Title: The efficacy of antibiotics to prevent respiratory diseases in swine: A protocol for a systematic review.

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Author contributions:
All authors contributed to the development of the review question and the methodology described in this proposal. JMS drafted the protocol, with input and final approval of all co-authors.

Registration:
This protocol is archived in the University of Guelph's institutional repository (The Atrium; https://atrium.lib.uoguelph.ca/xmlui/handle/10214/10046) and published online with Systematic Reviews for Animals and Food (SYREAF) available at: http://www.syreaf.org/. The systematic review will be reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines (Liberati et al., 2009). This protocol is reporting using the items (headings) recommended in the PRISMA-P guidelines (Moher et al., 2015).

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Introduction.

Rationale:

The treatment and prevention of infectious diseases in pigs is an important aspect of swine production worldwide. The prudent use of antimicrobials and other therapeutic drugs is a primary responsibility of swine producers and veterinarians and decisions surrounding the use of drug therapy include considerations such as cost, efficacy, and food safety. The World Health Organization has published numerous reports urging all stakeholders concerned with both food-producing animals and humans to establish recommended steps to enhance the prudent use of antimicrobials (WHO, 2015). Similarly, the Organization for Animal Health has also published recommendations and position statements regarding prudent use and risk management related to antimicrobial use in animals (OIE, 2017).

Respiratory diseases are an important cause of morbidity and mortality in intensively –reared pigs, leading to reduced swine welfare and economic losses due to reduced growth efficiency and the cost of treating illness (Sorenson et al., 2006). A variety of infectious disease agents are involved in respiratory disease in swine, including *Mycoplasma hyopneumoniae*, *Pasteurella multocida*, *Actinobacillus pleuropneumoniae*, swine influenza viruses, and porcine reproductive and respiratory syndrome virus (PRRSV) (Choi et al., 2003, Sorensen et al., 2006). Antibiotic therapy is used both to treat and to prevent respiratory diseases in pigs and there are numerous pathogenic organisms involved in all of the predominant swine respiratory diseases (Karriker, et al, 2012). However, while there are many studies that have assessed the efficacy of antibiotics for the prevention of pneumonia associated with one or more disease agent, they often report conflicting results, making decisions around treatment and prevention complex (Thacker and Minion, 2012).

Understanding the efficacy of antibiotics used to prevent respiratory diseases in swine is essential to optimizing their use; ineffective antibiotics should not be used for prevention or, if there are multiple efficacious antibiotics, then their importance to human medicine should be considered when making decisions on antibiotic use. Systematic reviews of randomized controlled trials, and network meta-analysis to provide input on relative antibiotic efficacy, will yield the highest level of evidence for efficacy of treatments under field conditions (Sargeant and O'Connor, 2014).

Objectives: The objective of this protocol is to describe the methods for a systematic review – network meta-analyses to address the question: "What is the efficacy of antibiotics to prevent respiratory disease in swine?"

The specific PICO elements, which will define the eligibility criteria, are as follows:

i. *Population:* Live swine at any stage of production.
ii. *Intervention:* Antibiotics licensed for use in swine administered parenterally, in the feed, or in the water at labelled therapeutic dose. Eligible antibiotics include any antibiotic licensed for use for respiratory disease in swine included in the OIE list of antimicrobial agents of veterinary importance[1] (see also appendix 1).
iii. *Comparator:* Placebo, untreated control group, or an alternative antibiotic treatment.
iv. *Outcomes:* The outcomes of interest are respiratory-related morbidity (as defined by the authors), mortality, and total antibiotic use over any period of time within the same production stage.

Methods

Eligibility criteria: In addition to eligibility criteria inherent in the PICO elements described above, eligibility includes publication in English. Both journal articles and other forms of research reports are eligible, provided they report the results of a primary research study with a

[1] OIE list of antimicrobial agents of veterinary importance (May 2015) available at: http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/Eng_OIE_List_antimicrobials_May2015.pdf

concurrent comparison group using an eligible study design and with a full text of more than 500 words.

