TR-326

INERT INGREDIENT INFORMATION IS NOT INCLUDED

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

Memorandum

Date: March 24, 1981

000326

Subject: EPA Reg. No. 5887-7 Black Leaf 40 Garden Spray
Caswell 597A

From: B. T. Backus
IRB/TSS

To: Mr. William Miller
Product Manager 16

Registrant: Black Leaf Products Co.
667 N. State St.
Elgin, IL 60120

Active Ingredient (label declaration):
Nicotine expressed as alkaloid.....40%
Inert Ingredients:.....60%

Background:

The current label bears the signal words DANGER and POISON in conjunction with the skull and crossbones motif.

The registrant (letter of Dec. 31, 1980) has indicated a desire to revise the labeling, and has proposed a signal word downgrading to CAUTION.

Comments and Recommendations:

1. Although the active ingredient is expressed as nicotine in the alkaloid form, the product, according to the confidential statement of formula, also contains [redacted]. This suggests the active ingredient in this formulation is really [redacted] nicotine sulfate, which is considerably less hazardous than the base.

2. The Registry of Toxic Effects of Chemical Substances 1979 gives the rat oral LD50 of 2:1 nicotine sulfate as 55 mg/kg, and the dermal (rat) LD50 value as 285 mg/kg.

3. This product contains about [redacted] nicotine sulfate. The expected rat oral LD50 would then be something like 110 mg/kg and the dermal LD50 value would be about 570 mg/kg.

4. The submitted studies are in Acc. 244635. These studies are IBT data that, according to our records, have not been validated. They indicate the product has a rat oral LD50 of between 50 and 500 mg/kg, and a rabbit dermal LD50 of above 200 mg/kg.

5. The product appears to meet the
The registrant should be informed

6. IRB/TSS would have no objection, on
animals, to revision of the signal w
proposed by the registrant) under the
additional label revisions as indicated

and domestic
(not CAUTION, as
port with the

Labeling:

1. The appropriate signal word is WARNING.

2. The active ingredient should be expressed as [redacted] Nicotine sulfate and its percentage should be approximately [redacted]

3. The STATEMENT OF PRACTICAL TREATMENT should be revised to something like:

   If swallowed: Speed is imperative. Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious or convulsing person. Apply artificial respiration if breathing stops.

   If on skin: Wash thoroughly and immediately with cold running water and/or dilute vinegar. Do not use soap.

   If in eyes: Flush with plenty of water. Get medical attention if irritation persists.

4. The statement under HAZARDS TO HUMANS AND DOMESTIC ANIMALS should be something like:

   WARNING: May be fatal if swallowed, inhaled or absorbed through the skin. Do not breathe vapors or spray mist. Do not get in eyes, on skin, or on clothing. If spilled on clothing, remove and wash clothing before reuse. Keep away from children, domestic animals, and foodstuffs.

5. The DISPOSAL statement should follow after the complete set of use directions.

Review:

The following studies were received at EPA on Dec. 21, 1980. Studies were conducted at Industrial Bio-Test Laboratories, Inc, Northbrook IL 60062, on the registered product. These studies are in Acc. 244635.

1. Minimum Emetic Dose Study with Black Flag 40 in Beagle Dogs (Acute Oral LD50-Dog). IBT No. J9168, dated Oct. 30, 1970.

   Procedure: Individual male purebred beagles, 10.0-12.5 kg, were given oral doses of 3.16, 4.64, 6.81, 10.0, 21.5, 31.6, 46.4, 100, 316 and 681 mg/kg of the subject product and were observed for a period of 14 days following dosage.

   Results: Emesis observed in all subjects receiving 6.81 mg/kg or more. Onset of emesis varied from 1 hr and 3 minutes after dosage (21.5 mg/kg) to 3 minutes afterwards (316 mg/kg). Animals receiving dosage levels of 100 and 316 mg/kg

died within one hr of treatment with gross signs of respiratory inhibition. Subject receiving 681 mg/kg survived, but showed clonic convulsions up to 4 hrs after dosage.

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Study Classification: Core Supplementary Data if validated (only one animal tested at each dosage level, no females tested).

2. Acute Oral Toxicity Study on Black Leaf 40 in Albino Rats (Acute Oral LD50-Rat). IBT No. A8836; dated July 28, 1970.

Procedure: Groups of 2M, 2F 166-196 g Charles River rats were orally intubated with dosage levels of 6.93, 10.4, 15.61, 23.41, 35.12 mg/kg, administered as a 1% w/v aqueous solution with subsequent 7-day observation.

Results: No mortalities. Symptoms included (seen at and above 15.61 mg/kg) hypoactivity, muscular weakness and tremors. At higher dosage levels animals showed spasms and convulsions, with recovery with 24 hrs.

Study Classification: Core Supplementary Data if validated.

3. Acute Oral Target Organ Study on Black Leaf 40 in Female Albino Rats (Acute Oral LD50-Rat). IBT No. A8777; dated June 29, 1970.

