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CASWELL FILE
OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS Branch
EPA SERIES 361

Dr. George E. Whitmore
Division of Toxicological Evaluation
Petitions Review Branch

June 11, 1965

Botran, tolerance request changes: apricots-10 ppm increased to 20 ppm;
leaf lettuce-5 ppm increased to 10 ppm.

PESTICIDE PETITION NO. 5F0434
(Final Evaluation)

Upjohn Chemical Company
Kalamazoo, Michigan
(AF 15-522)

By calculation, about 0.1 mg/day of Botran would be added to the human diet by the granting of the requested changes. Added to previously computed intake the resultant sum would be approximately 1.5 mg/day. This is the calculated safe amount that could be ingested based on a no effect level of 100 ppm in test animals with a safety factor of 100 fold. Although the petitioner submits some data indicating apricot residues are 10 ppm rather than 20, and that leaf lettuce can have 10 ppm residues in contrast to 5 ppm residues on head lettuce, it is the opinion of FSA that, had more extensive apricot residues been studied, the need for the 20 ppm tolerance already established for peaches would be evident, and that both leaf lettuce and head lettuce can have 10 ppm residues. If the calculated values are real the total possible residues would still be considered safe.

CONCLUSION:

The requested change of residue tolerance for apricots from 10 to 20 ppm and for lettuce from 5 to 10 ppm would be without hazard.

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cc:
FSA
TE
RSSE(Data Processing)
PP No. 5F0434

GEWhitmore:amp 6/11/65

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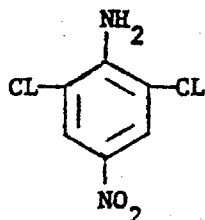
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Trade Name : Botran

Chemical Name: 2:6-dichloro-4-nitroaniline

Empirical formula : $C_6H_4N_2O_2Cl_2$

Structure :



Molecular wt : 207.03

Physical state : Solid

M.P. : 192-194°C

Color : Yellow

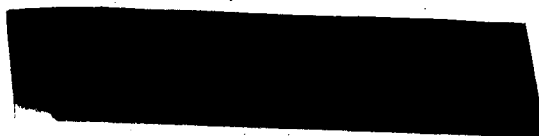
Solubility : Insoluble in water - poor solubility in most organic solvents

Co. : The Upjohn Company

Stability : Stable to hydrolysis - is reduced to the corresponding phenylenediamine by zinc and acid.

Use : Control of Botrytis (Grey Mold) in lettuce

Impurity



Acute Rat Oral :	LD ₅₀ = 4040 mg/kg
Acute Rat Oral (4% Formulation) :	LD ₅₀ = >8000 mg/kg
Acute Rat Oral (8% Formulation) :	LD ₅₀ = >8000mg/kg
Acute Rat Oral (50% Formulation) :	LD ₅₀ = >8000 mg/kg
Acute Mouse Oral :	LD ₅₀ = 1500-2500 mg/kg
Acute Cat Oral :	LD ₅₀ = >500 mg/kg
Acute Guinea Pig Oral :	LD ₅₀ = 1450 mg/kg
Acute Rat I.P. :	LD ₅₀ = 1460 mg/kg
Acute Mouse I.P. :	LD ₅₀ = 2500 mg/kg
Acute Mouse I.P. (8% Formulation):	LD ₅₀ = 2385 mg/kg
Acute Rat Subcutaneous :	LD ₅₀ = >5000 mg/kg
Acute Mouse Subcutaneous :	LD ₅₀ = >6000 mg/kg
Acute Mouse Dermal :	LD ₅₀ = >5000 mg/kg
Acute Rat Inhalation (7 hrs) :	No adverse effect at a 0.381 mg/ kg ^l conc
Acute Rat Inhalation (75% Formulation) (1hr) :	No adverse effect at a 21.6 mg/ kg ^l conc
Acute Guinea Pig Inhalation (7 hrs):	No adverse effect at a 0.381 mg/ kg ^l conc
Acute Rabbit Inhalation (7 hrs) :	No adverse effect at a 0.381 mg/ kg ^l conc
Acute Rabbit Dermal (75% Formulation) :	Slight irritant
Rabbit Eye Irritation (Tech) :	Slight irritant
Rabbit Eye Irritation(8% Formulation) :	Non-irritant
Rabbit Eye Irritation (75% Formulation)(5 day) :	Non to slight irritant

