories to perform the MIC testing minimized potential testing bias, and both laboratories adhered strictly to standard microbiological methods for veterinary susceptibility testing and quality-control standards published by CLSI. Finally, biases reported in other programs, such as a passive surveillance design, non-consideration in differences between livestock farm types and sizes, or prior treatment of animals with antibacterial agents, are acknowledged in this and other studies.[4,5] Furthermore, the lack of clinical breakpoints or interpretive criteria for certain antibacterial agents against pathogens to determine rates of susceptibility continue to be a limitation to veterinary surveillance. A greater collaborative effort among academic and industrial veterinary groups should be made to identify what gaps exist for available breakpoints and then establish CLSI-endorsed clinical breakpoints as long as a standardized approach is used.

The interpretation of MIC values from this study relies on clinical breakpoints to predict a potential susceptible, intermediate, or resistant outcome for use of an antibacterial agent to treat an infection.[8] The category of "susceptible" implies that an infection due to a bacterial pathogen may be susceptible to treatment with an antibacterial agent, taking into consideration the dosage regimen; the "intermediate" category implies that an infection due to a bacterial pathogen may be susceptible to treatment where the agent is physiologically concentrated and serves as a buffer zone against technical factors that may cause discrepancies in interpretation; the "resistant" category implies that resistant strains are not inhibited by the achievable concentrations of an antibacterial agent and resistance mechanisms are likely present within the pathogen.[8] In establishing veterinary-specific clinical breakpoints, a tripartite database, including minimal inhibitory concentration distribution data, pharmacokinetic-pharmacodynamic data, and clinical outcome data, are considered. It should be kept in mind that the purpose of antimicrobial susceptibility testing is not to mimic in vivo conditions, but to establish a method that provides reproducible results that may be correlated to clinical outcome, and that the in vitro antibacterial activity of an antimicrobial agent is only one component to consider for the likelihood of overall clinical efficacy in which pharmacokinetics and drug dosage also play a major role.[26] Additionally, other factors, such as health status of the animal, virulence factors of a pathogen, co-infections, stage of respiratory disease, and time point of antibacterial drug administration, among many other variables, must also be considered regarding clinical outcome by the attending veterinarian.[27]

The data presented from this current study, especially data that show a continued lack of susceptibility to certain antimicrobial agents such as tetracycline, should serve to underscore the importance of prudent use of these drugs when treating SRD. Although tetracycline has traditionally served as the "class representative" agent for in vitro susceptibility testing for veterinary tetracyclines, extrapolation of tetracycline susceptibility results may not necessarily be predictive of activity or clinical outcome for other tetracycline agents, such as oxytetracycline or chlortetracycline, due to differences in blood and lung-tissue concentrations and differences in bioavailability. Even though there are CLSI-established clinical breakpoints for tetracycline that were used in evaluating data in this study, it should be pointed out that these breakpoint values were derived partly from oxytetracycline pharmacokinetic data.[9]

The high levels of antimicrobial susceptibility observed in this study and others may be attributed to specific health management practices within swine herds, such as the "all-in, all-out" management practice system. This practice involves the commingling of pigs of similar age and weight, as well as group housing and pen cleaning between housing episodes, among other key components, and has been successful in combating the spread of certain infectious diseases.[28] Future studies may be able to determine if this management practice has an effect on antibiotic resistance changes over time, and if resistance reduction can be achieved through alternations in further enhanced housing and cleaning practices. Additionally, a pragmatic variation of the "all-in, all-out" model may represent an opportunity for other livestock practices to follow, especially since rates of antimicrobial resistance among cattle respiratory pathogens appear to be higher than those among swine respiratory pathogens.[4,29]

The results of this surveillance study using standardized susceptibility testing methods show high percentages of antimicrobial susceptibility among the major respiratory tract pathogens isolated from swine across the United States and Canada, except for tetracycline, and results from this 5-year SRD surveillance study are similar to those previously published.[4] This surveillance study continues to be useful in identifying the development of antimicrobial resistance among SRD target pathogens, which is crucial for the prudent use of antimicrobial agents in veterinary medicine.

