

US EPA ARCHIVE DOCUMENT

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

003801

SEP 09 1980

MEMORANDUM

OFFICE OF TOXIC SUBSTANCES

SUBJECT: PP#OF2351, OF2352, OF2353 and Registration 21137-4 (Triforine)
CASWELL#890AA

FROM: Charles Frick
Toxicology Branch, HED (TS-769)

TO: Henry Jacoby, PM#21
Registration Division (TS-767)

THRU: William Burnam, Acting Chief
Toxicology Branch, HED (TS-769)

Action Request:

EM Industries, Inc. petitions the Agency for residues of triforine in or on the following:

<u>CROPS</u>	<u>Residues</u>
almonds	0.01 PPM
apples	0.01 PPM
peaches	5.0 PPM
nectarines	2.0 PPM
apricots	3.0 PPM
cherries	2.0 PPM
plums	2.0 PPM
prunes	2.0 PPM
tomatoes	2.0 PPM
peppers	5.0 PPM
eggplant	1.0 PPM
strawberries	2.0 PPM
melons	1.0 PPM
cucumbers	0.5 PPM

Recommendation:

See end of review.

Chemical Name:

N,N'-[1,4-piperazinediyl-bis-(2,2,2-trichloroethylidene)]-bis-(formamide)

The two formulations of Triforine under consideration or registration and their toxicity profiles are as follows:

Handwritten initials/signature

Funginex emulsifiable concentrate (EC)

<u>Component</u>	<u>Percent</u>	<u>Purpose</u>
triforine (Tech) min. 97%	20.26	fungicide

*These inert materials have not been cleared for the proposed use.

The following were extracted from a review by Mr. R.B. Jaeger, 1/3/78 Reg.#239-EU11.

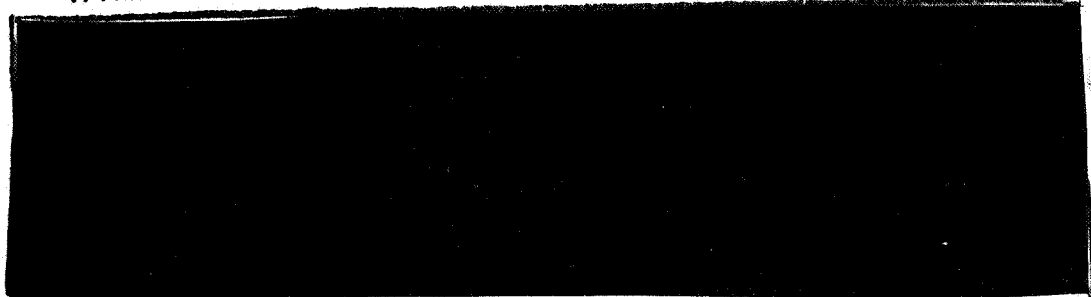
1. Acute Oral LD50 (Rat) = Males 5.7 - (4.0-8.2) gm/kg
Females - 3.8 (1.9-7.6) gm/kg
Core-Guidelines
2. Acute Dermal Toxicity - Male Rabbit = > 5 gm/kg
Core-Minimum
3. Primary Eye Irritation (Rabbit) = Category I
Core-Minimum
4. Primary Skin Irritation (Rabbit) P.I. 5.5/8.0
Category I
Core-Minimum
5. Inhalation LC50 (Rat) 21-Day = > 37.8 mg/L
Core-Minimum

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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Fungicide Wettable Powder

<u>Component</u>	<u>Percent</u>	<u>Purpose</u>
Triforine (Tech)	50	fungicide



Above inerts have been cleared.

Toxicity Profile

1. Oral LD50 (Rats) = > 5 gm/kg
Core-Minimum
2. Dermal LD50 (Rabbit) = > 2 gm/kg
Core-Guideline
3. Acute Inhalation LC50 4 hour exposure (Rat) = > 5.7 mg/L
4. Primary Skin Irritation (Rabbit) = Non irritating
Core-Guideline
5. Eye Irritation Study (Rabbit) = mildly irritating
Category I
Core-Guideline

Technical Triforine - 99%

The following summaries have been extracted from the review of PP#7F1921, by Dr. Reto Engler 4/7/77.