Subacute Rabbit Dermal Irritation	: Non-irritant
Subacute Rabbit Dermal Irritation (8% Formulation)	: Non-irritant
Subacute Rabbit Dermal Irritation (75% Formulation)(21 day)	: Slight irritant
Subacute Rabbit Dermal Irritation (75% Formulation)(5 day)	: Non to slight irritant
Guinea Pig Dermal Sensitization	: Not a sensitizer
Subacute Rat Oral (28 dyas)	: Liver enlargement
Subacute Rat Oral (28 days)	: Liver enlargement is reversible
Subacute Cat Oral	: Effect level \approx 200 mg/kg
Chronic Rat Oral (6 months)	: No effect level \approx 300 ppm (22-25 mg/kg)

Botran

#3

Chronic Dog Feeding (2 year)	:	One year results indicate hemotoxic properties
Chronic Rat Feeding (2 year)	:	One year results indicate possible liver effects. Yellow stain on coat and in urine
Synergism Mouse I.P. Study	:	Acts as a synergist for certain chemicals
Effect on Blood and Blood-forming tissues (Rats)	:	Caused growth inhibition and marked lymphopenia - no adverse effect on red cells
Methemoglobin in Cats	:	Methemoglobin levels were normal
Human Manufacturing Experience	:	No adverse effect

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Petitions Control Branch

March 23, 1965

Dr. C.E. Whitmore
Division of Toxicological Evaluation
Petitions Review Branch

Botran: Rat Reproduction Study (F₃ litter information received March 16, 1965). PF No. 5F0434 (Supplement to review of Feb. 23, 1965).

PESTICIDE-PETITION NO. 5F0434

Upjohn Chemical Company
Kalamazoo, Michigan
(AF 12-868)

The controls and the 100 ppm compound groups consisted of 20 rats of each sex as parents for two litters for each of 3 generations. The criteria studied were: number of litters per group, total number of still births, total number of live births, mean birth weight, percent of pups alive at weaning and mean weaning weight. Results were comparable between the controls and the compound fed groups.

Organ weights of the F₃ weaned rats were comparable between the control and compound groups. Tissue effects were absent as determined by histopathological examination of livers, hearts, kidneys, spleen, adrenals, thyroids, glands and bone marrow of these F₃ weaned rats.

CONCLUSION:

A diet level of 100 ppm of Botran fed for 3 generations to groups of 20 rats of each sex, was without effect.

This conclusion supports the statement in our Feb. 23, 1965 review that the establishment of the requested tolerances for Botran would be safe.

INIT:HB:ms:chf

cc:
TE
FSA
MSR (Data processing)
PF NO. 5F0434

GM:dm:gnj 03/23/65

Microcoulometric Analysis of 2,6-Dichloro-4-nitroaniline

Correction

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A description of the microcoulometric method for analysis for 2,6-dichloro-4-nitroaniline residues under the above title was included in "BOTRAN (2,6-dichloro-4-nitroaniline) Petition for Permanent Tolerance," January 6, 1965, page 117. Also, fifteen copies were furnished to Mr. Alpert of the FDA for distribution to regulatory laboratories. The following information should have been included:

Either of two columns may be used for the vapor phase chromatography.

- A. 4 foot, 1/4 inch O.D., aluminum, Chromosorb P coated with 5% silicone oil, viscosity 12,500. (Furnished by Dohrmann Instrument Co.)
- B. 4 foot, 1/4 inch O.D., aluminum, Anakrom ABS, 80/90 mesh, 5% D.C. silicone oil 200. (Prepared by our laboratories)

Column B is slightly superior to Column A.

G. A. Boyack
The Upjohn Company
3/23/65