



Knowledge

Compatibility of Denagard® and CTC explained

SUMMARY

In order to resolve or eliminate health challenges, an understanding of how animal health products work, disease dynamics (e.g., disease epidemiology and pathology) and disease interaction coupled with pig flow within an operation, is needed. Scientific studies help determine the effectiveness

of animal health products and allow veterinary practitioners to make educated decisions about their use to control, treat or eliminate disease.

Denagard® (tiamulin) 10 and chlortetracycline (CTC) are approved for concurrent use to provide enteric and respiratory disease coverage, respectively. The compatibility of these products is demonstrated in the following pages

through an explanation of how tiamulin and CTC work at a molecular level. Several trials are reviewed to demonstrate the effectiveness of Denagard Plus CTC in controlling disease. In numerous situations, Denagard Plus CTC demonstrates broad-spectrum protection against a variety of swine pathogens.

Denagard® (tiamulin) 10 and chlortetracycline (CTC) are approved for concurrent use to provide enteric and respiratory disease coverage, respectively. At 35 grams of tiamulin per ton of feed, Denagard controls swine dysentery associated with *Brachyspira* (formerly *Serpulina* or *Treponema*) *hyodysenteriae*. At 400 grams of chlortetracycline per ton of feed, CTC treats enteritis caused by *Escherichia coli* and *Salmonella choleraesuis*, and bacterial pneumonia caused by *Pasteurella multocida*. Research shows that tiamulin concentrates well in tissues where the indicated organism resides.¹ Trial results also show that tiamulin and CTC do not interfere with each other or

adversely affect their ability to control and treat their indicated diseases.²

Molecular action

Understanding tiamulin's molecular binding site at the ribosomal level helps explain how tiamulin interferes with the protein production of a cell. Tiamulin binds at the 50S ribosomal subunit location called the peptidyl transferase center (PTC), where amino acids are linked together to produce the primary protein structure. This binding directly inhibits peptide bond formation, and consequently, the cell's ability to produce proteins. This binding inhibits cell growth because the cell cannot repair its protein structure.



Chlortetracycline binds at the 30S ribosomal subunit, thus interfering with transfer RNA at the initiation of protein translation from the messenger RNA. This action contributes to chlortetracycline's inhibition of protein synthesis. Based on a review by Hammer, tiamulin affects a different ribosomal subunit than CTC, thus providing complementary activity at the molecular level.³ The review also states that understanding protein synthesis and antimicrobial interaction at the molecular level helps provide support for the ability of Denagard Plus CTC to improve health and performance of pigs.³

In summary, tiamulin and CTC affect protein synthesis in different ways by altering the ability of microorganisms to assemble proteins.

Clinical trials involving disease treatment and control

Pasteurella multocida

A trial was conducted to evaluate the effectiveness of medicated feed containing Denagard Plus CTC for controlling swine pneumonia in an induced *P. multocida* infection model⁴ (Table 1).

Protocol:

- Barrows averaging 26 lbs. were placed on non-medicated feed or medicated feed containing Denagard Plus CTC.
- Three days later, the pigs received an intranasal instillation of a broth culture of *P. multocida* Type A.
- Eleven days after infection, pigs were euthanized and their lungs were examined for pneumonic lesions and cultured for *P. multocida*.

Results:

- The medicated feed was effective in controlling pneumonia due to *P. multocida*.
- Clinical signs of pneumonia, pneumonic lesion development and number of pigs positive by culture were all reduced in the medicated group (Table 1).
- The results demonstrated reductions in coughing, difficulty breathing and lung lesions in the medicated group.
- In addition, the results demonstrated improved daily gain, feed consumption and feed efficiency in the medicated group. By reducing the disease burden, medicated pigs were better able to perform more closely to their full potential.

Salmonella choleraesuis

A trial was conducted to evaluate the efficacy of medicated feed containing Denagard Plus CTC in an *S. choleraesuis* challenge⁵ (Table 2).

Protocol:

- Pigs averaging 38.8 lbs. were started on medicated feed containing Denagard Plus CTC.
- Pigs were infected with *S. choleraesuis* through drinking water.

Results:

- Medicated pigs outperformed the non-medicated pigs (Table 2).
- The results demonstrate improved mortality rates, average daily gain, average daily feed intake and feed efficiency in the medicated group. By reducing the disease burden, medicated pigs were better able to perform more closely to their full potential.

Brachyspira hyodysenteriae

A trial was conducted to evaluate the effect of medicated feed containing Denagard Plus CTC in controlling swine dysentery (*B. hyodysenteriae*)⁶ (Table 3).

