JOURNAL OF CLINICAL MICROBIOLOGY, Sept. 1995, p. 2435–2444 Vol. 33, No. 9
0095-1137/95/$04.00+0
Copyright © 1995, American Society for Microbiology

Comparison of MICs of Ceftiofur and Other Antimicrobial Agents against Bacterial Pathogens of Swine from the United States, Canada, and Denmark

SARAH A. SALMON,[1]* JEFFREY L. WATTS,[1] CHERYL A. CASE,[1] LORRAINE J. HOFFMAN,[2] HENRIK C. WEGENER,[3] AND ROBERT J. YANCEY, JR.[1]†

Animal Health Discovery Research, The Upjohn Company, Kalamazoo, Michigan[1]; Veterinary Diagnostic Laboratory, Iowa State University, Ames, Iowa[2]; and National Veterinary Laboratory, DK-A90 Copenhagen, Denmark[3]

Received 26 January 1995/Returned for modification 28 April 1995/Accepted 19 June 1995

The MICs of ceftiofur and other antimicrobial agents, tested for comparison, for 515 bacterial isolates of pigs from the United States, Canada, and Denmark with various diseases were compared. The organisms tested included *Actinobacillus pleuropneumoniae*, *Escherichia coli*, *Pasteurella multocida*, *Salmonella choleraesuis*, *Salmonella typhimurium*, *Streptococcus suis*, *Streptococcus dysgalactiae* subsp. *equisimilis*, *Streptococcus equi* subsp. *equi*, and *Streptococcus equi* subsp. *zooepidemicus*. In addition to ceftiofur, the following antimicrobial agents or combinations were tested: enrofloxacin, ampicillin, sulfamethazine, trimethoprim-sulfadiazine (1:19), erythromycin, lincomycin, spectinomycin, lincomycin-spectinomycin (1:8), tilmicosin, and tetracycline. Tilmicosin was only tested against the U.S. isolates. Overall, ceftiofur and enrofloxacin were the most active antimicrobial agents tested against all isolates, with MICs inhibiting 90% of isolates tested (MIC_{90}s) of ≤2.0 and ≤1.0 μg/ml, respectively. Erythromycin, sulfamethazine, spectinomycin, and lincomycin demonstrated limited activity against all of the organisms tested, with MIC_{90}s of ≥8.0, ≥256.0, ≥32.0, and ≥16.0 μg/ml, respectively. Trimethoprim-sulfadiazine was active against isolates of *A. pleuropneumoniae*, *S. choleraesuis*, *S. typhimurium*, *P. multocida*, *S. equi*, and *S. suis* (MIC_{90}s, ≤0.5 μg/ml) but was less active against the *E. coli* strains tested (MIC_{90}, >16.0 μg/ml). Ampicillin was active against the *P. multocida*, *S. suis*, and *S. equi* isolates tested (MIC_{90}s, 0.5, 0.06, and 0.06 μg/ml, respectively) and was moderately active against *S. typhimurium* (MIC_{90}s, 2.0 μg/ml). However, this antimicrobial agent was much less active when it was tested against *A. pleuropneumoniae*, *S. cholerae-suis*, and *E. coli* (MIC_{90}s, 16.0, >32.0, and >32.0 μg/ml, respectively). Against the U.S. isolates of *A. pleuropneumoniae* and *P. multocida*, tilmicosin was moderately active (MIC_{90}s, 4.0 and 8.0 μg/ml, respectively). However, this compound was not active against the remaining U.S. isolates (MIC_{90}s, >64.0 μg/ml). Differences in the MICs from one country to another were not detected with enrofloxacin, ceftiofur, or lincomycin for the strains tested, but variations in the MICs of the remaining antimicrobial agents were observed.

A survey of producers rated swine respiratory disease (SRD) as the most important problem facing the swine industry (29). In the United States, it has been estimated that producers lose more than $210 million annually from SRD in production costs alone (6). These estimates do not include treatment and control costs or losses from deaths. SRD is a disease complex which includes atrophic rhinitis, pleuritis, pleuropneumonia, pneumonic pasteurellosis, and pneumonia. The bacteria isolated from swine with SRD include *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella choleraesuis*, and *Streptococcus suis* (5, 29, 33). *S. choleraesuis Streptococcus equi* subsp. *equi*, *Streptococcus equi* subsp. *zooepidemicus*, and *Escherichia coli* are also isolated from swine with septicemia-associated pneumonia (4, 19, 20, 29, 33, 36, 40). Antimicrobial agents are considered to be the primary tool for the treatment and control of SRD (18).

Salmonellosis is an important cause of enteritis in feeder-age pigs, and *S. choleraesuis* and *Salmonella typhimurium* are the two predominant *Salmonella* species involved (39). *S. choleraesuis* has not been isolated from Danish pig herds since 1968, and recently, *S. typhimurium* has been isolated in several outbreaks in Denmark (37a). *E. coli* also causes a number of intestinal and extraintestinal diseases in pigs. It is considered to be the single most important etiologic agent of diarrhea in neonatal and postweaning pigs (2). Other diseases caused by *E. coli* include edema disease, systemic *E. coli* infection in suckling pigs, and coliform mastitis (2).

Ceftiofur, a broad-spectrum cephalosporin antimicrobial agent originally developed for the treatment of bovine respiratory disease, has recently been approved for use in swine for the treatment of SRD worldwide. Previous studies have tested several antimicrobial agents against swine pathogens (9, 10, 12, 15–17, 25, 27, 28, 32–35, 41). Those studies either did not include ceftiofur (9, 10, 15–17, 25, 28, 32–35, 41) or tested only a limited number of strains against ceftiofur (27). Thus, only a limited amount of data is available on the activity of ceftiofur against swine pathogens. The purpose of the study described here was to compare the in vitro activity of ceftiofur with those of other antimicrobial agents currently in use or under development for use in swine against a large number of bacterial pathogens of pigs.

MATERIALS AND METHODS

Bacteria. A total of 515 porcine isolates were used in the study. From the United States, 250 isolates were tested, including 50 strains each of *A. pleuropneumoniae*, *P. multocida*, *S. suis*, and *S. cholerae-suis* obtained from swine with respiratory disease and 50 isolates of *E. coli* isolated from neonatal pigs with diarrhea. The isolates from Canada included in the study were *S. suis* (n = 25), *A. pleuropneumoniae* (n = 17), *E. coli* (n = 21), *S. equi* subsp. *equi* (n = 4), *S. equi*

* Corresponding author. Mailing address: Animal Health Discovery Research, 7923-190-MR, The Upjohn Company, 7000 Portage Rd., Kalamazoo, MI 49001. Phone: (616) 384-2328. Fax: (616) 384-2347.

† Present address: Central Research Division, Pfizer, Inc., Lincoln, NE 68501-0809.