Study designs eligible: Controlled trials with natural disease exposure (individual or cluster allocated) will be eligible for inclusion, although we will document the number of controlled trials with deliberate disease challenge and analytical observational studies at full text screening and also will identify the antibiotics used and whether any of the outcomes of interest were assessed for studies of these designs.

Information sources:

We will conduct the literature search in a range of relevant bibliographic databases and other information sources containing both published and unpublished literature. Table 1 presents the resources to be searched.

Table 1: Databases and information sources to be searched

Database / information source	Interface / URL
MEDLINE	PubMed
CAB Abstracts	CAB Interface
Science Citation Index	Web of Science
Conference Proceedings Citation Index – Science	Web of Science
Agricola	Proquest

The AASV maintains a searchable digital library of proceedings from the prominent swine conferences through the American Association of Swine Veterinarians website (Swine Information Library http://www.aasv.org/library/swineinfo/). Selected proceedings, as noted below, will be hand-searched for potentially relevant articles.

Resources to be searched on this site include proceedings from:
o AASV Annual Meeting (1999-2018)
o International Pig Veterinary Society Congress (2000, 2002, 2004, 2006, 2008, 2010, 2012, 2014, 2016, 2018)

A single reviewer will also search the USDA FDA FOI requests for antibiotics registered for prophylactic use for respiratory diseases of swine in the USA. A single reviewer will also check the reference lists of all included studies for any eligible studies that may have been missed by the database searches.

Search strategy:

A Science Citation Index (Web of Science) search strategy designed to identify studies of antibiotic use to prevent for respiratory disease in swine is presented in Table 2. The search strategy employs a multi-stranded approach to maximize sensitivity. The conceptual structure is as follows:

- Swine at any stage of production;

AND

- Antibiotics;

AND

- Respiratory outcomes

AND

- Disease prevention (as opposed to treatment)

Table 2: Search strategy to identify studies of antibiotics for the prevention of respiratory diseases in swine using Science Citation Index (Web of Science)

#1 TS= (swine OR pig* OR piglet* OR gilt* OR boar* OR sow* OR hog* OR wean* OR porcine NOT guinea) 910,721

#2 TS = (medicat* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR "anti-infect*" OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri*) 794,310

#3 TS = (amoxicillin OR amoxycillin OR ceftiofur OR danofloxacin OR enrofloxacin OR florfenicol OR gentamycin OR gentamicin OR lincomycin OR oxytetracycline OR penicillin OR spectinomycin OR streptomycin OR tilmicosin OR trimethoprim OR tulathromycin OR tylosin OR tildipirosin OR Neomycin OR Cefquinome OR Tylvalosin OR Phenoxymethylpenicillin OR Tiamulin OR Marbofloxacin OR Sulfadiazine OR Sulfamethazine OR Sulfadoxine OR Sulfamerazine OR Sulfapyridine OR sulfathiazole OR Tetracycline OR gamithromycin) 159,466

#4 TS = (ceffect OR ceftiocyl OR Baytril OR Kinetomax OR Marbox OR Forcyl OR Excede OR Excenel OR Naxcel OR Cevaxel OR Draxxin OR Zactran OR Zuprevo OR Lincomix OR Liquamycin OR Agrimycin OR Engemycin OR Nuflor OR Florkem OR “Agri-cillin” OR Depocillin OR Tylan OR Vetramoxin OR marobocyl OR “neo-chlor” OR “neo-tetramed” OR medprodex OR alamycin OR cyclosol OR “bio-mycin” OR oxymycine OR noromycin OR oxyvet OR oxy OR potencil OR parasail OR duphatrim OR Trimediazine OR tribrissen OR trimidox OR norovet OR borgal OR “dofatrim-ject” OR sulvit OR sulmed OR sulfavite OR sulfa OR onycin OR tetramed OR tiamulin OR denagard OR pulmotil OR tilmovet OR aivlosin OR sulfamed OR tetra) 61,748

#5 TS = (pneumonia OR pleuritis OR pleuropneumonia OR pleuropneumoniae OR respiratory OR SRD OR PRDC) 495,043

#6 TS = (prophyla* OR metaphyla* OR "meta-phyla*" OR “mass treatment” or “mass medication” or “blanket medication” or “blanket treatment” OR prevent* OR “in feed” OR “in-feed” OR “in-water” OR “in water” OR medicate) 1,822,316

#1 AND (#2 OR #3 OR #4) AND #5 AND #6 413

The search strategies will not be limited by date, language, or publication type.