Procedure: A group of 4F 161-170 g rats received a dosage level of 79.01 mg/kg with an additional 2F rats serving as controls. Animals were observed 60 hrs, then sacrificed. Brains were removed, preserved in buffered formalin (pH 7.0) and tissue sectioned and stained.

Results: No mortalities. Symptoms included hypoactivity, tremors, clonic convulsions, muscular weakness and ruffled fur, subsiding within 24 hrs. Necropsies showed no gross or microscopic brain lesions. Weight gains of 40 grams or more in 5-day period seen in 3 animals.

Study Classification: Core Supplementary Data if validated

4. Acute Oral Toxicity Study with Black Leaf 40 in Male and Female Albino Rats. IBT No. A9166; dated November 9, 1970.

Procedure: Groups of 2M, 2F Charles River strain rats were orally intubated at dosage levels of 266.7, 400, 600 and 900 mg/kg, with subsequent 14-day observation. Two females from this population were orally dosed with a 1% w/v aqueous solution of Black Leaf 40 at a dosage level of 266.7 mg/kg (others had been tested with undiluted product).

Results:

Dosage Level mg/kg	Mortalities M	F
266.7	0/2	0/2
400	2/2	0/2
600	2/2	1/2
900	2/2	2/2
266.7 (1% w/v aq. sol.)	-	2/2

Symptoms: Hypoactivity, muscular weakness, ruffled fur, prostration, convulsions
Oral LD50 (undiluted product) = 442.7 ± 84.29 mg/kg.

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Study Classification: Core Minimum Data if validated

Product Classification: Tox. Cat. II

5. Acute Oral Toxicity Study on Black Leaf 40 in Albino Rats. (Acute Oral LD50-Rat). IBT No. A8604, dated June 10, 1970.

   Procedure: Groups of 2M, 2F rats were orally intubated with dosage levels of 52.67, 79.01, 118.5, 177.8, and 266.7 mg/kg of the product, administered a a 1% w/v aqueous solution, with subsequent 14-day observation.

   Results:

Dosage Level mg/kg	Mortalities M	F
52.67	0/2	0/2
79.01	0/2	0/2
118.5	0/2	0/2
177.8	2/2	1/2
266.7	2/2	2/2

   Symptoms: Tremors, convulsions, hypoactivity, ruffled fur, muscular weakness. Oral LD50 = 160.7 ± 16.31 mg/kg. Males appear somewhat more susceptible than females.

   Study Classification: Core Minimum Data if validated

   Product Classification: Tox. Cat. II

6. Acute Oral Toxicity Study - Rat. IBT No. A8604, dated May 27, 1970.

   Procedure: 5M, 5F white rats were dosed at a level of 50 mg/kg of the product administered as a 1% w/v aqueous solution, with subsequent 14-day observation.

   Results: No mortalities. All animals gained weight during 2-week observation period. No report as to symptomatology or lack thereof.

   Study Classification: Core Supplementary Data if validated

7. Acute Dermal Toxicity Study - Rabbit. IBT No. A8604; dated May 27, 1970.

   Procedure: 2M, 2F NZ albino rabbits, 2.34-2.72 kg, with intact skin, received a dermal dosage level of 200 mg/kg of test substance with 24 hr occluded exposure, subsequent 14-day observation.

   Results: No mortalities. No symptoms. Dermal LD50 above 200 mg/kg.

   Study Classification: Core Supplementary Data if validated

   Product Classification: Probably Tox. Cat. II

8. Acute Vapor Inhalation Toxicity Study - Albino Rats. IBT No. A8604, dated May 27, 1970.

   Procedure: 5M, 5F rats were exposed to vapor generated by bubbling a stream of air through undiluted test material for one hour. Nominal vapor concentration was calculated to be 13 mg/L. There was a 14-day observation period, sacrifice and necropsies.

Results: No mortalities. No symptomatology observed. Necropsies were unremarkable.

Study Classification: Core Supplementary Data if validated (no information as to particle size distribution, nor were actual measurements made as to concentration of nicotine in inhalation chamber; no guarantee that most of nicotine was not simply retained in the test material and what rats were primarily exposed to was water vapor).

9. Eye Irritation Test on Black Leaf 40 in Albino Rabbits. IBT Study No. A8604, dated June 3, 1970.

Procedure: 0.1 ml test substance was applied to one eye of each of 6 rabbits, with no subsequent eyewash.

Results: No corneal opacity. Some iridial and conjunctival irritation in all 6 subjects, but all scores were zero at 72 hrs.

Study Classification: Core Minimum Data if validated

Product Classification: Tox. Cat. III

Byron T. Backus 3/24/81

Byron T. Backus
IRB/TSS

Nicotene sulfate toxicology review

Page _____ is not included in this copy.

Pages 6 through 8 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

X A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

___ The document is a duplicate of page(s) _____

___ The document is not responsive to the request

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