TABLE 1. Summary of MICs for all gram-negative isolates from all locations

Organism (no. tested) and antimicrobial agent	MIC (μg/ml)			
	Range	50%	90%	Mode
A. pleuropneumoniae (83)				
Ceftiofur	≤0.03–0.06	≤0.03	≤0.03	≤0.03
Ampicillin	≤0.03–32.0	0.13	16.0	0.13
Erythromycin	0.25–16.0	4.0	16.0	8.0
Tetracycline	0.25–>32.0	8.0	32.0	8.0
Enrofloxacin	≤0.03–1.0	≤0.03	0.13	≤0.03
Spectinomycin	8.0–128.0	32.0	128.0	16.0
Sulfamethazine	16.0–>512.0	512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	≤0.015–0.25	0.03	0.13	≤0.015
Lincomycin[a]	0.06–>64.0	8.0	16.0	8.0
Lincomycin-spectinomycin (1:8)[a]	0.25–>16.0	4.0	8.0	8.0
P. multocida (74)				
Ceftiofur	≤0.03–0.06	≤0.03	≤0.03	≤0.03
Ampicillin	0.06–32.0	0.13	0.5	0.13
Erythromycin	0.5–32.0	4.0	8.0	4.0
Tetracycline	0.25–32.0	1.0	16.0	0.25
Enrofloxacin	NR[b]	≤0.03	≤0.03	≤0.03
Spectinomycin	8.0–>128.0	32.0	>128.0	32.0
Sulfamethazine	16.0–>512.0	128.0	>512.0	128.0
Trimethoprim-sulfadiazine	≤0.015–0.5	0.06	0.25	0.06
Lincomycin	8.0–>64.0	32.0	64.0	32.0
Lincomycin-spectinomycin (1:8)[c]	4.0–>16.0	16.0	>16.0	16.0
S. typhimurium (98)				
Ceftiofur	1.0–2.0	1.0	2.0	1.0
Ampicillin	1.0–>32.0	2.0	2.0	2.0
Erythromycin	NR	>32.0	>32.0	>32.0
Tetracycline	1.0–>32.0	2.0	2.0	2.0
Enrofloxacin	0.06–0.5	0.06	0.13	0.06
Spectinomycin	32.0–>128.0	64.0	128.0	64.0
Sulfamethazine	64.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	≤0.015–>16.0	0.06	0.25	0.06
Lincomycin	64.0–>64.0	>64.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)	8.0–>16.0	8.0	16.0	8.0
S. cholerae-suis (50)				
Ceftiofur	1.0–2.0	1.0	1.0	1.0
Ampicillin	1.0–>32.0	>32.0	>32.0	>32.0
Erythromycin	NR	>32.0	>32.0	>32.0
Tetracycline	1.0–>32.0	>32.0	>32.0	>32.0
Enrofloxacin	0.13–1.0	0.13	0.13	0.13
Spectinomycin	32.0–64.0	64.0	64.0	64.0
Sulfamethazine	NR	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	0.13–0.5	0.25	0.25	0.13, 0.25
Lincomycin	NR	>64.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)	16.0–64.0	32.0	>64.0	32.0
E. coli (84)				
Ceftiofur	0.25–4.0	0.5	1.0	0.5
Ampicillin	1.0–>32.0	4.0	>32.0	>32.0
Erythromycin	16.0–>32.0	>32.0	>32.0	>32.0
Tetracycline	1.0–>32.0	>32.0	>32.0	>32.0
Enrofloxacin	≤0.03–16.0	≤0.03	0.06	≤0.03
Spectinomycin	16.0–>128.0	64.0	>128.0	>128.0
Sulfamethazine	16.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	0.03–>16.0	0.25	>16.0	0.25
Lincomycin	NR	>64.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)	2.0–>64.0	32.0	>64.0	>64.0

[a] Results are for 91 strains.
[b] NR, no range; the same value was obtained for all isolates.
[c] Results are for 76 strains.

TABLE 2. MICs of various antimicrobial agents for streptococci from all locations

Organism (no. of strains) and antimicrobial agent	MIC (μg/ml)			
	Range	50%	90%	Mode
S. suis (94)				
Ceftiofur	≤0.03–1.0	≤0.03	0.25	≤0.03
Ampicillin	≤0.03–8.0	≤0.03	0.06	≤0.03
Erythromycin	≤0.03–>32.0	16.0	>32.0	>32.0
Tetracycline	0.13–>32.0	32.0	>32.0	>32.0
Enrofloxacin	≤0.03–1.0	0.25	0.5	0.25
Spectinomycin	4.0–>128.0	16.0	>128.0	>128.0
Sulfamethazine	2.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	≤0.015–>16.0	0.06	0.5	0.03, 0.06
Lincomycin[a]	0.03–>64.0	32.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)[a]	0.06–>16.0	8.0	16.0	4.0
β-Hemolytic streptococci (24)				
Ceftiofur	≤0.03–0.06	≤0.03	≤0.03	≤0.03
Ampicillin	≤0.03–0.06	≤0.03	0.06	≤0.03
Erythromycin	≤0.03–>32.0	≤0.03	>32.0	≤0.03
Tetracycline	≤0.03–>32.0	1.0	32.0	2.0
Enrofloxacin	0.25–1.0	0.5	1.0	0.5
Spectinomycin	8.0–>128.0	32.0	64.0	32.0
Sulfamethazine	4.0–>512.0	32.0	>512.0	32.0
Trimethoprim-sulfadiazine	≤0.015–0.25	0.13	0.13	0.25
Lincomycin	≤0.06–1.0	0.5	1.0	0.5
Lincomycin-spectinomycin (1:8)	0.13–2.0	0.5	1.0	0.5

[a] A total of 100 isolates were tested.

subsp. *zooepidemicus* (n = 19), and *Streptococcus dysgalactiae* subsp. *equisimilis* (n = 1) (herein referred to as a group as β-hemolytic streptococci) and *P. multocida* (n = 1). The isolates from Canada were provided by K. B. Quinn, Upjohn Animal Health, Orangeville, Ontario, Canada. The isolates from Denmark tested in the study included *S. suis* (n = 25), *A. pleuropneumoniae* (n = 24), *E. coli* (n = 13), *S. typhimurium* (n = 98), and *P. multocida* (n = 25). Isolates were identified by conventional methods and were transferred to the Animal Health Discovery Research culture collection of The Upjohn Company. Upon receipt, the isolates were checked for purity and were stored in 1.0 ml of Trypticase soy broth (Difco, Detroit, Mich.) with 10% glycerol on 3-mm-diameter glass beads at −70°C. Isolates were subcultured twice on Trypticase blood agar base (BBL, Cockeysville, Md.) supplemented with 5% sheep blood or on chocolate agar supplemented with 2% supplement C (Difco) (*A. pleuropneumoniae* only) and were incubated at 35°C in 5% CO_2 for 18 to 24 h prior to MIC testing.