	Non-medicated control	Medicated
Pig days with coughing, %	21.8	4.6 ^a
Pig days with dyspnea, %	15.7	1.1 ^a
Pigs with lung lesions due to <i>P. multocida</i> , %	70.0	25.0 ^a
Pigs with lung culture positive, for <i>P. multocida</i> , %	35.0	5.0 ^a
Average daily gain, lb.	0.950	1.354 ^a
Average daily feed, lb.	2.184	2.429 ^a
Feed/gain	2.294	1.792 ^a

- a. Medicated treatment significantly different from non-medicated control treatment ($P \leq .05$).

- Barrows averaging 26 lbs. body weight; five pigs/pen; four pens/treatment; 14-day trial; pigs infected three days after start of medication.

	Non-medicated control	Medicated
Mortality, %	10.0	0.0
Average daily gain, lb.	0.12	1.06 ^a
Average daily feed, lb.	1.38	2.34 ^a
Feed/gain	11.63	2.2 ^a

- a. Medicated treatment significantly different from non-medicated control treatment ($P \leq .05$).

- Pigs averaging 38.8 lbs. body weight; five pigs/pen; four pens/treatment; 14-day trial.

Protocol:

- Pigs averaging 30.3 lbs. were placed on medicated feed containing Denagard Plus CTC, Denagard alone or on non-medicated feed.
- Pigs were infected with *B. hyodysenteriae*.

Results:

- Treatment in all groups was limited to the first 14 days of the trial, but improvement in overall health in the group medicated with feed containing Denagard Plus CTC extended for the duration of the six-week trial.
- Both groups of medicated pigs had improved scores in all measured parameters including mortality rate, diarrhea score, diarrhea days and bloody feces (Table 3).
- The results also demonstrate improved average daily gain and feed efficiency in the medicated groups. By reducing the disease burden, medicated pigs were better able to perform more closely to their full potential.

Results from the field

Respiratory and enteric disease challenges are present in varying degrees even on the most well-managed farms. While these diseases may be subclinical much of the time, they still limit pig performance and profitability. Subclinical disease may become clinical when pigs are stressed from being weaned or handled, if their environments are changed, or when they are commingled. Critical periods to monitor disease include the first two weeks post-weaning in the nursery and the first two weeks after placement into the grow/finish barn.⁷ The cited studies demonstrate that strategically using Denagard Plus CTC during high stress periods in the growing herd allow pigs to achieve and maintain better performance.

A study by Campbell et al. emphasizes the value of utilizing

Table 3. Effect of medicated feed on swine dysentery (*B. hyodysenteriae*)

	Non-medicated control	Denagard	Denagard Plus CTC
Diarrhea score (0-3)	0.79 ^a	0.044	0.014
Pig days with diarrhea, %	50.5 ^a	3.2	1.1
Pig days with bloody feces, %	21.3 ^a	0.1	0.0
Mortality, %	36.7 ^a	0	0
Average daily gain, lb.	0.32 ^a	1.25	1.32
Average daily feed, lb.	1.42 ^a	2.99	3.03
Feed/gain	4.444 ^a	2.421	2.309

- a. Non-medicated control group significantly different from medicated group (P ≤ .01).
- Pigs averaging 30.3 lbs. body weight; five pigs/pen; six pens/treatment; 42-day trial; medicated days 0-14 only.

Table 4. Percent improvement in performance of average daily gain (Non-medicated control serves as a benchmark for Trials 1-4, carbadox serves as a benchmark for Trial 5)*

	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
Non-medicated control	0% ^a	0% ^a	0% ^a	0% ^a	NT
Carbadox	- 9.1% ^a	19% ^b	0.08% ^{b,c}	NT	0% ^a
Tylosin and sulfamethazine	NT	NT	0.07% ^b	0.03% ^{a,b}	NT
Neomycin and oxytetracycline	13% ^{a,b}	NT	NT	0.03% ^{a,b}	-9.7% ^a
Denagard and CTC	41% ^b	36% ^c	11% ^c	0.07% ^b	13% ^b
P value	< .05	< .01	< .10	< .02	< .06

- * Adapted from Campbell et al.⁸
- a,b,c. Values in same column with different superscripts are significant at P ≤ .06, with the exception of Trial 3.
- NT – Not tested in trial.

