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A Comparison of Potential Oxytetracycline Hydrochloride Immersion-Marking Solutions And Their Effect on Water Acidification

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Addendum: In January 2011, one of the products tested in this study (Pennox® 343) was approved by FDA's Center for Veterinary Medicine for the skeletal marking of finfish fry and fingerlings.

Oxytetracycline hydrochloride (OTC) water soluble powder is approved in the USA for use in the skeletal marking of finfish fry and fingerlings by immersion at dosages of 200 - 700 mg per L active OTC for 2 - 6 h. The three approved OTC products distributed in the USA for finfish are *Oxytetracycline HCl Soluble Powder-343* (75.6% active OTC; Phoenix Scientific, Inc., St. Joseph, Missouri USA 64503; ANADA 200-247); *Terramycin-343*® (75.6% active OTC; Pfizer, Inc., New York, New York USA 10017; NADA 008-622); and *TETROXY*® *Aquatic Soluble Powder* (36.6% active OTC; Cross Vetpharm Group Ltd., Dublin, Ireland; ANADA 200-460). As OTC is an acidic compound, it must be buffered to prevent or minimize mortality in treated fish due to low pH. Methods for using anhydrous sodium phosphate dibasic as a buffer have been well-documented and recommended (Fielder 2002; Carty et al. 2007).

At the time of this publication, two of the three above-referenced approved products for use in fish are currently not being marketed, and the remaining product is not being used as it results in excessive acidification of treatment water. This situation jeopardizes USA fisheries programs that depend on immersion skeletal-marking operations to assess their natural resource conservation and management goals. Several generic versions of the pioneer product (*Terramycin-343*®; NADA 008-622) exist on the market, but presently their labels do not contain indications for fish. This study was conducted to determine the effect two generic OTC products have on the pH of different source waters as compared to the effect produced by *Terramycin-343*®. It was intended that data generated from this study could be used to help identify a new, suitable OTC product(s) for potential future approval and labeling for the skeletal marking of finfish.

Methods

Test articles were (a) *Pennox*® *343* (PennField Animal Health, 14040 Industrial Road, Omaha, Nebraska USA 68144; ANADA 200-026), (b) *Agrimycin*®*-343* (Agri Laboratories, Ltd., P.O. Box 3103, St Joseph, Missouri USA 64503; ANADA 200-066), and (c) *Terramycin-343*® (Pfizer, Inc., 235 East 42nd St., New York, New York USA 10017; NADA 008-622). All test articles contained 102.4 g active OTC per 135.5 g premix (i.e., 75.6% active OTC). Two different source waters were used in the study. One source water was 100% Bozeman Fish Technology Center (BFTC) warm spring water (20±1°C), while the other source water was 50% BFTC warm spring water mixed with 50% de-ionized (DI) water. Each of the three test articles (7.04g) was added to 2-gal samples of each source water (n = 6) to produce a non-buffered, 700 mg per L active OTC solution. The pH of each source water sample was measured using an YSI EcoSense pH and Temperature Pen (YSI Inc., Yellow Springs, Ohio USA) before and after each test article was added and mixed. The percent differences (to the nearest 0.1%) in pH measurements between source water and OTC solution were used to draw comparisons among the three test articles with respect to water acidification.

Results

In all treatment groups, pH decreased after OTC was added to obtain a 700 mg per L active solution (Table 1). For all three test articles, the pH changes observed in the source water with a higher natural buffering capacity (100% BFTC warm spring water; 159 mg per L $CaCO_3$) were more gradual and of less magnitude (mean difference, 28.5%; SD±2.0%) than pH changes observed in the source water with a moderate natural buffering capacity (50% BFTC warm spring water mixed with 50% DI water; 80 mg per L $CaCO_3$; mean difference, 54.6%; SD±1.4%). The patterns and magnitude of change in pH observed in this study parallel those reported in a study conducted by Carty et al. (2007) evaluating one of the currently approved OTC products, *Oxytetracycline HCl Soluble Powder-343*.

Discussion

As OTC is an acidic compound, it was anticipated that all treatments would result in a decrease in pH of source water. It was also anticipated, and observed, that the natural buffering capacity of source water would affect the magnitude

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of observed pH change. Although it was unknown to what extent each of the products tested would decrease pH, it is interesting to note that all products tested (each of which contained 75.6% active OTC; 343 g active OTC per 454 g premix) decreased pH of source water by a similar magnitude when used to achieve a 700 mg per L active OTC solution. Hence, as *Terramycin-343®* has a relatively long history of successful use in aquaculture as an immersion skeletal marking agent, it would appear that both *Pennox® 343* and *Agrimycin®-343* would in fact be suitable candidates for potential future expanded approvals for similar use as immersion skeleton marking products.

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References

Carty, D., J.D. Bowker, M.P. Bowman, and B. Johnson. 2007. Buffering oxytetracycline hydrochloride immersion-marking solutions with sodium phosphate dibasic. *Drug Research Information Bulletin No. 1*. U.S. Fish & Wildlife Service, Aquatic Animal Drug Approval Partnership, Bozeman, Montana USA.

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Note

At the time of this publication, and due in part to the results observed in this study, PennField Animal Health is currently in the process of expanding their current label for *Pennox® 343* to include use for skeletal marking of finfish fry and fingerlings.

Table 1. Change in pH of source water following administration of test articles to achieve a 700 mg per L active OTC solution.

Source Water; Drug	TA[1]	pH Reduction	% pH Difference
High TA[2]; **without** Pennox®-343	159	2.50	30.5%
High TA; **with** Pennox®-343	159		
Low TA[3]; **without** Pennox®-343	80	4.23	56.0%
Low TA; **with** Pennox®-343	80		
High TA; **without** Agrimycin®-343	159	1.98	26.6%
High TA; **with** Agrimycin®-343	159		
Low TA; **without** Agrimycin®-343	80	3.73	53.1%
Low TA; **with** Agrimycin®-343	80		
High TA; **without** Terramycin-343®	159	2.24	28.5%
High TA; **with** Terramycin-343®	159		
Low TA; **without** Terramycin-343®	80	3.92	54.5%
Low TA; **with** Terramycin-343®	80		

[1] Total Alkalinity (mg per L as $CaCO_3$)
[2] High TA water is 100% warm spring water
[3] Low TA water is 50% warm spring water and 50% DI water