We will conduct searches using each database listed in the protocol, translating the strategy appropriately to reflect the differences in database interfaces and functionality.

Study records:

Data management: We will download the results of searches in a tagged format, load them into bibliographic software (EndNote) and de-duplicate the citations. We will save results from resources that do not allow export in a format compatible with EndNote in Word or Excel documents as appropriate and manually de-duplicate. The de-duplicated search results will be uploaded into online systematic review software (DistillerSR®, Ottawa, ON, Canada). Reviewers will have training in epidemiology and in systematic review methods. Prior to both abstract and full-text screenings, data extraction, and risk of bias assessment, the reviewers assigned to each step will undergo training to ensure consistent data collection using the forms created in DistillerSR®.

Selection process: In the first round of screening, abstracts and titles will be screened for eligibility. Two reviewers will independently evaluate each citation for relevance using the following questions:

1) Is this a primary study evaluating the use of one or more antibiotics to prevent respiratory disease in swine?
   YES (neutral response), NO (EXCLUDE), UNCLEAR (neutral response)
2) Is there a concurrent comparison group? (i.e. controlled trial with natural or deliberate disease exposure or analytical observational study)?
   YES (neutral response), NO (EXCLUDE), UNCLEAR (neutral response)
3) Is the full text available in English? [language of publication can be included as a field in DistillerSR]
   YES (include for full text screening), NO (EXCLUDE), UNCLEAR (include for full text screening)

Citations will be excluded if both reviewers responded “no” to any of the questions. Any disagreements will be resolved by consensus. If consensus cannot be reached, the article will be marked as “unclear” and will advance to full text screening. A pre-test will be conducted by

all reviewers on the first 250 abstracts to ensure clarify of questions and consistency of understanding of the questions.

Following title/abstract screening, eligibility will be assessed through full-text screening, using the questions included below. Two reviewers will independently evaluate the full text articles, with any disagreements resolved by consensus. If consensus cannot be reached, a third reviewer will be used. A pre-test will be conducted by all reviewers on the first 10 full texts to ensure clarify of questions and consistency of understanding of the questions.

1) Is the full text available with > 500 words?
   YES (neutral response), NO (EXCLUDE)
2) Is the full text available in English?
   YES (neutral response), NO (EXCLUDE)
3) Eligible population: Does the study evaluate live swine?
   YES (neutral response), NO (EXCLUDE)
4) Eligible intervention: Does the study assess the use of one or more of the antibiotics of interest* for the PREVENTION of respiratory disease(s)?
   * One or more of the antibiotics licensed for respiratory disease at the labelled dose
   YES, at the approved dose (neutral response), YES, but at a different dose (EXCLUDE), NO (EXCLUDE)
5) Are at least one of the following outcomes described: respiratory disease related morbidity, mortality, antibiotic use.
   YES (neutral response), NO (EXCLUDE)
6) Is there a concurrent comparison group? (i.e. controlled trial with natural or deliberate disease exposure or analytical observational study)?
   YES (neutral response), NO (EXCLUDE)
7) Eligible study design: Is the study a controlled trial with natural disease exposure?
   Yes (moves to data extraction stage),
   No, the study is a controlled trial with deliberate disease induction (indicate the antibiotic(s) evaluated, but exclude from data extraction)
   No, the study is an observational study (indicate the antibiotic(s) evaluated but exclude, from data extraction)

Data collection process: Data will be extracted by two reviewers working independently. Any disagreements will be resolved by consensus or, if consensus cannot be reached, a third reviewer will be used. Authors will not be contacted to request missing data or to clarify published results. A form for data extraction will be created for this review in DistillerSR® and pre-tested on 4 full text articles to ensure question clarity.