Table 5. Summary of growth trial with feeder pigs commingled from two sources

	Non-medicated control	Denagard Plus CTC	Carbadox
Average daily gain, lb.	1.151 ^a	1.422 ^b	1.276 ^c
Average daily feed intake, lb.	2.272 ^a	2.53 ^b	2.401 ^{ab}
Feed/gain	1.982 ^a	1.774 ^b	1.885 ^{ab}
% test days with diarrhea	45.6 ^a	23.3 ^b	47.8 ^a

- a,b,c. Values in same row with different superscripts are significant at P ≤ .05.
- Pigs averaging 32 lbs. body weight; six pigs/pen; six pens/treatment; 14-day trial; pigs commingled from two sources.

antimicrobials to offer broad-spectrum activity against both enteric and respiratory pathogens in weanling pigs derived from both high-health status herds and conventional health pigs⁸ (Table 4).

Protocol:

- All five trials were conducted in the first two weeks post-weaning.

- Trial 1 – Conventionally weaned pigs averaging 13.8 lbs. were placed on standard nursery diet; mild post-weaning diarrhea occurred naturally.
- Trials 2, 3 and 4 – Terminal cross barrows and gilts were weaned at 16-18 days of age and moved off-site to a nursery building; minimal clinical disease was observed.
- Trial 5 – Terminal cross pigs

were weaned at 18 days of age and moved into nursery rooms on an all-in/all-out basis; natural exposure to existing enteric and respiratory pathogens occurred, but no clinical signs were observed.

Results:

- Trial 1 – The only treatment group to have a significant reduction in diarrhea was the group receiving medicated feed containing Denagard Plus CTC.
- Trial 1 – Collectively, the data demonstrates improved average daily gain in the medicated groups receiving Denagard Plus CTC.
- Performance was positively impacted in all trials regardless of perceived health status.

A trial by Anderson et al. with commingled feeder pigs was conducted to evaluate performance of pigs treated with Denagard Plus CTC against non-medicated pigs and pigs treated with carbadox⁷ (Table 5).

Protocol:

- Feeder pigs from two sources were trucked approximately 30 and 100 miles, respectively, to the test site.
- Three pigs from each source were allotted to each pen on the basis of weight and gender.
- Average initial weight was 32 lbs.
- Pigs were observed daily and rated for diarrhea.
- Pigs were provided with feed containing carbadox, Denagard Plus CTC or no medication.

Results:

- The data demonstrates increased average daily gain in the medicated groups, however, pigs receiving medicated feed containing Denagard Plus CTC had significantly higher average daily gains compared to the pigs given carbadox or non-medicated controls (Table 5).
- Only pigs receiving Denagard Plus CTC had improvements in feed consumption and feed efficiency, and diarrhea scores compared to non-medicated controls.
- By reducing the disease burden, medicated pigs receiving Denagard Plus CTC were better able to perform more closely to their full potential.

Denagard Plus CTC – a valuable tool for producers

Throughout these trials, there was consistent improvement in performance – average daily gain, average feed intake and feed to gain ratio – regardless of health status among medicated pigs.



By reducing the disease burden, medicated pigs were better able to perform more closely to their full potential.

Denagard Plus CTC offers:

- Powerful broad-spectrum activity from two antibiotics, whose individual action complements each other.
- Enteric and respiratory disease control, respectively.
- Convenience of feed medication.
- Strategic applications for cost-effective performance.

Strategically used during the high-stress periods such as post-weaning or at times of health challenges in a grow/finish unit, Denagard Plus CTC allows pigs to achieve and maintain better performance.

Caution: Do not feed Denagard 10 undiluted. Do not use in feeds for animals other than swine. Not for use in swine weighing over 250 lbs.

Contraindications: Swine being treated with Denagard (tiamulin) should not have access to feeds containing polyether ionophores (e.g., lasalocid, monensin, narasin, salinomycin and semduramicin) as adverse reactions may occur.

Warning: Observe label withdrawal times.

See product label for directions for use and additional information.

1. Anderson MD, Stroh SL, Rogers S. Tiamulin (Denagard®) activity in certain swine tissues following oral and intramuscular administration. AASV. 1994.
2. Freedom of Information Summary, NADA 140-011. Denagard® 10; chlortetracycline premixes. August 1996.
3. Hammer M. Concurrent applications of Denagard/Tiamulin and Tetracyclines – control of mycoplasmal and mixed respiratory infections in practice. IPVS. 2006.

4. Data on file. Novartis Animal Health US, Inc.
5. Data on file. Novartis Animal Health US, Inc.
6. Data on file. Novartis Animal Health US, Inc.
7. Anderson M, Campbell J, Walter D. Comparative performance of selected feed medications during critical production periods in SEW and conventional pigs. AASV. 1997.

8. Campbell J, Walter D, Prince TJ, Haydon K, Risley CR, Sweet LA, Williams N. Comparative productivity and health status of SEW nursery pigs fed different type of dietary antimicrobials. IPVS. 1998.



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