UNITED ST ES ENVIRONMENTAL PROTECTION GENCY

(2-3-81) ✓
CASWELL FILE

DATE: FEB 3 1981

SUBJECT: FAP OH5265, Allethrin, Piperonyl Butoxide, and N-octylbicycloheptene Dicarboximide for Use in Food Handling Establishments.
TOX Chem. Nos. 25, 613, 670

FROM: John D. Doherty 12/31/80
Toxicology Branch/HED (TS-769)

ABK 1/23/81

TO: F. D. R. Gee, PM #17
Registration Division (TS-767)

Background:

The McLaughlin, Gormley and King Company has submitted FAP OH5265 for the use of allethrin, piperonyl butoxide and N-octylbicycloheptene dicarboximide for use in food handling establishments. RCB (see M. Bradley memo dated December 4, 1980) has recommended for the proposed food additive regulations provided that toxicological considerations permit. The purpose of this memo is to clarify Toxicology Branch's position related to the use of allethrin.

Conclusion:

The petitioner must submit or reference adequate studies demonstrating the safety of allethrin. In a meeting held at Waterside Mall, December 12, 1979, between EPA and representatives from the McLaughlin, Gormley and King Company, John Doherty (EPA) presented to Mr. Baker and Dr. F. Preiss a list of studies that should be submitted or referenced. To this date, the company has not responded.

This list is attached for reference.

Attachment:

OPP:HED:TOX: J.DOHERTY:sb 12/30/80 X73710 Rm. 814 CM 2 #m5

EPA Form 1320-6 (Rev. 3-76)

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Copy of list of required studies as presented to Mr. Baker and Dr. Preiss on December 12, 1 9.

The following is a list of "at least" studies normally required to support a food additive regulation or registration for the indoor use of a pesticide product. Additional studies may be required if the EPA deems necessary.

STUDY	STATUS WITH ALLETHRIN	BASIS FOR NEED
A. Basic requirements with technical material		
1.) Acute oral LD_{50}	O.K.	Standard
2.) Acute dermal LD_{50}	O.K.	"
3.) Acute Inhalation LC50	Needs	"
4.) Eye Irritation	Needs	"
5.) Dermal Irritiation	Needs	"
6.) Sensitization-skin	Needs	Use pattern:repeated human exposure and chemi prediction.
7.) 90 day rat oral feeding	Needs	Use pattern:FAP, frequent human exposure
8.) 2 generation reproduction	Needs	Use pattern: FAP and ffequent human exposure
9.) Teratology-1	O.K.	
10) Teratology-2	Needs	Use pattern; FAP and frequent female exposure
11.) Chronic feeding-6 month dog	Needs	Use pattern:FAP, indoor
12.) chronic feeding/oncogenesis	Needs	Use pattern:FAP, indoor
13.) oncogenesis-2nd species	Needs	Use pattern:FAP,indoor us
B. Requirements for a synthetic pyrethrin		
1.) Neurotoxicity	Needs	Chemical class history has a characteristic neuropathy
2.) "cough potential" in guinea pigs	Needs	chemical class history h indicated possible respiratory hazard.

C. Requirements for formulation

1.) Acute oral LD_{50}	Needs	Labelling
2.) Acute dermal LD_{50}	Needs	"
3.) Acute Inhalation LC_{50}	Needs	"
4.) Eye Irritation	Needs	"
5.) Dermal Irritation	Needs	"
6.) 90 day subchronic inhalation	Needs	Use patter: indoor use ar applicators may have a near daily exposure, forr ation may have different toxic properties than the technical material.

* O.K. indicates that the requirement has been satified or that an adequate study has been reviewed by Toxicology Branch. Needs indicates that no study has been reviewed by Toxicology Branch although the study may exist. It is the registrants responsibility to request review of studies to support thier product.

The registrant is reminded that they may request a specific waiver in writing for any of the above tests if they feel the above requirements are not warranted.

In addition, Residue Chemistry Branch may deterine that allethrin results in metabolites (photo or otherwise) that are of toxicological significance. In this case, Toxicology Branch may require additional tests on these metabolites when and if these metabolites are determined.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: DEC 4 1980

Doherty sue

SUBJECT: FAP#OH5265 Allethrin in food handling establishments.
Amendment of October 2,1980.

FROM: Martha J. Bradley, Chemist Martha J. Bradley
Residue Chemistry Branch, HED (TS-769)

TO: Gee/Heyward (PM No. 17)
Registration Division (TS-767)

and

Toxicology Branch (TS-769) ✓
Hazard Evaluation Divison

THRU: R.S. Quick, Section Head RM
Petition Evaluation Section
Residue Chemistry Branch, HED (TS-769)

R.D. Schmitt, Deputy Chief
Residue Chemistry Branch, HED (TS-769) R D Schmitt

Willa Y. Garner, Acting Chief
Residue Chemistry Branch, HED (TS-769)

McLaughlin Gormley King Company has submitted this amendment in response to the deficiencies in our memo of 9/6/80 (M. Bradley).

The deficiencies in order are:

1. The current manufacturing process for allethrin should be submitted.

Allethrin is currently produced by the esterification of dl 2-allyl 4-hydroxy 3-methyl 2-cyclopenten 1-one with dl-cis -trans chrysanthemum monocarboxylic acid chloride. Racemic allethrin consists of eight diastereoisomers with the most active component, d-trans allethrin, representing 15% of the technical product. Racemic allethrin is ca 94% esters with up to 3% each of free chrysanthemum carboxylic acid with its anhydrides and free allethrolone.

