



## High susceptibility of pig respiratory and systemic bacteria to HydroTrim®

### Trial description

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#### Objective

- ▶ Successful treatment of bacterial infections can only be achieved when bacteria are highly susceptible to corresponding antibiotics and antibiotic combinations.
- ▶ Sulfonamides and trimethoprim are classified by the European Medicines Agency (EMA) as category D, which promotes their use by veterinarians as first-line treatments compared to other families of antibiotics.
- ▶ Minimum Inhibitory Concentrations (MIC) were determined for sulfadiazine and trimethoprim (HydroTrim®), which are registered for treatment of diverse pig infections, to investigate the susceptibility of respiratory and systemic pathogens to sulfadiazine and trimethoprim alone and in combination (ratio 5:1).

#### Set-up

- ▶ Forty-nine pathogenic bacteria comprising 12 *P. multocida*, 14 *S. suis*, 13 *A. pleuropneumoniae*, and 10 *G. parasuis* were used for MIC determination (broth microdilution method).
- ▶ The Fractional Inhibitory Concentration Index (FICI) was determined and classified:
  - S = synergistic,  $FICI \leq 0.5$
  - P = partial synergistic,  $0.5 < FICI < 1$
  - AD = additive,  $FICI = 1$
  - I = indifferent,  $1 < FICI < 4$
  - AN = antagonistic,  $FICI \geq 4$

## Results

**Table 1.** MIC<sub>90</sub> values and MIC ranges (µg/ml) of sulfadiazine (SD) and trimethoprim (TMP) in single and combined administration against four bacteria species

Bacteria	MIC values	Sulfadiazine	Trimethoprim	SD-TMP (5:1 ratio)
<i>P. multocida</i>	MIC <sub>90</sub> Range	> 5120 2560->5120	256 128-256	<b>256</b> 256
<i>S. suis</i>	MIC <sub>90</sub> Range	> 5120 160->5120	256 64-256	<b>256</b> 4-256
<i>A. pleuropneumoniae</i>	MIC <sub>90</sub> Range	5120 80-5120	16 0.5-128	<b>4</b> 0.5-8
<i>G. parasuis</i>	MIC <sub>90</sub> Range	2560 10-5120	128 2-128	<b>32</b> 2-64

**Table 2.** Combination efficacy (ratio 5:1) between sulfadiazine and trimethoprim against four bacteria species

Bacteria	N° of isolates	Com eff. S	Com eff. P	Com eff. AD	Com eff. I	Com eff. AN
<i>P. multocida</i>	12	0%	0%	0%	100% (12/12)	0%
<i>S. suis</i>	14	71.4% (10/14)	0%	0%	21.4% (3/14)	7.1% (1/14)
<i>A. pleuropneumoniae</i>	13	61.5% (8/13)	7.7% (1/13)	0%	15.4% (2/13)	15.4% (2/13)
<i>G. parasuis</i>	10	60% (6/10)	20% (2/10)	0%	20% (2/10)	0%

S = synergistic, FICI ≤ 0.5; P = partial synergistic, 0.5 < FICI < 1; AD = additive, FICI = 1; I = indifferent, 1 < FICI < 4; AN = antagonistic, FICI ≥ 4

## Conclusions

- ▶ The MIC results reveal modifications and reductions in MIC<sub>90</sub> values and MIC ranges due to sulfadiazine/trimethoprim combined use.
- ▶ A synergistic effect of the combination sulfadiazine/trimethoprim was found for three tested pig pathogens.
- ▶ The results illustrate the importance that both molecules sulfadiazine and trimethoprim reach sufficiently the target tissue in the animal.