Data items:

Study level data to be extracted include:

- Country where trial was conducted (if not stated, use country affiliation of corresponding author)
- Commercial versus research trials
- Number of herds enrolled in study
- Year(s) the study was conducted
- Months of data collection
- Stage(s) of production

Arm level data collected:

- Antibiotic name(s)
- Dose / route / frequency of administration
- Unit of allocation (individual, pen)
- Description of comparison group
- Number of animals enrolled
- Number of pens enrolled
- Number of animals / pens lost to follow up
- Number of animals / pens analyzed
- Any additional concurrent treatments given to both intervention groups.
- The approach used in the analysis to account for non-independent observations (not applicable, not reported, random effects, GEE, other)

Outcomes and prioritization:

- Respiratory-related morbidity,
- Mortality,
- Total antibiotic use,

These outcomes were prioritized based on their impact on animal health and welfare and their economic importance. Formal evaluation of these criteria for prioritization was not undertaken.

The specific outcome data, as described below, will be extracted only for experimental studies with natural disease exposure.

Outcome data to be collected:

1) Respiratory-related morbidity
    a. Case definition
    b. Time period for assessing outcome, frequency of outcome assessment
    c. Level at which outcome data were measured (animal / pen / herd)

2) Mortality
    a. Level at which outcome data were measured (animal / pen / herd)

b. Time period for assessing outcome

3) Total antibiotic use
    a. Measure used to define outcome
    b. Time period for assessing outcome
    c. Antibiotic(s) used

For each outcome, we will extract the possible metrics in the following order:

- 1st priority: Adjusted summary effect size ($_{adjusted}$ risk ratio or $_{adjusted}$ odds ratio, mean differences for continuous outcomes) and variables included in adjustment and corresponding precision estimate
- 2nd priority: Unadjusted summary effect size
- 3rd priority: Arm level risk of the outcome, or arm level mean of the outcome (continuous outcomes)
- Variance components.

Risk of bias in individual studies: Risk of bias will only be assessed for controlled trials with natural disease exposure. Risk of bias assessment will be performed at the outcome level for each outcome using the Cochrane risk of bias instrument (Higgins et all, 2016), with the signaling questions modified as necessary for the specific review question. The ROB-2.0 for clustered RCTs and individual RCTs will be used depending on the study design (Higgins et al., 2016). These tools are available at https://sites.google.com/site/riskofbiastool/welcome/rob-2-0-tool.

Data synthesis:

Network meta-analysis. Network meta-analysis (aka mixed treatment comparison meta-analysis) will be conducted for each outcome. Network meta-analysis will use the approach described by NICE Decision Support Unit technical document (Dias et al., 2014; O'Connor et al., 2013; O'Connor et al., 2016). The approach to reporting will use the PRISMA- NMA (http://www.prisma-statement.org/Extensions/NetworkMetaAnalysis.aspx). Planned a priori sub-group analyses will be conducted for randomized versus non-randomized trials.

Meta-bias(es): Small study effects ("publication bias") will be assessed for all antibiotic-comparator combinations where there are at least 10 studies in the meta-analysis. If feasible, we will use approaches to assessing publication bias in the network of evidence using previously proposed approaches (Mavridis et al., 2013; Mavridis et al., 2014).

Confidence in cumulative evidence: The quality of evidence for each outcome will be assessed using the approach proposed by GRADE (GRADE, 2015, Puhan et al., 2014), while also

considering the nature of the network meta-analysis (Jansen et al., 2011). If feasible, we will use the framework from the CINeMA platform for conveying the impact of risk of bias on the network performance.

Discussion:

This systematic review will provide a synthesis of the current evidence regarding the efficacy of antibiotics used to prevent respiratory diseases in swine. Results will be helpful for veterinarians and swine producers when making evidence-informed decisions regarding treatment options to reduce respiratory illness and death, and potentially reduce the need to use antibiotics to treat respiratory diseases. The results also will be helpful for identifying specific gaps in knowledge related to the efficacy of prophylactic antibiotics for respiratory disease to target additional research.