MIC determinations. The following antimicrobial agents and combinations of antimicrobial agents were tested: enrofloxacin, ceftiofur, ampicillin, sulfamethazine, trimethoprim-sulfadiazine (1:19), erythromycin, lincomycin, spectinomycin, lincomycin-spectinomycin (1:8), tetracycline, and tilmicosin. The dilution ranges used for these antimicrobial agents were as follows: enrofloxacin, cefitiofur, ampicillin, erythromycin, and tetracycline, 0.03 to 32.0 μg/ml; sulfamethazine, 0.5 to 512.0 μg/ml; trimethoprim-sulfadiazine, 0.015 to 16.0 and 0.3 to 304 μg/ml; respectively; spectinomycin, 0.13 to 128.0 μg/ml; lincomycin and tilmicosin, 0.06 to 64.0 μg/ml; and lincomycin-spectinomycin, 0.06 to 64.0 and 0.5 to 512.0 μg/ml, respectively. MIC determinations for enrofloxacin, ceftiofur, ampicillin, erythromycin, sulfamethazine, trimethoprim-sulfadiazine, spectinomycin, and tetracycline were obtained by using a commercially prepared, dehydrated MIC panel. These panels were stored at room temperature. Similar determinations were made for lincomycin, lincomycin-spectinomycin (1:8), and tilmicosin by using the microdilution method of the National Committee for Clinical Laboratory Standards (NCCLS) for organisms that grow aerobically (22). The MIC panels used for these antimicrobial agents were prepared in-house and were stored at −70°C. The panels were thawed to room temperature prior to inoculation. All MIC panels were inoculated by following NCCLS guidelines (22). Briefly, three to five colonies of a 24-h culture were removed, suspended in 5.0 ml of sterile 0.85% saline, and adjusted to a 0.5 McFarland barium sulfate turbidity standard with a nephelometer. A 0.01-ml aliquot of this suspension was then transferred to 10.0 ml of cation-supplemented Mueller-Hinton broth (Sensititre, Westlake, Ohio). Haemophilus test medium broth (Remel, Lenexa, Kans.) was used to test the *A. pleuropneumoniae* isolates. A 0.05-ml aliquot of this suspension was then dispensed into each well of a 96-well microdilution plate containing either dehydrated, prediluted antimicrobial agent (Sensititre) or antimicrobial agent diluted in the appropriate growth medium by using an automated inoculator. These panels were then either sealed with the supplied adhesive seals (commercially prepared panels) or wrapped in plastic to prevent dehydration and were incubated at 35°C for 18 to 24 h. The MIC for each isolate was read as the lowest dilution demonstrating no visible growth. The final well in each row contained no antimicrobial agent and served as a positive growth control on both panels. The following quality control strains recommended by NCCLS were included with each batch of organisms tested: *Staphylococcus aureus* ATCC 29213, *E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, and *Enterococcus faecalis* ATCC 29212.

RESULTS AND DISCUSSION

Previous studies testing bacterial isolates from swine have included a number of antimicrobial agents and have used various methodologies (9, 10, 12, 15–17, 25, 27, 28, 32–35, 41). While most of those studies have also reported MIC data (9, 10, 15–17, 25, 27, 35), a number of the studies have interpreted MIC data by categorizing isolates as susceptible or resistant (9, 10, 15–17, 28, 33–35, 41). The interpretive criteria used for those studies were based on human pharmacokinetics and treatment regimens; however, the validity of using human breakpoints for veterinary isolates has not been established. Because interpretive criteria with pathogens isolated from pigs are not available for all antimicrobial agents tested, isolates in the present study should not be classified as susceptible or resistant; therefore, only MIC data are presented. The MICs for the isolates tested are summarized in Tables 1 to 8. The MICs for the quality control strains are summarized in Tables 9 and 10. Out-of-range values were obtained with enrofloxacin, ceftiofur, spectinomycin, and trimethoprim-sulfadiazine against older strains of *P. aeruginosa* and *E. coli* (22, 30). This was resolved when the strains were replaced with new isolates.

The fluoroquinolones are a class of antimicrobial agents derived from the naphthyridine nalidixic acid (26). This class of agents generally exhibits good activity against gram-negative bacilli, moderate activity against the staphylococci, and fair to poor activity against streptococci and anaerobes (26). Of these compounds, enrofloxacin has been developed solely for veterinary use. Previous studies have shown enrofloxacin to be efficacious in the treatment of SRD and other bacterial diseases

TABLE 3. MICs of various antimicrobial agents for gram-negative organisms from the United States

Organism (no. of strains) and antimicrobial agent	MIC (μg/ml)			
	Range	50%	90%	Mode
A. pleuropneumoniae (50)				
Ceftiofur	NR[a]	≤0.03	≤0.03	≤0.03
Ampicillin	≤0.03–32.0	0.13	16.0	0.06
Erythromycin	0.25–16.0	2.0	4.0	2.0
Tetracycline	0.25–>32.0	8.0	32.0	8.0
Enrofloxacin	≤0.03–0.13	≤0.03	0.06	≤0.03
Spectinomycin	8.0–>128.0	16.0	64.0	16.0
Sulfamethazine	16.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	≤0.015–0.06	≤0.015	0.03	≤0.015
Lincomycin	0.06–>64.0	4.0	16.0	8.0
Lincomycin-spectinomycin (1:8)	0.5–>64.0	8.0	16.0	8.0
Tilmicosin	1.0–>64.0	2.0	4.0	2.0
P. multocida (50)				
Ceftiofur	≤0.03–0.06	≤0.03	≤0.03	≤0.03
Ampicillin	0.06–32.0	0.13	0.25	0.13
Erythromycin	0.5–8.0	4.0	8.0	4.0
Tetracycline	0.25–32.0	1.0	16.0	1.0
Enrofloxacin	NR	≤0.03	≤0.03	≤0.03
Spectinomycin	8.0–64.0	32.0	32.0	32.0
Sulfamethazine	16.0–256.0	128.0	256.0	128.0, 256.0
Trimethoprim-sulfadiazine	≤0.015–0.25	0.06	0.25	0.06
Lincomycin	8.0–64.0	32.0	32.0	32.0
Lincomycin-spectinomycin (1:8)	16.0–64.0	16.0	32.0	16.0
Tilmicosin	0.5–8.0	4.0	8.0	4.0
S. cholerae-suis (50)				
Ceftiofur	1.0–2.0	1.0	1.0	1.0
Ampicillin	1.0–>32.0	>32.0	>32.0	>32.0
Erythromycin	NR	>32.0	>32.0	>32.0
Tetracycline	1.0–>32.0	>32.0	>32.0	>32.0
Enrofloxacin	0.13–1.0	0.13	0.13	0.13
Spectinomycin	32.0–64.0	64.0	64.0	64.0
Sulfamethazine	NR	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	0.13–0.5	0.25	0.25	0.13, 0.25
Lincomycin	NR	>64.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)	16.0–64.0	32.0	>64.0	32.0
Tilmicosin	NR	>64.0	>64.0	>64.0
E. coli (50)				
Ceftiofur	0.25–4.0	0.5	1.0	0.5
Ampicillin	1.0–>32.0	16.0	>32.0	>32.0
Erythromycin	16.0–>32.0	>32.0	>32.0	>32.0
Tetracycline	1.0–>32.0	>32.0	>32.0	>32.0
Enrofloxacin	≤0.06–16.0	0.06	0.06	0.06
Spectinomycin	16.0–>128.0	64.0	>128.0	>128.0
Sulfamethazine	15.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	0.03–>16.0	0.25	>16.0	0.25
Lincomycin	NR	>64.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)	8.0–>64.0	32.0	>64.0	>64.0
Tilmicosin	NR	>64.0	>64.0	>64.0