1. Oral LD50 (Mice) = 6 gm./kg
Oral LD50 (Rat) = 13 gm/kg
Dermal LD50 (Rat) = 10 gm/kg
Skin and Eye Irritation = Not irritating

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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2. 90-Day Feeding (Rat) - NEL = 500 PPM
3. 90-Day Feeding (Dog) - NEL = 100 PPM
4. Mutagenicity - Negative (male dominant lethal mouse)
5. 3-Generation Reproduction Study (Rat) - NEL = 2500 PPM
(reproduction) HLT.
6. Metabolism (Rat) Two Studies - Satisfactory to determine
major metabolites.

The following studies have been reviewed by Charles Frick for the purpose of assigning Core-Classification.

1. Teratology + Fetotoxicity (Rat) - NEL = 400
Possible fetotoxicity
effects at 800 and HLT
1600 PPM.
Core-Minimum
2. 18-Month Mouse Feeding Study - Negative for oncogenicity
at 750 PPM (HLT)
Core-Guideline
3. 2-Year Dog Feeding Study - NEL = 100 PPM (HLT 1000 PPM)
Core-Minimum
4. 2-Year Rat Feeding Study - NEL = 625 PPM
No oncogenic effects at 3125 PPM
HLT.
Core-Minimum

ADI, maximum permissible intake (MPI) and theoretical maximal
residue concentration (TMRC).

Based on the NEL (100 PPM) observed in the dog study using a 100 fold safety factor, the ADI is 0.025 mg/kg/bw/day; for a 60 kg man the MPI thus is 1.5 mg/kg/day. The TMRC was calculated.

Recommendation:

1. The existing data base gives no indication of any hazards associated with level of exposure of Technical Triforine that would result from the proposed tolerance request however, under the proposed guidelines of August 22, 1978, the teratology requirement consists of teratogenic testing in two species therefore, a second teratology study will be required.
2. The toxicology data on the formulation of Triforine (Funginex WP) is adequate.
3. The formulation of Triforine (Funginex EC) [REDACTED] inert ingredients, as noted in review, that have not been cleared for the proposed use.
4. Residue Chemistry Branch considerations are not available at the time of this review.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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NO CFR NUMB

Triforin

9/2/80

003801

File last updated 9/2/80

ACCEPTABLE DAILY INTAKE DATA

Dog mg/kg	NOEL ppm	S.F.	ADI mg/kg/day	MPI mg/day (60kg)
2.500	100.00	100	0.0250	1.5000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Cranberries (44)	0.100	0.03	0.00005
Blueberries (18)	0.100	0.03	0.00005
Peaches (114)	0.100	0.90	0.00135

MPI 1.5000 mg/day (60kg) TMRC 0.0014 mg/day (1.5kg) % ADI 0.10

Current Action: 0F2351, 0F2352, 0F2353

CROP	Tolerance	Food Factor	mg/day (1.5kg)
Almonds (1)	0.010	0.03	0.00000
Apples (2)	0.010	2.53	0.00038
Peaches (114)	4.900	0.90	0.06610
Nectarines (100)	2.000	0.03	0.00090
Apricots (3)	3.000	0.11	0.00506
Cherries (30)	2.000	0.10	0.00307
Plums, not prunes (124)	2.000	0.09	0.00276
Prunes (130)	2.000	0.04	0.00123
Tomatoes (163)	2.000	2.87	0.08624
Peppers (120)	5.000	0.12	0.00920
Eggplant (53)	1.000	0.03	0.00045
Strawberries (152)	2.000	0.18	0.00552
Melons (92)	1.000	2.50	0.03005
Cucumbers, inc pickl (46)	0.500	0.73	0.00544

MPI 1.5000 mg/day (60kg) TMRC 0.2178 mg/day (1.5kg) % ADI 14.52

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