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Appendix 1: Antibiotics approved for use in swine from OIE list, with trade names and labelling

Antibiotic	Trade name	Dose
Amoxicillin	Vetramoxin LA	15 mg/kg twice, 48h apart
Amoxicillin (trihydrate)	amoxicillin SP	20 mg (16 mg amoxicillin trihydrate)/kg b.w. daily, equivalent to 1 g Amoxicillin SP/50 kg b.w./day, for 3-5 consecutive days.
Cefquinome	Ceffect 25 mg/ml Suspension for Injection for Cattle and Pigs (BAYER)	For respiratory disease administer 2 mg cefquinome/kg bodyweight (2 ml/25 kg bodyweight) once daily for 3 consecutive days.
Ceftiofur (cystalline free acid)	Excede® 100 Sterile Suspension (Pr) (Zoetis)	Give single dose in post-auricular region of neck of 5 mg ceftiofur equivalents/kg (1 mL/20 kg) b.w.
Ceftiofur (hydrochloride)	Ceftiocyl (Pr)(Vetoquinol), Cevaxel® RTU Sterile Suspension (Pr) (Ceva Animal Health). Excenel/Excenel RTU EZ	3 mg/kg b.w. (1 mL/17 kg b.w.). Repeat q24h for 3 treatments. Do not inject more than 10 mL/site // 3-5 mg/kg SID q3 days
Ceftiofur (sodium)	Ceftiofur Sodium for Injection (Pr) (Bio Agri Mix), Excenel® Sterile Powder (Pr) (Zoetis), Naxcel/Cevaxel	1 mL/17 kg (3 mg/kg) b.w. Repeat q24h for 3 treatments.
Danofloxacin		1.25 mg/kg SID 3 days
Enrofloxacin	Baytril 100 (Bayer), Kinetomax, Baytril Max, Baytril OneJect	Administer once, behind the ear, a S.C. dose of 7.5 mg/kg (0.75 mL/10 kg) b.w.
Florfenicol	Florkem® (Pr) (Ceva Animal Health), Nuflor® (Pr) (Merck Animal Health), Nuflor Swine injectible	15 mg/kg (2.25 mL/45 kg) b.w. in the neck only. Repeat in 48h.
Gamithromycin	Zactran	6 mg/kg once

Gentamycin (sulfate)	Gentamycin 50 / Gentamycin 100/ Genta-100	2 mg/kg to 5 mg/kg BID q 3days
lincomycin (hydrochloride)	Lincomycin 110 Premix (Bio Agri Mix)	Growing swine: 2 kg/tonne of complete feed (220 g lincomycin base/tonne). Feed as sole ration for 21d.
	lincomix 100/300 mg/ml)	5 mg/lb (2.27 mg/kg) once
	Lincomycin 44 Premix (Bio Agri Mix)	" "
	Lincomycin 44 G Premix (Bio Agri Mix)	Growing swine: 5 kg/tonne of complete feed (220 g lincomycin base/tonne). Feed as sole ration for 21d.
	Lincomix® 44 Premix (Zoetis)	" "
Marbofloxacin	Marbox/Marobocyl (100mg/ml)/Forcyl Swine (160mg/ml)	2 mg/kg SID q 3 days / 8mg/kg once
Neomycin sulfate, tetracycline	Neo-Chlor® (Pr) (Vetoquinol)	Swine and newborn piglets: 100 g, 10 kg sizes: Dissolve 4 g powder/170 mL water/45 kg b.w. as a drench or dissolve 200 g (2 pouches) powder/225 L water for 4-5d. 400 g size: Dissolve 4 g powder in 170 mL water/45 kg b.w. as a drench or dissolve 800 g (2 pouches)/900 L water for 4-5d.
	Neo-Tetramed (Medprodex)	Swine: 2 g/170 mL of water per 45 kg b.w. as a drench OR 100 g/225 L drinking water for 4-5 d. Newborn piglets: 4 g/60 mL water and give 5 mL/piglet q12h for 4-5d.
Oxytetracycline	Alamycin LA (Pr) (Vetoquinol), Cyclosol 200 LA (Dominion), Liquamycin LA-200® (Zoetis), Bio-Mycin® 200 (Pr) (Boehringer), Oxymycine LA (Zoetis), Noromycin LA (Kane Veterinary Supplies)	1 mL/10 kg (20 mg /kg) b.w as a single dose. Maximum 5 mL/injection site. 1 mL/10 kg (20 mg/kg) b.w. Maximum 5 mL/injection site. Pigs <10 kg b.w.: Give 1 mL/animal.