Additionally, understanding the in vitro susceptibility of SRD pathogens isolated in the United States and Canada continues to be an important component of antimicrobial stewardship. Even though this study shows high rates of susceptibility for antimicrobial agents against SRD pathogens, public perceptions, as well as regulatory pressures, continue to drive the need for newer, alternative treatment options which may include novel antibacterial classes, re-evaluation of older or discontinued antibacterial agents, posology, and alternative approaches such as bacteriophages and peptides.[30]

## Implications

- Key antimicrobial agents approved for treatment of SRD in the United States and Canada have high rates of susceptibility for *A pleuropneumoniae, P multocida, S suis,* and *B bronchiseptica*.
- Under the conditions of this study, the lowest rates of susceptibility are seen with tetracycline against *A pleuropneumoniae, P multocida,* and *S suis,* and with ampicillin and florfenicol against *B bronchiseptica*.
- Continuous monitoring of antimicrobial susceptibility among swine pathogens provides up-to-date information about susceptibility trends for commonly used antimicrobial agents and is an important component of responsible use and antimicrobial stewardship.


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### Conflict of interest

Authors MTS, CL, LJ, LM, MKS, RM, SFK, RT, and JLW were employed by Zoetis; and authors DB and CM were employed by Microbial Research, Inc, at the time this study was being planned and performed.

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* Non-refereed references.

# Conversion tables

**Weights and measures conversions**

| Common (US) | Metric | To convert | Multiply by |
|---|---|---|---|
| 1 oz | 28.35 g | oz to g | 28.4 |
| 1 lb (16 oz) | 453.59 g | lb to kg | 0.45 |
| 2.2 lb | 1 kg | kg to lb | 2.2 |
| 1 in | 2.54 cm | in to cm | 2.54 |
| 0.39 in | 1 cm | cm to in | 0.39 |
| 1 ft (12 in) | 0.31 m | ft to m | 0.3 |
| 3.28 ft | 1 m | m to ft | 3.28 |
| 1 mi | 1.6 km | mi to km | 1.6 |
| 0.62 mi | 1 km | km to mi | 0.62 |
| 1 $in^2$ | 6.45 $cm^2$ | $in^2$ to $cm^2$ | 6.45 |
| 0.16 $in^2$ | 1 $cm^2$ | $cm^2$ to $in^2$ | 0.16 |
| 1 $ft^2$ | 0.09 $m^2$ | $ft^2$ to $m^2$ | 0.09 |
| 10.76 $ft^2$ | 1 $m^2$ | $m^2$ to $ft^2$ | 10.8 |
| 1 $ft^3$ | 0.03 $m^3$ | $ft^3$ to $m^3$ | 0.03 |
| 35.3 $ft^3$ | 1 $m^3$ | $m^3$ to $ft^3$ | 35 |
| 1 gal (128 fl oz) | 3.8 L | gal to L | 3.8 |
| 0.264 gal | 1 L | L to gal | 0.26 |
| 1 qt (32 fl oz) | 946.36 mL | qt to L | 0.95 |
| 33.815 fl oz | 1 L | L to qt | 1.1 |

**Temperature equivalents** (approx)

| °F | °C |
|---|---|
| 32 | 0 |
| 50 | 10 |
| 60 | 15.5 |
| 61 | 16 |
| 65 | 18.3 |
| 70 | 21.1 |
| 75 | 23.8 |
| 80 | 26.6 |
| 82 | 28 |
| 85 | 29.4 |
| 90 | 32.2 |
| 102 | 38.8 |
| 103 | 39.4 |
| 104 | 40.0 |
| 105 | 40.5 |
| 106 | 41.1 |
| 212 | 100 |

°F = (°C × 9/5) + 32
°C = (°F - 32) × 5/9

**Conversion chart, kg to lb (approx)**

| Pig size | Lb | Kg |
|---|---|---|
| Birth | 3.3-4.4 | 1.5-2.0 |
| Weaning | 7.7 | 3.5 |
| | 11 | 5 |
| | 22 | 10 |
| Nursery | 33 | 15 |
| | 44 | 20 |
| | 55 | 25 |
| | 66 | 30 |
| Grower | 99 | 45 |
| | 110 | 50 |
| | 132 | 60 |
| Finisher | 198 | 90 |
| | 220 | 100 |
| | 231 | 105 |
| | 242 | 110 |
| | 253 | 115 |
| Sow | 300 | 135 |
| | 661 | 300 |
| Boar | 794 | 360 |
| | 800 | 363 |

1 tonne = 1000 kg
1 ppm = 0.0001% = 1 mg/kg = 1 g/tonne
1 ppm = 1 mg/L