[a] NR, no range; the same value was obtained for all isolates.

of swine (7, 13, 17, 31, 32, 42). For these reasons, enrofloxacin was included in the present as a representative of this class of antimicrobial agents. Enrofloxacin demonstrated excellent activity against the gram-negative isolates tested, with an MIC inhibiting 90% of isolates tested (MIC_{90}) of ≤0.13 μg/ml for isolates of *A. pleuropneumoniae*, *P. multocida*, and *E. coli* from all three countries. The results are similar to those found by Gutiérrez et al. (17), who reported an MIC_{90} of ≤0.06 μg/ml for *A. pleuropneumoniae*. Enrofloxacin also exhibited excellent activity against the isolates of *S. typhimurium* from Denmark and the isolates of *S. choleraesuis* isolated from pigs in the United States (MIC_{90}s, 0.13 μg/ml for both organisms). Enrofloxacin was less active against the streptococci than the gram-negative bacilli. However, this antimicrobial agent was still active against these organisms (MIC_{90}s, 1.0 μg/ml for both the β-hemolytic streptococci and *S. suis*). For a single strain of *E. coli* from the United States, the enrofloxacin MIC was 16.0 μg/ml.

Similar to its activity against bovine respiratory disease pathogens (37), ceftiofur was highly active against the SRD pathogens tested. For all isolates of *A. pleuropneumoniae* and *P. multocida* tested, the ceftiofur MIC_{90}s were ≤0.03 μg/ml.

TABLE 4. MICs of various antimicrobial agents for *S. suis* isolates from the United States[a]

Antimicrobial agent	MIC (μg/ml)			
	Range	50%	90%	Mode
Ceftiofur	≤0.03–1.0	≤0.03	0.13	≤0.03
Ampicillin	≤0.03–8.0	≤0.03	0.06	≤0.03
Erythromycin	≤0.03–>32.0	0.5	>32.0	>32.0
Tetracycline	0.5–>32.0	32.0	>32.0	32.0
Enrofloxacin	≤0.03–0.5	0.25	0.5	0.25
Spectinomycin	4.0–>128.0	16.0	32.0	16.0
Sulfamethazine	4.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	≤0.015–0.25	0.13	0.13	0.13
Lincomycin[a]	0.06–>64.0	16.0	>64.0	32.0
Lincomycin-spectinomycin (1:8)[b]	0.5–>64.0	8.0	16.0	8.0
Tilmicosin	0.06–>64.0	>64.0	>64.0	>64.0

[a] A total of 50 *S. suis* isolates were tested.
[b] A total of 47 isolates were tested.

MIC_{90}s of 0.25 μg/ml were obtained for isolates of *S. suis* from all three countries and MICs of 1.0 μg/ml were obtained for isolates of *E. coli* from all three countries. Ceftiofur was also active against the β-hemolytic streptococcal isolates (MIC_{90}s, ≤0.03 μg/ml) and the *S. typhimurium* and *S. choleraesuis* isolates (MIC_{90}s, 1.0 μg/ml for both isolates). Of the isolates tested, for only a single *E. coli* isolate from the United States was the ceftiofur MIC 4.0 μg/ml. For the remaining isolates, ceftiofur had MICs of ≤2.0 μg/ml. These results are similar to those obtained in a previous study in which the MIC_{90}s of ceftiofur were reported to be ≤0.125, ≤0.125, and ≤1.0 μg/ml for *A. pleuropneumoniae*, *P. multocida*, and *S. choleraesuis*, respectively (27). For the strain of *E. coli* for which the ceftiofur MIC was high, the MIC of enrofloxacin was also high.

Ampicillin is often used for the treatment of SRD and other porcine diseases (11, 14, 23, 24). Ampicillin demonstrated excellent activity against *P. multocida*, β-hemolytic streptococci, and *S. suis* (MIC_{90}s, ≤0.03, ≤0.03, and 0.13 μg/ml, respectively) and moderate activity against *S. typhimurium* (MIC_{90}s, 2.0 μg/ml). These results are in agreement with previously reported MICs (10, 33, 34). Fales et al. (10) found the MIC_{90} of ampicillin to be ≤0.25 μg/ml for *P. multocida*. Turgeon et al. (34, 35) found that ≥90% of strains of *S. suis* were inhibited by 0.12 μg of ampicillin per ml. Ampicillin was much less active when it was tested against *E. coli* and *S. choleraesuis* (MIC_{90}s, >32.0 μg/ml). Against *A. pleuropneumoniae* isolates from the United States, ampicillin was also less active (MIC_{90}s, 16.0 μg/ml); however, against the Canadian and Danish strains of this organism, ampicillin was much more active (MIC_{90}s, 0.25 and 0.5 μg/ml, respectively). These results are similar to those reported previously for *A. pleuropneumoniae* isolates from various countries (9, 12, 15–17).

Sulfonamides and the potentiated sulfonamides (trimethoprim-sulfonamide combinations) have also been widely used for the treatment of numerous swine diseases (11, 14, 23, 24). Sulfamethazine was tested in the present study as a rep-

TABLE 5. MICs of various antimicrobial agents for gram-negative isolates from Canada

Organism (no. of strains) and antimicrobial agent	MIC (μg/ml)			
	Range	50%	90%	Mode
A. pleuropneumoniae (10)				
Ceftiofur	NR[a]	≤0.03	≤0.03	≤0.03
Ampicillin	0.13–0.5	0.25	0.25	0.25
Erythromycin	8.0–16.0	8.0	8.0	8.0
Tetracycline	0.25–16.0	8.0	8.0	8.0
Enrofloxacin	0.06–0.13	0.13	0.13	0.13
Spectinomycin	64.0–128.0	64.0	128.0	64.0
Sulfamethazine	128–512.0	256.0	512.0	256.0
Trimethoprim-sulfadiazine	0.06–0.13	0.06	0.13	0.06, 0.13
Lincomycin	1.0–32.0	8.0	16.0	8.0
Lincomycin-spectinomycin (1:8)	0.25–8.0	2.0	4.0	2.0
E. coli (21)				
Ceftiofur	0.25–1.0	0.5	1.0	0.5
Ampicillin	2.0–>32.0	4.0	>32.0	4.0
Erythromycin	32.0–>32.0	>32.0	>32.0	>32.0
Tetracycline	1.0–>32.0	>32.0	>32.0	>32.0
Enrofloxacin	≤0.03–0.5	≤0.03	≤0.03	≤0.03
Spectinomycin	16.0–>128.0	128.0	>128.0	>128.0
Sulfamethazine	128.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	0.03–>16.0	0.5	>16.0	>16.0
Lincomycin	NR	>64.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)	2.0–>16.0	16.0	>16.0	>16.0

[a] NR, no range; the same value was obtained for all isolates.