	liquamycin LA-200 (200mg/ml)/Agrimycin 200/Engemycin (100 mg/ml)	9 mg/lb (4.1 mg/kg) once / 5 mg/kg to 10 mg/kg once Individual treatment: 5 g/1,000 kg b.w. dissolved in water, q12h for 2-3d. Mass medication: 10 g/900 kg b.w. in drinking water consumed daily.
	Oxytetracycline HCl Soluble Powder 1000 (Bio Agri Mix)	Individual treatment: 5 g/1,000 kg b.w. dissolved in water, q12h for 2-3d. Mass medication: 10 g/900 kg b.w. in drinking water consumed daily.
	Oxyvet® 200 LA (Pr) (Vetoquinol)	`
	Oxy 250 (Medprodex)	1 g/25 kg b.w. q12h as a drench OR 2 g/4 L of water OR 100 g/200 L drinking water for 4-5d.
	Oxy 1000 (Jaapharm)	1 tsp/1,000 kg (2,200 lb.) b.w. for 3-4d.
	Oxyvet® 100 LP (Pr) (Vetoquinol), Oxymycine LP (Zoetis)	3 mL/45 kg b.w. q24h for 2-3d.
Penicillin	Agri-cillin / Depocillin 300 mg/ml	3000 units per lb SD q 4 days / 15 I.U./kg SID q 4 days
Penicillin (G procaine)	Depocillin® (Pr) (Merck Animal Health)	1 mL/20 kg b.w. (15,000 IU/kg b.w.) q24h until 2d after clinical signs disappear.
Phenoxymethylpenicillin (potassium)	Potencil 10% Premix for PigsBy CompanyPotencil 10% Premix for Pigss (Elanco Animal Health)	For oral administration after incorporation in pelleted feed or meal at an inclusion level of 2 kg Potencil per tonne of feed. This is approximately equivalent to 10 mg phenoxymethyl penicillin potassium per kg bodyweight daily.
Streptomycin (amphotericin B)	ParaSail™ (Merial)	Healthy swine >=3 weeks of age: 1 mL reconstituted vaccine.

Sulfadiazine	Duphatrim IS Injectible (Zoetis)	15mg of active ingredients per kilogram bodyweight (1ml per 16kg bodyweight) once by intramuscular or slow intravenous injection.
	Trimediazine 15% Premix for Medicating feeding stuff (vetoquinol)	Feed intake per day per kg bodyweight Inclusion rate per tonne of feed Up to 35 g --- 2.75–5.5 kg 35–40 g --- 2.50–5.0 kg 40–45 g ----2.25–4.5 kg 45–50 g---2.00–4.0 kg 50–55 g---1.75–3.5 kg 55–65 g---1.50–3.0 kg
	Tribrissen 48 % suspension for injection	1 ml per 32 kg (70 lb) body weight daily, i.e. equivalent to 15 mg active ingredients/kg body weight. In cases of severe infection the dose may be increased to 1.5 ml per 32 kg (70 lb) daily i.e. equivalent to 22.5 mg active ingredients/kg body weight.
Sulfadoxine (trimethoprim)	Trimidox (Pr) (Vetoquinol), Norovet TMPS (Pr) (Kane Veterinary Supplies), Borgal® (Pr) (Merck Animal Health), Dofatrim-ject (Pr) (Rafter 8)	1 mL/15 kg (16 mg/kg) b.w. q24h. Piglets <4.5 kg (10 lb): 0.5 mL maximum.
Sulfamerazine (in combo with: calcium chloride, calcium pantothenate, magnesium sulfate, niacinamide, potassium chloride, riboflavin (vitamin B2), sodium acetate, sodium chloride, sulfamerazine, sulfamethazine, sulfathiazole, vitamin A, vitamin B12, vitamin D3)	3-Sulvit (Pr) (Vetoquinol)	Dissolve 450 g (1 pouch)/2,700 L drinking water for 5-10d. Automatic proportioners: Stock solution: 450 g (1 pouch) of powder in 20.25 L of water. Medicates 2,700 L. Set to distribute 30 mL stock solution/4 L of water.
Sulfamerazine (electrolytes, sulfamethazine, sulfathiazole, vitamins	Sulmed Plus (Medprodex)	```
	Sulfavite (Dominion)	Sulfavite (Dominion)

