# FINDING OF NO SIGNIFICANT IMPACT

for

## IVOMEC SR Bolus for Cattle

## NADA 140-988

**Merck & Co., Inc.**
**Rahway, NJ**

**FOR PUBLIC DISPLAY**

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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 that, therefore, an environmental impact statement will not be prepared.

Merck & Co. Inc. has submitted a new animal drug application for IVOMEC SR Bolus as a treatment for the control of endo- and ectoparasites in cattle weighing 125-300 kg. The bolus provides for the sustained release of ivermectin into the rumen/reticulum at a uniform rate of approximately 12 mg/day for about 135 days. The bolus is targeted at beef (cow/calf operations) and dairy (replacement cattle) calves, and stocker cattle within the allowed weight range in pasture environments. In support of the application, Merck & Co. has submitted an Environmental Assessment (EA), dated October 15, 1996, for the manufacture and use of IVOMEC SR Bolus as required under 21 CFR 25.31a(a) for new animal drug applications. The EA describes use patterns for the SR Bolus in targeted cattle weighing between 100 and 300 kg. After the development of the use pattern data, the permitted weight class was changed to 125 - 300 kg. This change does not alter the validity or conclusions of the EA.

The EA provides information on environmental introductions of the drug substance, ivermectin, due to manufacturing, emissions, and use of the product. The bulk drug substance (ivermectin) will be produced at Merck facilities in Danville, PA, Elkton, VA, and Barceloneta, Puerto Rico. The SR Bolus will be manufactured at the Merck facility in West Point, PA, and packaged at Merck facilities in West Point, PA, and Haarlem, Holland. Citations of applicable laws and regulations and certifications that the manufacturing sites are in compliance with applicable environmental and occupational safety requirements are provided. Material Safety Data Sheets (MSDS) for ivermectin and IVOMEC SR Bolus are provided.

Merck has submitted a data package to address potential environmental effects from the use of this product. The package contains environmental fate and effects studies for

ivermectin. These studies enable the sponsor to provide estimates of terrestrial and aquatic concentrations of ivermectin residues and to prepare an exposure assessment, based on physical/chemical and environmental fate data; and an effects assessment, based on a series of indicator organism toxicity tests. Environmental hazard assessments are provided for both aquatic and terrestrial ecosystems. Comparisons of predicted environmental concentrations and toxicity values for indicator organisms provide sufficient safety margins. Experimental data indicate that ivermectin residues would be expected to remain appreciably bound in soils.

To address concerns that the use of IVOMEC SR Bolus in pastured cattle in the U.S. may adversely impact dung dependent arthropods and dung degradation processes, Merck has provided the following assessments and studies. The assessments consider additive effects from injectable, topical, and sustained release formulations.

- To estimate the levels of ivermectin residues introduced into pastures, Merck provides data on the percentage of all pastured cattle that are treated on a monthly basis with anthelmintics for 10 distinct U.S. regions. Based on drug metabolism and dung residue data for injectable, pour-on, and sustained release formulations, Merck provides estimates of the percentage of pastured cattle excreting anthelmintics by region and by month. A discussion of the potential for off-label use of the SR Bolus is provided.

- To evaluate the effects of ivermectin residues on dung beetle populations, Merck provides detailed information on the ecology of dung beetles. A review of the scientific literature on the effect of different ivermectin formulations on beetle larvae and adults is provided. Use and exposure scenarios evaluate the exposure of beetle populations to ivermectin residues.

- A detailed discussion of the biological, physical, and mechanical components of dung degradation is provided along with a comprehensive literature review on the effects of ivermectin residue on dung pat degradation.

- The following studies were conducted by the sponsor to measure potential effects of ivermectin on dung degradation:

  1. Baggott, D.G., S.D., Wratten and M. Mead-Briggs. 1990. The Effect of Treating Cattle with Ivermectin Through Two Grazing Seasons on the Persistence of Dung on the Pasture in England.

  2. Heinze-Mutz, E.M. and D. Barth. 1990. The Degradation of Dung Pats from Cattle Treated with an Ivermectin Sustained-Release Bolus in Germany.

  3. Wallace, D.H. and J.E. Holste. 1989. The Degradation of Dung Pats from Ivermectin-Treated Cattle Under Field Conditions in Missouri.

The EA supports the conclusion that sufficient ivermectin-free dung would be available in pasture environments to maintain beetle populations and that effects on beetle populations and/or dung degradation rates, if any, would be short-lived and would not be expected to be ecologically significant.

We have reviewed the EA and available scientific information and conclude that the EA provides adequate information to determine that the manufacture and use of IVOMEC SR Bolus as described in the EA would not be expected to cause a significant impact on the quality of the human environment.

11/1-3/96 R. C. Livingston

Date Director, Office of New Animal Drug Evaluation, HFV-100

Attachment: October 15, 1996, Environmental Assessment