TABLE 6. MICs of various antimicrobial agents for gram-positive isolates from Canada

Organism (no. of strains) and antimicrobial agent	MIC (μg/ml)			
	Range	50%	90%	Mode
β-Hemolytic streptococci (24)				
Ceftiofur	≤0.03–0.06	≤0.03	≤0.03	≤0.03
Ampicillin	≤0.03–0.06	≤0.03	0.06	≤0.03
Erythromycin	≤0.03–>32.0	≤0.03	>32.0	≤0.03
Tetracycline	≤0.03–>32.0	1.0	32.0	2.0
Enrofloxacin	0.25–1.0	0.5	1.0	0.5
Spectinomycin	8.0–>128.0	32.0	64.0	32.0
Sulfamethazine	4.0–>512.0	32.0	>512.0	32.0
Trimethoprim-sulfadiazine	≤0.015–0.25	0.13	0.13	0.25
Lincomycin	≤0.06–1.0	0.5	1.0	0.5
Lincomycin-spectinomycin (1:8)	0.13–2.0	0.5	1.0	0.5
S. suis (22)				
Ceftiofur	≤0.03–0.25	≤0.03	0.25	≤0.03
Ampicillin	≤0.03–0.25	≤0.03	0.13	≤0.03
Erythromycin	≤0.03–>32.0	>32.0	>32.0	>32.0
Tetracycline	0.25–>32.0	32.0	>32.0	32.0
Enrofloxacin	0.13–1.0	0.25	0.5	0.25
Spectinomycin	8.0–>128.0	16.0	>128.0	16.0
Sulfamethazine	2.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	≤0.015–0.06	0.03	0.5	0.13
Lincomycin[a]	1.0–>64.0	>64.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)[a]	1.0–>16.0	4.0	16.0	4.0

[a] A total of 25 isolates were tested.

resentative of the sulfonamide class of antimicrobial agents. We found that sulfamethazine was not active against the organisms tested when MIC_{90}s were determined for isolates from all countries grouped together (MIC_{90}s, >512.0 μg/ml). Some minimal activity was observed against *P. multocida* strains from the United States when they were assessed separately (MIC_{90}s, 256.0 μg/ml). These results agree with those from previous reports with sulfonamides against swine pathogens (8–10, 16). While sulfamethazine was found to be inactive against most of the strains tested, the potentiated sulfonamide tested was found to have good activity against most of the strains tested. Trimethoprim-sulfadiazine exhibited good activity against *A. pleuropneumoniae*, *S. choleraesuis*, *S. typhimurium*, *P. multocida*, β-hemolytic streptococci, and *S. suis* (MIC_{90}s, ≤0.25 μg/ml). However, trimethoprim-sulfadiazine was found to be inactive against the *E. coli* isolates at the concentration tested (MIC_{90}s, >16.0 μg/ml). These results are also in agreement with those reported previously for *A. pleuropneumoniae*, *S. choleraesuis*, and *S. suis* (8–10, 27, 34, 35). However, Raemdonck et al. (27) found the MIC_{90} of trimethoprim-sulfadiazine for *P. multocida* to be 8.0 μg/ml, which is much higher than those found for the isolates tested in the present study. These differences could be due to differences in the sources of isolates of *P. multocida* used in the present study. Our isolates were only from Denmark and the United States, whereas Raemdonck et al. (27) tested 931 isolates from 13 countries.

Erythromycin has been widely used for the treatment of bacterial infections of swine in some countries (11, 14, 23). This antimicrobial agent was found to have limited activity against the isolates tested. Overall, erythromycin was inactive against *S. suis*, β-hemolytic streptococci, *S. typhimurium*, *S. choleraesuis*, and *E. coli* isolates at the concentrations tested (MIC_{90}s, >32.0 μg/ml). Against isolates of *P. multocida* and *A. pleuropneumoniae*, erythromycin exhibited limited activity (MIC_{90}s, 8.0 and 16.0 μg/ml, respectively). These results are similar to those reported for recent isolates of *A. pleuropneumoniae*, *P. multocida*, and *S. choleraesuis* (9, 10, 15, 17, 27). Earlier studies found the MIC_{90} of erythromycin for *A. pleuropneumoniae* to be 2.0 μg/ml (9) and 4.0 μg/ml (14), and the MIC_{90} for *P. multocida* was 4.0 μg/ml (10). These data probably suggest that resistance to erythromycin has increased over the last 10 years. An MIC_{90} of erythromycin for *S. choleraesuis* has recently been reported (27) to be >64.0 μg/ml, which is in agreement with the results of the present study.

Lincomycin, spectinomycin, and lincomycin-spectinomycin in combination have also been proven to be efficacious in the treatment of various diseases of pigs (11, 14, 21, 23). Previous studies testing lincomycin and spectinomycin in combination have tested these antimicrobial agents at a 1:2 ratio (8). We tested lincomycin-spectinomycin at a 1:8 ratio, the ratio of concentrations achieved in porcine plasma after intramuscular dosing, to more accurately reflect in vivo concentrations (38). At the concentrations tested, lincomycin and lincomycin-spectinomycin were not active against most of the gram-negative organisms tested (MIC_{90}s, ≥32.0 μg/ml). Against the β-hemolytic streptococci (MIC_{90}s, 1.0 μg/ml for lincomycin and lincomycin-spectinomycin) and *A. pleuropneumoniae* (MIC_{90}s, 16.0 and 8.0 μg/ml for lincomycin and lincomycin-spectinomycin, respectively) these compounds were more active. Spectinomycin was not active against the majority of the organisms tested (MIC_{90}s, ≥32.0 μg/ml). These results concur with recently reported data for lincomycin, spectinomycin, and lincomycin-spectinomycin tested against *A. pleuropneumoniae*, *P. multocida*, and *S. choleraesuis* (9, 10, 27).

Against the majority of the isolates tested, tetracycline showed little activity (MIC_{90}s, ≥16.0 μg/ml). However, tetracycline showed moderate activity (MIC_{90}s, 2.0 μg/ml) against the *S. typhimurium* isolates from Denmark. These data are similar to those presented in previous reports (9, 10, 27).

