



• May 26, 1998

NADA 141-101

Dr. Elizabeth Dunlap  
MS Bioscience  
Division of Milk Specialties Company  
P.O. Box 278  
Dundee, IL 60118

Dear Dr. Dunlap:

We refer to your April 7, 1998 submissions of promotional materials for the competitive exclusion product PREEMPT™, NADA 141-101. The materials consist of three single-sheet promotional pieces and one press release. You state in your letter that the promotional materials are being disseminated in conjunction with the marketing of the product. The materials under review are classified as promotional labeling for an Over-The-Counter product.

In reviewing your promotional pieces, we make reference to the **Indications for Use** as is the subject of your NADA approval. The approved claim is "PREEMPT™ is indicated for the early establishment of intestinal micro flora in chickens to reduce *Salmonella* colonization." In consideration of this claim, we note our objections to the following promotional statements:

**Promotional Piece #1**

- 1) "... specifically formulated to reduce **both the incidence and severity** of *Salmonella* colonization by . . ."

As will be repeated later in this letter, the product is approved for use in reducing *Salmonella* colonization. Modifiers such as "incidence" and "severity" imply product effectiveness against animal disease. The statement goes outside the approved claim and so should be revised.

- 2) "... provides chicks with the bacteria needed to establish a **healthy** gut flora at a time when they are vulnerable to **infection**."

The term "healthy" implies a health- or disease-associated benefit of the product, which is outside the approved claim. In the term "normal" may be used instead. The term infection is outside the approved claim. The term "colonization" should be used

instead.

- 3) “PREEMPT™’s defined cultures of 29 nonpathogenic bacterial strains readily colonize the chick’s intestinal tract, competitively excluding **infectious pathogens, such as *Salmonella***.”

The product is approved for use only to reduce *Salmonella* colonization. This claim implies that the product is effective against additional pathogens, which is outside the approved claim. The statement should be revised. Further, use of terms such “infectious” and “pathogen” should not be used since these terms imply product-derived health or disease benefits, which are outside the approved claim.

- 4) “PREEMPT™ is a *preventive* treatment.”

This statement implies a product-derived health or disease benefit, which is outside the approved claim. The statement should be deleted.

- 5) “Rapidly establishes **healthy**, mature gut flora in day-old chicks.”

The term “healthy” implies a product-derived health or disease benefit, which is outside the approved claim. In the term “normal” may be used instead.

- 6) “Reduce the **incidence and severity** of *Salmonella* **infection** in chicks.”

All three words imply a product-derived health or disease benefit, which is outside the approved claim. The statement should be revised.

- 7) “Decreases producers’ dependence on antibiotics.”

This statement implies a product-derived health or disease benefit, which is outside the approved claim. The statement should be deleted

## Promotional Piece #2

We have reviewed this promotional piece and have filed it without comment.

## Promotional Piece #3

As have been stated before, the product is approved for use in reducing *Salmonella* colonization. We further note that the preapproval efficacy trials involved *Salmonella* spp. and certainly not anyone specific *Salmonella* species. Finally, preapproval studies certainly did not involve any other genus, other than *Salmonella*.

This promotional piece inappropriately indicates the effectiveness of PREEMPT™ in decreasing the “incidence of infection by various pathogens” that include *S. typhimurium*, *S. enteritidis* PT4, *S. typhimurium* DT104, *Clostridium perfringens*, *Escherichia coli* O157: H7, and *Listeria monocytogenes*. We object to the reference to any of these organisms and to the use of the terms “incidence,” “infection,” “pathogen,” and “mortality.”

We acknowledge that the promotional piece lists both published and unpublished references to support the summarized data. However, we remind you that an approved supplemental application is first required if a product is to be marketed with any additional claims for approved use.

Regarding the reverse side of the promotional piece, we do not consider the tables on *Salmonella* in poultry litter as outside the approved label claim, provided there is adequate data to support the table claims. We request that you submit the referenced studies so that we review the study data.

Additionally, we ask that you reconsider the use of the term "incidence" in describing litter contamination. Incidences in more appropriately used to describe the rate at which new events occur with time in animals or humans. The promotional piece uses the term to describe the proportion of litter that cultures positive for *Salmonella*, which we do not consider as an appropriate use of the term.

### Press Release

- 1) "... these beneficial microbes establish a **healthy** ecosystem which naturally inhibits the growth of **all types of *Salmonella*** bacteria."

The term "healthy" implies a product-derived health or disease benefit, which is outside the approved claim. In the term "normal" may be used instead.

The product was approved for use in reducing the colonization of *Salmonella* species in general. The approval did not involve determining efficacy against each of all the *Salmonella* species as the Press Release implies. The phrase should be deleted.

- 2) "... hens would pass the **good** microbes - **and disease resistance** - onto their chicks."

The term "good" implies a product-derived health or disease benefit, which is outside the approved claim. In the term "normal" may be used instead. Similarly the phrase "disease resistance" is outside the approved claim and should be deleted.

- 3) "While down on the farm, poultry producers share an increasing concern over the indiscriminate use of antibiotics."

"Until now, producers have relied primarily on antibiotics to curb pathogenic infections in poultry. Not only are these antibiotics expensive, but their overuse could lead to the emergence of new bacterial "super strains" which are highly resistant to conventional medication. PREEMPT™ is among the first of a new generation of microbial products which enhance an animal's own natural defenses against infection through the process of competitive exclusion."

These statements imply a product-derived health or disease benefit, which are outside the approved claim. The statements should be deleted.

- 4) "Beyond treating chickens, the implications for products like PREEMPT™ are exciting. This patented technology could be used to create a new class of live microbial products for poultry, cattle, swine, dogs, cats . . . and ultimately, human beings . . . 'future products could be biologically designed to treat severe diarrhea, to alleviate stomach upset, to mitigate the side-effects of chemo and radiation therapy - in short, to correct any condition which threatens the body's' beneficial microbes.'"

While many of the statements may be truthful in part, these extra label claims are inappropriate for promoting the approved product. The statements imply health and disease benefits that are outside the approved claim and that is not attributable to any approved competitive exclusion product. The paragraph should be deleted.

In light of these objections, we request that distribution of the promotional pieces be ceased immediately. We remind you of the commitment you made when you signed the new animal drug application (NADA) Form FDA-356 that labeling and advertising would be neither false nor misleading in any particular. We will expect to receive your response within 30 days of receipt of this letter. If you have any questions, you should contact the Product Manager, Dr. Neal Bataller at (301) 827-0163.

Sincerely,



Vitolis E. Vengris, D.V.M., PhD  
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and Regulatory Review  
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