Sulfamethazine	Sodium Sulfamethazine Solution 25% (Dominion), Sodium Sulfamethazine Solution 25% (P.V.L.), Sulfa 25% Solution (Bimeda-MTC)	25 mL/40 kg b.w. for first day, then reduce dose by 1/2 for next 3d.
	Sodium Sulfamethazine Solution 12.5% (Dominion)	2.5 mL/45 kg b.w. for first day, then reduce dose by 1/2 for next 3d.
Sulfamethazine (sulfathiazole)	Sulfa MT (Jaapharm), 2 Sulfamed (Medprodex	Group treatment: Dissolve 567 g in 10 L of water. Add this stock solution to 350 L of drinking water for the 1st day. For each of the next 5d, add the same quantity of stock solution to 500 L of drinking water. Individual treatment: Prepare either a 12.5% OR a 25% solution by dissolving 567 g or 1134 g, respectively, in water to make a total volume of 4.5 L. As a drench: 80 mL of 12.5% solution, OR 40 mL of 25% solution, per 50 kg b.w. the first day, and per 100 kg b.w. per day for the next 3d. Dosage calculations are based on a water consumption of 23-38 L/head/day. Herd medication: Dissolve 400 g (1 pouch)/8 L water. Add this to each 260 L of water on Day 1 and to each 355 L of water Days 2-4. Automatic proportioner: Set apparatus to deliver 30 mL stock solution/3.78 L water (1 oz/gal U.S.). Prepare stock solution by dissolving 400 g (1 pouch)/2 L water for Day 1 and 400 g (1 pouch)/2.8 L water Days 2-4.
	Sulfa-MT (Pr) (Vetoquinol), Sulfa 2 Soluble Powder (Dominion)	

	Powder 21 (P.V.L.)	Pre-mix 1 package in 11 L water. Add to each 400 L of drinking water on the first day, and to each 500 L on the second and subsequent days. Drench: Give 60 mL of a 12.5% solution OR 30 mL of a 25% solution per 34 kg b.w. Reduce dose by 1/2 on the second, third, and fourth days. 12.5% solution: Dissolve 1 package/4.5 L water 25% solution: Dissolve 2 package/4.5 L water.
Sulfapyridine (sulfamethazine, sulfathiazole)**	Neutral Sulfa (P.V.L.)	75 mL/4.5 L of water. Give treated water as sole source of drinking water for 3-5d. 400 g: Dissolve 1 g/25 kg b.w. q12h, given as a drench using a dose syringe or 2 g/4 L or 400 g (1 pouch)/800 L drinking water for 4-5d. 10 kg: Dissolve 1 g powder/25 kg b.w. q12h, given as a drench using a dose syringe or 2 g/4 L or 100 g/200 L drinking water for 4-5d. Automatic proportioner: 400 g: Set to distribute 30 mL/4 L drinking water (1 oz/gal U.S.). Prepare stock solution by dissolving 400 g (1 pouch)/6 L water. This will medicate 800 L drinking water. 10 kg: Set to distribute 30 mL/4 L drinking water (1 oz/gal U.S.). Prepare stock solution by dissolving 200 g/3 L water. This will medicate 400 L drinking water.
Tetracycline	Tetracycline 250 (Vetoquinol)	
	Tetracycline Hydrochloride (P.V.L.), Tetracycline Hydrochloride (Dominion)	2 tsp/2.5 L of water or milk.