Tilmicosin is a semisynthetic macrolide antibiotic that has recently been approved for use in the United States for the treatment of bovine respiratory disease. While injection of this product has been shown to be fatal in swine, it has displayed some efficacy in the treatment of SRD when used as a feed

TABLE 7. MICs of various antimicrobial agents for gram-negative isolates from Denmark

Organism (no. of strains) and antimicrobial agent	MIC (μg/ml)			
	Range	50%	90%	Mode
A. pleuropneumoniae (22)				
Ceftiofur	≤0.03–0.06	≤0.03	≤0.03	≤0.03
Ampicillin	0.13–0.5	0.25	0.5	0.13
Erythromycin	2.0–16.0	8.0	16.0	8.0
Tetracycline	0.5–8.0	1.0	8.0	1.0
Enrofloxacin	0.06–1.0	0.06	0.13	0.06
Spectinomycin	32.0–128.0	64.0	128.0	64.0
Sulfamethazine	128.0–>512.0	256.0	512.0	512.0
Trimethoprim-sulfadiazine	0.03–0.25	0.06	0.13	0.13
Lincomycin[a]	1.0–64.0	16.0	32.0	16.0
Lincomycin-spectinomycin (1:8)[a]	1.0–4.0	2.0	4.0	2.0
P. multocida (24)				
Ceftiofur	≤0.03–0.06	≤0.03	≤0.03	≤0.03
Ampicillin	0.13–0.5	0.13	0.25	0.13
Erythromycin	2.0–32.0	8.0	8.0	8.0
Tetracycline	0.25–16.0	0.25	0.5	0.25
Enrofloxacin	NR[b]	≤0.03	≤0.03	≤0.03
Spectinomycin	16.0–>128.0	64.0	>128.0	64.0
Sulfamethazine	32.0–>512.0	256.0	>512.0	128.0
Trimethoprim-sulfadiazine	≤0.015–0.5	0.06	0.25	0.06
Lincomycin	32.0–>64.0	32.0	>64.0	32.0
Lincomycin-spectinomycin (1:8)	4.0–>16.0	8.0	16.0	8.0
S. typhimurium (98)				
Ceftiofur	1.0–2.0	1.0	2.0	1.0
Ampicillin	1.0–>32.0	2.0	2.0	2.0
Erythromycin	NR	>32.0	>32.0	>32.0
Tetracycline	1.0–>32.0	2.0	2.0	2.0
Enrofloxacin	0.06–0.5	0.06	0.13	0.06
Spectinomycin	32.0–>128.0	64.0	128.0	64.0
Sulfamethazine	64.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	≤0.015–>16.0	0.06	0.25	0.06
Lincomycin	64.0–>64.0	>64.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)	8.0–>16.0	8.0	16.0	8.0
E. coli (13)				
Ceftiofur	0.25–1.0	0.5	0.5	0.5
Ampicillin	1.0–>32.0	4.0	>32.0	4.0
Erythromycin	32.0–>32.0	>32.0	>32.0	>32.0
Tetracycline	1.0–>32.0	>32.0	>32.0	>32.0
Enrofloxacin	≤0.03–0.06	≤0.03	≤0.03	≤0.03
Spectinomycin	16.0–>128.0	32.0	>128.0	>128.0
Sulfamethazine	64.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	0.03–>16.0	0.25	>16.0	0.25
Lincomycin	NR	>64.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)	2.0–>16.0	16.0	>16.0	2.0

[a] Results are for 41 isolates.
[b] NR, no range; the same value was obtained for all isolates.

additive (1, 3). Tilmicosin was active against the isolates of *A. pleuropneumoniae* (MIC_{90}, 4.0 μg/ml) and *P. multocida* (MIC_{90}, 8.0 μg/ml) tested in the study; however, tilmicosin was not active against *S. suis*, *E. coli*, or *S. choleraesuis* (MIC_{90}s, >64.0 μg/ml for all three strains). These results support those reported previously in studies in which tilmicosin was tested against porcine pathogens (25).

Differences were not detected for ceftiofur, enrofloxacin, and lincomycin when comparing MIC data from one country with those from another. However, differences from country to country were detected for the remaining antimicrobial agents. Ampicillin and tetracycline were less active against isolates of *A. pleuropneumoniae* from the United States (MIC_{90}s, 16.0 and 32.0 μg/ml, respectively) than against isolates from Canada and Denmark (MIC_{90}s, 0.25 and 0.5 μg/ml, respectively, for ampicillin and 8.0 μg/ml for tetracycline). In contrast, MICs of erythromycin for *A. pleuropneumoniae* were slightly higher for isolates from Canada and Denmark (MIC_{90}, 8.0 μg/ml for isolates from both countries) than for isolates from the United States (MIC_{90} = 4.0 μg/ml). For the lincomycin-spectinomycin combination, MICs were slightly higher for the U.S. isolates of *A. pleuropneumoniae* and *P. multocida* (MIC_{90}s, 16.0 and 32.0 μg/ml, respectively) than for the Canadian and Danish isolates. Differences by location were also detected with spectinomycin. For the Danish *P. multocida* strains, the MIC_{90}s of spectinomycin were higher (MIC_{90}, >128.0 μg/ml) than those for the U.S. strains (MIC_{90}s, 32.0 μg/ml). This loss of activity against the *P. multocida* strains from Denmark was also observed with

TABLE 8. Summary of MICs for *S. suis* isolates from Denmark[a]

	MIC (μg/ml)			
	Range	50%	90%	Mode
Ceftiofur	≤0.03–0.5	≤0.03	0.13	≤0.03
Ampicillin	≤0.03–0.06	≤0.03	≤0.03	≤0.03
Erythromycin	≤0.03–>32.0	0.13	>32.0	>32.0
Tetracycline	0.13–>32.0	2.0	>32.0	2.0
Enrofloxacin	0.13–1.0	0.5	1.0	0.5
Spectinomycin	8.0–>128.0	16.0	32.0	16.0
Sulfamethazine	4.0–>512.0	>512.0	>512.0	>512.0
Trimethoprim-sulfadiazine	≤0.015–>16.0	0.13	2.0	0.13
Lincomycin	0.25–>64.0	4.0	>64.0	>64.0
Lincomycin-spectinomycin (1:8)	0.13–>16.0	1.0	16.0	1.0

[a] A total of 25 *S. suis* isolates were tested.

sulfamethazine. Also, sulfamethazine was more active against U.S. strains of *E. coli* (MIC_{90}s, 256.0 μg/ml) than against the strains from Canada and Denmark (MIC_{90}s, >512.0 μg/ml for isolates from both countries). Differences were also observed with trimethoprim-sulfadiazine from one country to another. For isolates of *A. pleuropneumoniae* from the United States, the MIC_{90}s of trimethoprim-sulfadiazine (MIC_{90}s, 0.03 μg/ml) than did those were slightly lower than those for isolates from Canada and Denmark (MIC_{90}s, 0.13 μg/ml for isolates from both countries). Also with trimethoprim-sulfadiazine, the MIC_{90}s for *S. suis* strains were higher (MIC_{90}s, 2.0 μg/ml) than those of trimethoprim-sulfadiazine for *S. suis* strains from the United States and Canada (MIC_{90}s, 0.13 and 0.5 μg/ml, respectively).

