

**Environmental Assessment**

**for**

**Tylosin**

**for**

**Prevention and Treatment of American Foulbrood  
Disease (AFB) in Honey Bees**

USDA  
National Research Support Program-7

January 28, 2003

For Public Display  
HFV-305



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
Rockville MD 20857

January 28, 2003

Dr. Gregg Claycamp  
Environmental Safety Team  
HFV-103  
FDA/Center for Veterinary Medicine  
7519 Standish Place  
Rockville, MD 20855

re: INAD 10-772

Dear Dr. Claycamp:

The NRSP-7 would like to address the environmental component of our project investigating the use of tylosin for the prevention and treatment of American foulbrood disease (AFB) of honey bees. This project is coordinated by Dr. Arthur Craigmill, the Animal Drug Coordinator for NRSP-7's Western Region.

**PROPOSED USE**

The recommended dose is 200 mg of tylosin per hive once weekly for 3 weeks. The dosage form to be used is the water soluble powder. The powder is mixed with confectioner's sugar and dusted into the hive across the tops of the frames. This provides oral administration as the bees ingest the sugar and drug as part of their 'housekeeping'. The antibiotic/sugar mixture is cleaned up within 24 hours of administration. These worker bees then feed the larvae thus administering the drug to the affected part of the hive. American Foulbrood is a bacterial disease affecting the larvae.

**RATIONALE**

The use of tylosin to treat American Foulbrood in honey bees will be a very small use as compared to other approved uses in major species. Tylosin is approved under 132 NADAs (some of these have been voluntarily withdrawn) alone and in combination. The following are representative formulations, species, and dosages for the most significant NADA approvals.

Tylosin tartrate:

Formulation	Species	Dose	Duration
Soluble powder	Chickens	50 mg per lb BW	1 to 5 days as sole source of water
	Turkeys	60 mg per lb BW	2 to 5 days as sole source of water
	Swine	250 mg/gallon of drinking water	3 to 10 days as sole source of water

Tylosin phosphate:

Formulation	Species	Dose	Duration
Type A Medicated Article	Cattle	8 to 10 g per ton of feed	Feed continuously
	Swine	10 to 100 g per ton of feed	3 days to 6 weeks (depends on claim)

Tylosin:

Formulation	Species	Dose	Duration
Injection (IM)	Cat	3 to 5 mg/lb BW	Up to 5 days, once or twice per day
	Dog	3 to 5 mg/lb BW	Up to 5 days, once or twice per day
	Cattle	8 mg/lb BW	Up to 5 days, once daily
	Swine	4 mg/lb BW	Up to 3 days, twice daily

REGULATORY OPTIONS

This proposed use does not clearly qualify for a categorical exclusion from the requirement to provide an environmental assessment (21 CFR 25.33). Although bees are a minor species, there is no directly comparable major species using similar management practices (21 CFR 25.33 (d) (4)).

Alternatively, we propose that the VICH Guidance #89, Environmental Impact Assessments (EIA's) for Veterinary Medicinal Products (VMP's) – Phase 1, be used to determine that this use can be limited to a Phase I assessment. The criterion that qualifies this proposed use is described in Question 17. "Is the predicted environmental concentration of the VMP in soil ( $PEC_{soil}$ ) less than 100 ug/kg?" The guidance states, "This value is below the level shown to have effects in ecotoxicity studies conducted on earthworms, microbes, and plants with VMPs currently registered in the US." The guidance concludes that if the calculated  $PEC_{soil}$  value for the VMP entering the environment is less than 100 ug/kg, then the VMP may stop at Phase I.

CALCULATIONS

We are assuming that bees correspond to 'pasture animals' since they range over a large area gathering nectar and are not confined to their hives. The guidance states "The  $PEC_{soil}$  estimate for a VMP excreted onto pasture assumes direct entry into soil with even distribution in the upper 5 cm of soil. This estimate for whole herd/flock treatments is based upon:

- (1) dose/animal based on mg/kg and body-weight of animal;
- (2) percentage of dose excreted by the treated animals (use 100% if no excretion data are available);
- (3) stocking density of treated animals (animals/hectare);
- (4) excreted VMP is distributed in soil to 5 cm; and
- (5) bulk density of soil. Effectively, this means that for a soil bulk density of 1,500 kg/m<sup>3</sup>, the total dose/hectare is distributed in 750,000 kg of soil."

For the following questions, information has been gathered from *The New Complete Guide to Beekeeping* by Roger A. Morse (The Countryman Press, Woodstock, VT 1994).

- (1) Dose/animal – The dose per bee can be estimated for an average hive number. An optimum colony contains 50,000 to 60,000 bees (p. 68). The proposed dose is 200 mg of tylosin per hive once weekly for 3 weeks. This becomes 0.004 mg of tylosin per bee per treatment assuming 50,000 bees in the hive.
- (2) Percentage of dose excreted by the treated animals - We will assume 100%.
- (3) Stocking density (animals/hectare) – “While it is true that a bee may fly as much as eight or nine miles, if necessary, to collect pollen and nectar, research shows that colonies that gather most of their food within a half-mile radius prosper much more than those whose field force must fly further.” (p. 20). One-half mile = 2640 ft. The area of a circle with that radius = 21,884,544 sq ft. An acre = 43,560 sq ft. A hectare = 2.471 acres. Therefore, a hectare = 107,636.76 sq ft. This makes the range of the bees 203.32 hectares. The stocking density then becomes 245.9 bees per hectare per hive.
- (4) Assume that the excreted VMP is distributed in soil to 5 cm.
- (5) If we assume a soil bulk density of 1,500 kg/m<sup>3</sup>, the total dose per hectare is distributed in 750,000 kg of soil. If we assume the total dose administered to the hive is distributed over the calculated 203.32 hectares, then 200 mg per treatment would be distributed over this area. The prescribed 3 treatments would provide a total of 600 mg distributed over the area. This would reduce to 2.95 mg per hectare or 750,000 kg of soil or 0.000003935 mg/kg. This is the equivalent of 0.003935 ug/kg of soil. Since this is considerably below the 100 ug/kg threshold, this environmental impact assessment is limited to Phase I.

The number of hives per acre for pollination ranges from 1 to 5 depending on the crop to be pollinated and the number of other wild pollinators available. Some information about this is attached. Hives are also often placed in one location in a large orchard since the bees have a considerable range. If all 5 hives were treated for the 3 treatments, we can assume that the total exposure would increase five-fold. This is actually not likely since the bees probably range over a larger area. In any case, this exposure would still be only 0.01973 ug/kg of soil. Again, this is well below the threshold value.

It should also be kept in mind that for human food safety reasons, treatment will not be administered during the time that the bees are producing honey. The label will advise that the drug should be applied in early spring or the fall and consumed by the bees before the main honey flow to avoid contamination of the production honey. The use will be discontinued at least 6 weeks prior to main honey flow. This means that the bees are unlikely to have an opportunity to contaminate the areas they pollinate.

We believe that this use will not present a danger to the environment and that these calculations should complete the environmental component for a new animal drug application for this indication.

Please feel free to contact me if you have any questions.

Sincerely,

*Meg R. Oeller, DVM*

Meg R. Oeller, D.V.M.  
FDA Liaison to NRSP-7

Attachments

cc: ADR 217  
Craigmill