	Onycin 1000 (Pr) (Vetoquinol), Tetra 1000 and 250 (Dominion), Tetramed 1000 and 250 (Medprodex)	1000: 1 g/100 kg b.w. q12h, given as a drench, OR 1 g/8 L of water, OR 25 g pouch/200 L of drinking water for 4-5d. Automatic proportioner: Set to distribute 30 mL/4 L drinking water (1 oz/gal). Prepare stock solution by dissolving 50 g powder/3 L water. This will medicate 400 L drinking water. 250: 1 g/25 kg b.w. q12h, given as a drench OR 2 g/4 L of drinking water, OR 1x100 g pouch/200 L, OR 1x400 g pouch/800 L of drinking water for 4-5d.
Tetracycline (neomycin sulfate)	Neo-Chlor® (Pr) (Vetoquinol)	Swine and newborn piglets: 100 g, 10 kg sizes: Dissolve 4 g powder/170 mL water/45 kg b.w. as a drench or dissolve 200 g (2 pouches) powder/225 L water for 4-5d. 400 g size: Dissolve 4 g powder in 170 mL water/45 kg b.w. as a drench or dissolve 800 g (2 pouches)/900 L water for 4-5d. Swine: 2 g/170 mL of water per 45 kg b.w. as a drench OR 100 g/225 L drinking water for 4-5 d. Newborn piglets: 4 g/60 mL water and give 5 mL/piglet q12h for 4-5d.
	Neo-Tetramed (Medprodex)	1000: 225 mg/100 lb b.w. q12h for 3-4d. 250: Swine: 2.5 g (5/8 tsp)/5 L water or milk for 4-5d. Newborn Piglets: 2 g (1/2 tsp)/32 mL water. Give 5 mL q24h for 3d.
	Tetra 1000 and 250(Jaapharm) and 55	55:Swine: 11.2 g/5 L water or milk for 4-5d. Newborn pigs: 8 g/28 mL water. Give 5 mL q24h for 3d.

Tiamulin	Tiamulin HF 10% (Bio Agri Mix)	1.65 kg/tonne feed. Feed as sole ration for 14d.
	Denagard™ 10% GF Premix (Pr) (Elanco (Novartis))	1.65 kg/tonne for 14d.
Tildipirosin	Zuprevo (40 mgéml)	4 mg/kg once
Tilmicosin	Pulmotil™ Premix (Pr) (Elanco (Novartis)), Tilmovet® Premix (Huvepharma AD)	1) 2 kg/998 kg (400 g tilmicosin/tonne) in complete feed. Feed for 21d, beginning ~7d before anticipated disease outbreak. Feed continuously as sole ration. 2)1 kg/999 kg (200 g tilmicosin/tonne) in complete feed. Feed for 21d, beginning ~7d before anticipated disease outbreak. Feed continuously as sole ration.
	Pulmotil™ AC (Pr) (Elanco (Novartis))	Administer continuously in drinking water for 5 consecutive days at a concentration of 200 mg tilmicosin/L (80 mL Pulmotil AC/100 L water), which is equivalent to a daily dose of 20 mg tilmicosin/kg b.w. for pigs that are drinking 10% of their body weight.
Trimethoprim (with sulfadoxine)	Trimidox (Pr) (Vetoquinol), Norovet TMPS (Pr) (Kane Veterinary Supplies), Dofatrim-ject (Pr) (Rafter 8)	1 mL/15 kg (16 mg/kg) b.w. q24h. Piglets <4.5 kg (10 lb): 0.5 mL maximum. Treat 2-3d after symptoms have subsided, 5d maximum.
	Borgal® (Pr) (Merck Animal Health)	3 mL/45 kg (16 mg/kg) b.w. q24h. Piglets <4.5 kg b.w.: 0.5 mL maximum.
Tulathromycin	Draxxin® 25 Injectable Solution (Pr) (Zoetis), Draxxin®100 Injectable Solution (Pr) (Zoetis)	2.5 mg/kg (1 mL/10 kg) b.w. in the neck.
Tylosin	Tylan™ 200 Injection (Pr) (Elanco (Novartis))	1/2-2 mL/45 kg (100 lb) b.w./day [2.2-8.8 mg/kg b.w. or 1-4 mg/lb b.w.].

Tylvalosin (tartrate)	Aivlosin® Water Soluble Granules (Pr) (Pharmgate Animal Health)	5 mg tylvalosin/kg b.w./day. Use continuously for 5 consecutive days.