We consider this deficiency resolved.

5. The petitioner should submit a revised Section F to conform to existing regulations for allethrin, piperonyl butoxide and N-octylbicycloheptene dicarboximide.

The petitioner has submitted revised regulations to conform with our recommendations (see attached proposals for 21 CFR 193).

We consider this deficiency resolved.

We now recommend for the proposed Food Additive Regulations for allethrin, piperonyl butoxide and N-octylbicycloheptene dicarboximide provided toxicological considerations permit.

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

Attachment 1

Section 193._____

Allethrin

The food additive allethrin, composed of any combination of the isomers found in racemic allethrin, may be safely used in place of pyrethrins to treat food processing areas and food storage areas provided:

(1) That the food is removed or covered well prior to such use.

(2) It is used or intended for use in combination with piperonyl butoxide and N-octylbicycloheptene dicarboximide for insect control in accordance with 193.320.

(3) A tolerance of one part per million is established for residues of allethrin in or on foods treated in accordance with 193.320.

(4) To assure safe use of the additive, its label and labeling shall conform to that registered with the U.S. Environmental Protection Agency, and it shall be used in accordance with such label and labeling.

(5) Where tolerances are established under Sections 408 and 409 of the Act on both raw agricultural commodities and processed foods made therefrom, the total residues of allethrin in or on the processed food shall not be greater than that permitted by the larger of the two tolerances.

193.360 Piperonyl butoxide.

The food additive piperonyl butoxide may be safely used in accordance with the following prescribed conditions:

(a) It is used or intended for use in combination with pyrethrins for control of insects:

(1) In cereal grain mills and in storage areas for milled cereal grain products, whereby the amount of piperonyl butoxide is at least equal to but not more than 10 times the amount of pyrethrins in the formulation.

(2) On the outer ply of multiwall paper bags of 50 pounds or more capacity in amounts not exceeding 60 milligrams per square foot, whereby the amount of piperonyl butoxide is equal to 10 times amount of pyrethrins in the formulation. Such treated bags are to be used only for dried foods.

(3) On cotton bags of 50 pounds or more capacity in amounts not exceeding 55 milligrams per square food of cloth, whereby the amount of piperonyl butoxide is equal to 10 times the amount of pyrethrins in the formulation. Such treated bags are constructed with waxed paper liners and are to be used only for dried foods that contain 4 percent fat or less.

(4) In two-ply bags consisting of cellophane/polyolefin sheets bound together by an adhesive layer when it is incorporated in the adhesive. The treated sheets shall contain not more than 50 milligrams of piperonyl butoxide per square foot (538 milligrams per square meter). Such treated bags are to be used only for packaging prunes, raisins, and other dried fruits and are to have a maximum ratio of 3.12 milligrams of piperonyl butoxide per ounce of fruit (0.10 milligram of piperonyl butoxide per gram of product).

(5) In food processing and food storage areas: Provided, That the food is removed or covered prior to such use.

(b) It is used or intended for use in combination with pyrethrins and N-octylbicycloheptene dicarboximide for insect control in accordance with § ~~122~~ 193.320.

(c) The food additive piperonyl butoxide may be safely used in accordance with the following prescribed conditions:

(1) It is used or intended for use in combination with any one or any combination of allethrin isomers for control of insects:

(2) In food processing and food storage areas: Provided, that the food is removed or well covered prior to such use.

(3) It is used or intended for use in combination with allethrins and N-octylbicycloheptene dicarboximide for insect control in accordance with 192.320.

(d) A tolerance of 10 parts per million is established for residues of piperonyl butoxide in or on:

(1) Milled fractions derived from cereal grains when present therein as a result of its use in cereal grain mills and in storage areas for milled cereal grain products.

(2) Dried foods when present as a result of migration from its use on the outer ply of multiwall paper bags of 50 pounds or more capacity.

(3) Foods treated in accordance with § 193.320.

(4) Dried foods that contain 4 percent fat, or less, when present as a result of migration from its use on the cloth of cotton bags of 50 pounds or more capacity constructed with waxed paper liners.

(5) Foods treated in accordance with paragraph (a) (4) and (5) of this section.

(e) To assure safe use of the additive, its label and labeling shall conform to that registered with the U.S. Environmental Protection Agency, and it shall be used in accordance with such label and labeling.

(f) Where tolerances are established under sections 408 and 409 of the Act on both raw agricultural commodities and processed foods made therefrom, the total residues of piperonyl butoxide in or on the processed food shall not be greater than that permitted by the larger of the two tolerances.

193.320 N-Octylbicycloheptene dicarboximide.

The food additive N-octylbicycloheptene dicarboximide may be safely used in accordance with the following prescribed conditions:

(a) It is used in combination with piperonyl butoxide and pyrethrins or any one or any combination of allethrin isomers for insect control in food-processing and food-storage areas, provided that the food is removed or covered prior to such use.

(b) Residues in food resulting from the use described in paragraph (a) of this section shall not exceed 10 parts per million of N-octylbicycloheptene dicarboximide, 10 parts per million of piperonyl butoxide, and 1 part per million of pyrethrins or allethrin.

(c) To assure safe use of the additive, its label and labeling shall conform to that registered with the U.S. Environmental Protection Agency and it shall be used in accordance with such label and labeling.