These differences in antimicrobial activity against isolates from the three countries could be attributed to many factors. Variations in antimicrobial agent usage from one country to another could be a reason. Another factor would be differences in the serotypes of an organism from one country to another. Reams et al. (28) reported differences in antibiograms on the basis of the serotypes of U.S. isolates of *S. suis*; conversely, Fales et al. (9) found no correlation between antibiograms and

TABLE 9. Summary of MIC ranges for NCCLS quality control organisms with Mueller-Hinton broth in commercially prepared panels

Antimicrobial agent	MIC range (μg/ml)			
	E. coli ATCC 25922	*P. aeruginosa* ATCC 27853	*E. faecalis* ATCC 29212	*S. aureus* ATCC 29213
Enrofloxacin				
Expected	0.03–0.13	2.0–8.0	0.5–2.0	0.06–0.25
Obtained	≤0.03–0.25	1.0–2.0[a]	0.5	0.13–0.25
Ceftiofur				
Expected	0.25–1.0	>16.0	2.0–8.0	1.0–4.0
Obtained	0.5–1.0	8.0–32.0[a]	1.0–8.0	1.0–2.0
Ampicillin				
Expected	2.0–8.0	NA[b]	0.5–2.0	0.25–1.0
Obtained	2.0–8.0	>32.0	0.5–1.0	0.25–0.5
Erythromycin				
Expected	≥16.0	>16.0	1.0–4.0	≤0.13–0.5
Obtained	>32.0	>32.0	1.0–4.0	0.5
Spectinomycin				
Expected	4.0–16.0	>16.0	>16.0	>16.0
Obtained	16.0–64.0	>512.0	512.0–>512.0	128.0–>512.0
Sulfamethazine				
Expected	NA	NA	NA	NA
Obtained	256.0–>512.0	>512.0	512.0–>512.0	128.0–>512.0
Tetracycline				
Expected	≤2.0–4.0	8.0–≥16.0	8.0–>16.0	NA
Obtained	1.0	8.0–>16.0	16.0	0.25–32.0
Trimethoprim-sulfadiazine				
Expected	≤0.06/1.19	NA	≤0.13/2.38	≤0.25/4.75
Obtained	0.06–0.25	8.0–>16.0	≤0.015–0.13	0.13

[a] Out-of-range values were obtained with enrofloxacin, ceftiofur, spectinomycin, and trimethoprim-sulfadiazine against an old strain of *P. aeruginosa*. This was resolved when the strain was replaced with a new isolate.
[b] NA, not available.

TABLE 10. Summary of MIC ranges for NCCLS quality control organisms with Mueller-Hinton broth and manually prepared panels

Antimicrobial agent	MIC range (μg/ml)			
	E. coli ATCC 25922	*P. aeruginosa* ATCC 27853	*E. faecalis* ATCC 29212	*S. aureus* ATCC 29213
Lincomycin				
Expected	NA[a]	NA	NA	NA
Obtained	>64.0	>64.0	32.0	0.25–2.0
Lincomycin-spectinomycin (1:8)				
Expected	NA	NA	NA	NA
Obtained	4.0–16.0	>64.0	8.0–64.0	1.0–4.0
Tilmicosin				
Expected	NA	NA	NA	0.5–2.0
Obtained	>64.0	>64.0	>64.0	0.5

[a] NA, not available.

the serotypes of *A. pleuropneumoniae* strains isolated in the United States.

Overall, against the porcine bacterial isolates tested in the present study, ceftiofur and enrofloxacin exhibited the broadest spectra of activity. The activities of the remaining antimicrobial agents varied, depending on the organism and the country in which the organism originated.

