UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

006986

JUN 9 1989

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Hartz Response to Previous Toxicology Reviews of Blockade Formulation Studies

TO: Mr. George LaRocca, PM 32
Registration Division (TS-767)

FROM: Byron T. Backus, Toxicologist
Fungicide/Herbicide/Antimicrobial Toxicology Branch
HED (TS-769C)

THROUGH: K. Clark Swentzel
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Fungicide/Herbicide/Antimicrobial Toxicology Branch
HED (TS-769C)

and

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HED (TS-769C)

EPA Record Nos. 235863, 235865, 235872, 235876, 235879, 235880, 235882, 235883

Project No. 9-0513

EPA Reg. Nos. 2596-114, 2596-115

Tox. Chem. 346, 77A

Action Requested:

Review responses from the registrant (Hartz Mountain Corporation) to a previous series of Toxicology Branch reviews on the subject formulation.

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Comments and Recommendations:

1. The Blockade dog 4X application study was previously reviewed May 9, 1988 and was classified as core supplementary data. There were concerns regarding what the 1X application level was, particularly as there had been a 1986 study (conducted prior to product marketing) in which 136 applications were made from 50 cans.

   The registrant has stated that the cans in this pre-marketing study contained 175 g of product, and that an average of 25 g remained in each can, for a dose of 4.1 g/kg. This indicates a total of 150 gm/can x 50 cans = 7500 g of formulation was applied, and a single dose was 7500 grams ÷ 136 = 55.147 g; dividing this through by the 4.1 g/kg dosage gives 13.45 kg as the mean weight of the dogs used in this study, a reasonable value.

   Additionally, 1.5 g/kg has been defined as a "normal" dose of the product, not to be applied more frequently than every 7 days.

   After considering these arguments, the study is upgraded to core minimum data.

2. The Blockade cat 4X application study was previously reviewed May 9, 1988 and at that time was classified as core supplementary data. As in the 4X dog application study there were concerns regarding whether the indicated 1X level (2.69 g/kg) was in fact reasonable. Additionally, there were concerns regarding the reporting that cats were not observed to preen.

   After examining the arguments and considering that current labeling specifies to apply the product lightly, we can accept 2.7 g/kg as a reasonable approximation of the 1X dose level. It is the understanding of this reviewer that current labeling specifies not to apply this product more than once every 7 days. Regarding the lack of preening, it is noted that the laboratory conducting this study has been recently audited, and the minor deviations found had no adverse effect on any of the findings of the audited studies.

   The Blockade cat 4X application study is upgraded to core minimum data.

3. Since the dosage levels of 1.5 g/kg (for dogs) and 2.7 g/kg (for cats) have been accepted above as reasonable approximations of a 1X dose level, then the high-dose studies (review

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dated September 19, 1988) can also be upgraded to core minimum data. Concern was also expressed in the previous review regarding the lack of reports of any adverse signs or possible effects during the subsequent observation period. Again, this concern has now been alleviated by the recent audit of this facility, which was found to be adherent to GLP standards.

4. Both the cat and dog oral NOEL and LEL studies were previously classified as "acceptable" (protocols for these studies are not specifically outlined in the Subdivision F Guidelines, so core classification was not used). The registrant's comments are directed only at the interpretation of the cat oral study, and specifically effects in one cat that did not vomit until 6 hours after treatment, and showed depressed appetite for the remainder of the day. The registrant has stated an opinion that the [redacted] alone may have been responsible for these symptoms. The original DER (attached to a memorandum dated May 17, 1988) states, in part: "These delayed symptoms may have been due to either the deet or fenvalerate." The other 3 cats showing symptoms after Blockade dosage at 250 mg/kg all vomited at least once within an hour after dosage. This one cat did not vomit until about 6 hours later, and so presumably absorbed more of the formulation (which would have included [redacted], deet and fenvalerate). Perhaps a better statement is that these delayed symptoms were due to either the [redacted] or the deet or fenvalerate, or some combination thereof.

   The registrant has no comments regarding the dog study.

5. In a previous review the rat oral LD_{50} study was classified as core minimum data. Because the female LD_{50} was reported as 5420 mg/kg with 95% confidence limits of 4517 to 6504 mg/kg, a range which includes values below 5000 mg/kg, the recommendation was made for toxicity category III labeling with respect to potential oral exposure. The registrant has stated that category III toxicity labeling for this product should not be necessary; one of the arguments used is that the material tested was 30% more concentrated than that which is in the final product.

   After considering the registrant's arguments, the position of the Toxicology Branch is that toxicity category III labeling for oral exposure would be desirable for this formulation, but this is not a requirement that can be imposed.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

6. The study was previously classified as conditionally acceptable, with a clarification needed regarding the reporting of the residue weight for sample 1C. This clarification has now been made (sample weight for the 4-hr sample was 80 mg/kg, rather than 170 mg). This study is now classified as acceptable.

7. The registrant has stated that: "Comments regarding the Rat Inhalation Test (Hartz Test No. 1004) will be the subject of a separate communication."

8. The registrant has submitted revised supplemental labeling (received at EPA 12-28-88) which consists of a tag including the following restrictions:

   - Do not use Blockade Cat Flea and Tick Repellent on young (less than one year old) or pregnant cats.
   - Do not use Blockade Dog Flea & Tick Repellent on young (less than 3 months old) puppies.
   - Apply lightly. Do not saturate animal's coat. Spray approximately 2 seconds for each pound of pet's body weight.
   - Do not apply more often than every seven days.
   - Do not use this or any other pesticide on sick, old or debilitated pets.

   At the present time, HED believes that no further revisions in this labeling are necessary.

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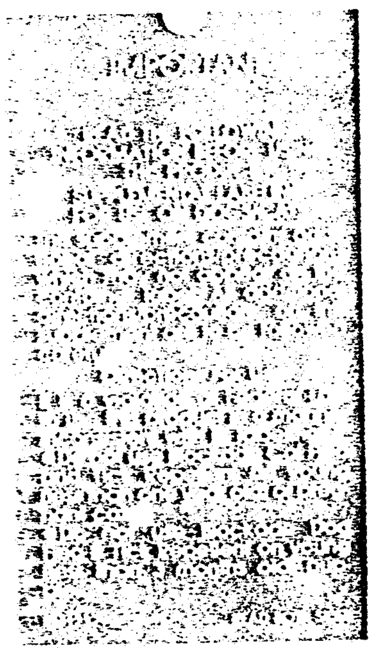
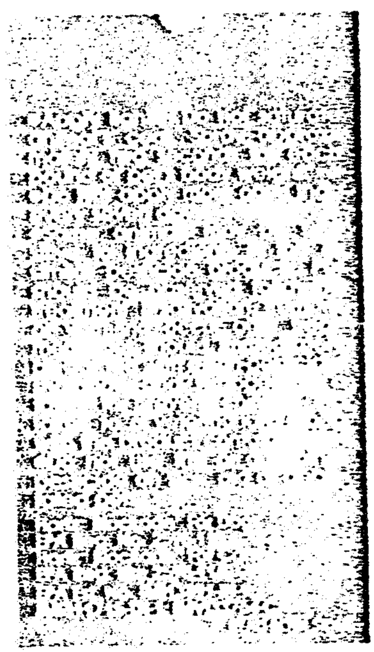
Hartz Blockade for Dogs
EPA Reg. No. 2596-115

Hartz Blockade for Cats
EPA Reg. No. 2596-114

Revised Supplemental Labeling

submitted with letter dated 12/23/86





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