

Finding of No Significant Impact (FONSI)
for
TYLAN Soluble
(Tylosin tartrate)

in
Broiler Chickens

Elanco Animal Health
Greenfield, IN

The Center for Veterinary Medicine has considered the potential environmental impact of this action and has concluded that this action will not have a significant impact on the quality of the human environment and, therefore, an environmental impact statement will not be prepared.

Elanco Animal Health is requesting the approval of a supplemental new animal drug application (NADA) for the use of TYLAN Soluble (tylosin tartrate) for the control of mortality caused by necrotic enteritis associated with *Clostridium perfringens* in broiler chickens. The product would be administered orally in drinking water at a concentration of up to 375 ppm for five days and will be dispensed by prescription (Rx). In support of the application, Elanco Animal Health has provided an Environmental Assessment (EA) signed February 10, 2012. A copy of the EA is attached.

The EA consists of an exposure and effects assessment that generally follows the recommendations presented in Guidance for Industry (GFI) 89 (Environmental Impact Assessments for Veterinary Medicinal Products – Phase I (GL6)) and GFI 166 (Environmental Impact Assessments for Veterinary Medicinal Products – Phase II (GL38)). These guidance documents were developed by the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Products (VICH). The EA describes the proposed use of the product, the chemical characteristics of tylosin tartrate, its fate in the environment, effects to terrestrial and aquatic organisms, and risk characterization.

Tylosin is metabolized to a certain extent within chickens. After dosing chickens with ¹⁴C-tylosin, the parent compound and various metabolites were identified in excreta including tylosin factors A, B, D, 20-dihydrodesmycosin, and unidentified polar compounds. When the biological potencies of tylosin factors A, B, D, and 20-dihydrodesmycosin were taken into account, it was conservatively estimated that 25% of tylosin factor A equivalent potency was lost through metabolism.

Tylosin was also found to degrade in chicken manure and soil. In an aerobic manure degradation study, tylosin factors A, B, C, and D were not detected after 30 days. Although this study did not examine the presence of other degradation products, it does demonstrate that the tylosin factors degraded rapidly in chicken manure. In soils, the sum of tylosin factors A, B, C, and D degraded slowly (20% to 30% degradation after 120 days). Due to the rapid degradation of tylosin factors in manure, and the eventual degradation in soil, accumulation in soil is not expected to occur.

The predicted environmental concentrations for tylosin in soil (PEC_{soil}) and water (PEC_{water}) were calculated based on the expected use of the product and metabolism data. The PEC_{soil} and PEC_{water} were calculated to be 379 $\mu\text{g}/\text{kg}$ and 4.3 $\mu\text{g}/\text{L}$, respectively.

Terrestrial toxicity studies on tylosin were conducted for plants (tomato, soybean, oat), earthworms, and soil microorganisms. Aquatic toxicity studies were conducted on algae (*Pseudokirchneriella subcapitata*), the water flea (*Daphnia magna*), and rainbow trout (*Oncorhynchus mykiss*). Based on the results of these toxicity tests, the most sensitive terrestrial and aquatic species were tomato (based on emergence data) and algae. The calculated predicted no effects concentrations (PNEC) for these two species were 430 $\mu\text{g}/\text{kg}$ and 9.9 $\mu\text{g}/\text{L}$, respectively. Based on this data, the corresponding risk quotients, defined as the $PEC/PNEC$ ratio, were 0.88 (tomato) and 0.43 (algae). These risk quotients are below a value of one, indicating little or no potential for effects on terrestrial and aquatic organisms.

Based on available information, no significant environmental impacts are expected from the proposed use of tylosin tartrate in broiler chickens.

{see appended electronic signature page}

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Enclosure:
Environmental Assessment for the Use of Tylosin Tartrate for Control of Necrotic Enteritis in Broiler Chickens

Electronic Signature
Addendum for Submission ID

Signing Authority (Role)	Letter Date
Elizabeth Rettie (Office Director) - Acting	4/13/2012

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