REFERENCES

1. **Bäckström, L., W. B. Chung, M. T. Collins, and E. Ose.** 1991. Efficacy of tilmicosin for control of atrophic rhinitis. *In* Proceedings of the 12th Annual Meeting of the International Pig Veterinary Society. Animal Health Service, Boxtel, The Netherlands.
2. **Bertcshinger, H. U., J. M. Fairbrother, N. O. Nielsen, and J. F. Pohlenz.** 1992. *Escherichia coli* infections, p. 552–559. *In* A. D. Leman, B. E. Straw, W. L. Mengeling, S. D'Allaire, and D. J. Taylor (ed.), Diseases of swine, 7th ed. Iowa State University Press, Ames, Iowa.
3. **Binder, S., A. Lackhoff, N. B. Lee, H. Berner, and J. Bauer.** 1991. Efficacy of food-medication with tilmicosin in respiratory disorders of swine. *In* Proceedings of the 12th Annual Meeting of the International Pig Veterinary Society. Animal Health Service, Boxtel, The Netherlands.
4. **Blood, D. C., and O. M. Radostits.** 1984. Veterinary medicine, 6th ed. p. 328. London, Bailliére Tindall.
5. **Christensen, G., and J. Mousing.** 1992. Respiratory system, p. 138–162. *In* A. D. Leman, B. E. Straw, W. L. Mengeling, S. D'Allaire, and D. J. Taylor (ed.), Diseases of swine, 7th ed. Iowa State University Press, Ames.
6. **Daniel, G. M., W. Freese, S. Henry, E. Stevermer, B. Straw, and W. P. Switzer.** 1986. An up-to-date review of atrophic rhinitis. Vet. Med. **81:**735–744.
7. **Doporto, D. J. M., O. M. E. Trujillo, and J. Zuñiga.** 1992. Comparative efficiency of two quinolones against natural infection by *Actinobacillus pleuropneumoniae*. *In* Proceedings of the 12th Annual Meeting of the International Pig Veterinary Society. Animal Health Service, Boxtel, The Netherlands.
8. **Eaves, L. E., P. J. Blackwell, and M. Fegan.** 1989. Characterization and antimicrobial sensitivity of haemophili isolated from pigs. Aust. Vet. J. **66:** 1–4.
9. **Fales, W. H., L. G. Morehouse, K. R. Mittal, C. Bean-Knudsen, S. L. Nelson, L. D. Kintner, J. R. Turk, M. A. Turk, T. P. Brown, and D. P. Shaw.** 1989. Antimicrobial susceptibility and serotypes of *Actinobacillus* (*Haemophilus*) *pleuropneumoniae* recovered from Missouri swine. J. Vet. Diagn. Invest. **1:**16–19.
10. **Fales, W. H., J. R. Turk, M. A. Miller, C. Bean-Knudssen, S. L. Nelson, L. G. Morehouse, and H. S. Gosser.** 1990. Antimicrobial susceptibility of *Pasteurella multocida* type D from Missouri swine. J. Vet. Diagn. Invest. **2:**80–81.
11. **Farrington, D. O.** 1986. Pneumonic pasteurellosis, p. 436–444. *In* A. D. Leman, B. Straw, R. D. Glock, W. L. Mengeling, R. H. C. Penny, and E. Scholl (ed.), Diseases of swine, 6th ed. Iowa State University Press, Ames.
12. **Fedorka-Cray, P. J., L. J. Hoffman, W. C. Cray, Jr., J. T. Gray, S. A. Breisch, and G. A. Anderson.** 1993. *Actinobacillus* (*Haemophilus*) *pleuropneumoniae*. Part I. History, epidemiology, serotyping, and treatment. Comp. Continuing Ed. **15:**1447–1454.
13. **Food and Chemical News.** 1994. Limited fluoroquinolone use in food animals endorsed by advisory groups. Food Chem. News, 23 May, p. 6–9.
14. **Friendship, R. M.** 1993. Antimicrobial drug use in swine. *In* J. F. Prescott and J. D. Baggot (ed.), Antimicrobial therapy in veterinary medicine. Iowa State University Press, Ames.
15. **Gilbride, K. A., and S. Rosendal.** 1984. Antimicrobial susceptibility of 51 strains of *Haemophilus pleuropneumoniae*. Can. J. Comp. Med. **48:**47–50.
16. **Gutiérrez, C. B., S. Píriz, S. Vadillo, and E. F. Rodríguez Ferri.** 1992. *In vitro* activity of 22 antimicrobial agents against *Actinobacillus pleuropneumoniae* strains isolated in Spain. *In* Proceedings of the 12th Annual Meeting of the International Pig Veterinary Society. Animal Health Service, Boxtel, The Netherlands.
17. **Gutiérrez, C. B., S. Píriz, S. Vadillo, and E. Rodríguez-Ferri.** 1993. In vitro susceptibility of *Actinobacillus pleuropneumoniae* strains to 42 antimicrobial agents. Am. J. Vet. Res. **54:**546–550.
18. **Hannan, P. C. T., P. J. O'Hanlon, and N. H. Rogers.** 1989. *In vitro* evaluation of various quinolone antibacterial agents against veterinary mycoplasmas and porcine respiratory bacterial pathogens. Res. Vet. Sci. **46:**202–211.
19. **Henry, S. C.** 1986. Evaluating the alternative therapies for swine respiratory disease. Vet. Med. **81:**763–770.
20. **Hommez, J., L. A. Devriese, F. Castryck, and C. Miry.** 1991. Beta-hemolytic streptococci from pigs: bacteriological diagnosis. J. Vet. Med. **37:**441–444.
21. **Kim, B. H., and H. B. Kwon.** 1992. Effect of Linco-Spectin 44 premix in diets on the performance and the prevention of respiratory disorders and diarrhoea of weaners and growing-finishing pigs. *In* Proceedings of 12th Annual Meeting of the International Pig Veterinary Society. Animal Health Service, Boxtel, The Netherlands.
22. **National Committee for Clinical Laboratory Standards.** 1990. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, 2nd ed. Approved standards. NCCLS document M7-A2. National Committee for Clinical Laboratory Standards, Villanova, Pa.
23. **Nicolet, J.** 1986. *Haemophilus* infections, p. 426–433. *In* A. D. Leman, B. Straw, R. D. Glock, W. L. Mengeling, R. H. C. Penny, and E. Scholl (ed.), Diseases of swine, 6th ed. Iowa State University Press, Ames.
24. **Nielsen, R.** 1988. Seroepidemiology of *Actinobacillus pleuropneumonia*. Can. Vet. J. **29:**580–581.
25. **Ose, E. E.** 1987. *In vitro* antibacterial properties of EL-870, a new semisynthetic macrolide antibiotic. J. Antibiot. **40:**190–194.
26. **Prescott, J. F., and J. D. Baggot.** 1993. Fluoroquinolones. *In* J. F. Prescott and J. D. Baggot (ed.), Antimicrobial therapy in veterinary medicine. Iowa State University Press, Ames.
27. **Raemdonck, D. L., A. C. Tanner, S. T. Tolling, and S. L. Michener.** 1994. Antimicrobial susceptibility of *Actinobacillus pleuropneumoniae*, *Pasteurella multocida* and *Salmonella choleraesuis* isolates from pigs. Vet. Rec. **134:**5–7.
28. **Reams, R. Y., L. T. Glickman, D. D. Harrington, T. L. Bowersock, and J. L. Thacker.** 1993. *Streptococcus suis* infection in swine: a retrospective study of 256 cases. Part I. Epidemiologic factors and antibiotic susceptibility patterns. J. Vet. Diagn. Invest. **5:**363–367.
29. **Schultz, R. A.** 1986. Swine pneumonia: assessing the problem in individual herds. Vet. Med. **81:**757–762.
30. **Sensititre Systems Group.** 1991. Custom plate user manual. Sensititre, Westlake, Ohio.
31. **Smith, I. M., A. Mackie, and J. Lida.** 1991. Effect of giving enrofloxacin in the diet to pigs experimentally infected with *Actinobacillus pleuropneumoniae*. Vet. Rec. **129:**25–29.
32. **Stiplovits, L. G. Laber, D. G. C. Burch, and D. J. S. Miller.** 1992. Comparative studies of the antimicrobial sensitivity of mycoplasmas and bacteria isolated from the respiratory tract of swine. *In* Proceedings of 12th Annual Meeting of the International Pig Veterinary Society. Animal Health Service, Boxtel, The Netherlands.
33. **Touil, F., R. Higgins, and M. Nadeau.** 1988. Isolation of *Streptococcus suis* from diseased pigs in Canada. Vet. Microbiol. **17:**171–177.
34. **Turgeon, P. L., R. Higgins, M. Gottschalk, and M. Beaudoin.** 1992. Antimicrobial susceptibility of *Streptococcus suis* isolates in Quebec. *In* Proceedings of the 12th Annual Meeting of the International Pig Veterinary Society.

Animal Health Service, Boxtel, The Netherlands.
35. **Turgeon, P. L., R. Higgins, M. Gottschalk, and M. Beaudoin.** 1994. Antimicrobial susceptibility of *Streptococcus suis* isolates. Br. Vet. J. **150:**263–269.
36. **Turk, J. R., W. H. Fales, C. Maddox, M. Miller, L. Pace, J. Fischer, J. Kreeger, G. Johnson, S. Turnquist, J. A. Ramos, and H. S. Gosser.** 1992. Pneumonia associated with *Salmonella choleraesuis* infection in swine: 99 cases (1987–1990). J. Am. Vet. Med. Assoc. **10:**1615–1616.
37. **Watts, J. L., R. J. Yancey, Jr., S. A. Salmon, and C. A. Case.** 1994. A 4-year survey of antimicrobial susceptibility trends for isolates from cattle with bovine respiratory disease in North America. J. Clin. Microbiol. **32:**725–731.
37a. **Wegener, H. C.** Personal communication.
38. **Wegener, H. C., J. L. Watts, S. A. Salmon, and R. J. Yancey, Jr.** 1994. Antimicrobial susceptibility of *Staphylococcus hyicus* isolated from exudative epidermitis in pigs. J. Clin. Microbiol. **32:**793–795.
39. **Wilcock, B. P., and K. J. Schwartz.** 1992. Salmonellosis, p. 570–579. *In* A. D. Leman, B. E. Straw, W. L. Mengeling, S. D'Allaire, and D. J. Taylor (ed.), Diseases of swine, 7th ed. Iowa State University Press, Ames.
40. **Wilson, M. R., R. Takov, R. M. Friendship, S. W. Martin, I. MacMillan, R. R. Hacker, and S. Swaminathan.** 1986. Prevalence of respiratory diseases and their association with growth rate and space in randomly selected swine herds. Can. J. Vet. Res. **50:**209–216.
41. **Wray, C. Y., E. Beedell, and I. M. McLaren.** 1991. A survey of antimicrobial resistance in salmonellae isolated from animals in England and Wales during 1984–1987. Br. Vet. J. **147:**356–369.
42. **Yeh, J., and B. Kim.** 1992. Effect of enrofloxacin on post weaning diarrhea in pigs. *In* Proceedings of the 12th Annual Meeting of the International Pig Veterinary Society. Animal Health Service, Boxtel, The Netherlands.