Toxicology Branch/HED Review

RCB 5352

FEB 15 1983

Caswell No(s).: 470 A (2-15-83)

To: Henry Jacoby

Registration No(s).: Related action: 359-685

Pesticide Petition No(s).: 3F2810

Chemical(s): Iprodione

Requested Action(s): Tolerance: 20 ppm in/on Stone fruit

Recommendation: "Stone fruit" has not yet been approved as a tolerance category. Tolerance for apricots plums and prunes can be toxicologically supported at 20 ppm.

Inert(s) cleared 180.1001: yes

% of ADI occupied: Existing: 5.67 Resulting: 8.17

Resulting % increase in TMRC: 2.50

Data considered in setting the ADI: 3-generation reproduction in rat NOEL: 500 ppm

Attached (?): ADI printout: (YES)/NO ; TOX "one-liner": (YES) NO ; DER: YES (NO)

Existing regulatory actions against registration: none

RPAR status: none

New Data: none

Data gaps: Teratology (in a second species); Mutagenicity including at least the following: (1) DNA repair (2) Gene mutation, mammalian, preferably in vitro, (3) Chromosomal aberration, mammalian, preferably in vitro.

Comments: Defer Tolerance category consideration to RCB. "Stone fruit" may become an approved category in the near future.

Reviewer: Thomas Edwards 2-3-83 Date:

Section Head: William M Butler 2-14-83 Branch Chief: [signature] 2/14/83

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CFR 180.39 Iprodione 1/28/83

File last updated 1/28/83

ACCEPTABLE DAILY INTAKE DATA

RAT,Older NOEL mg/kg	ppm	S.F.	ADI mg/kg/day	MPI mg/day(60kg)
25.000	500.00	100	0.2500	15.0000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Kiwi Fruit(204)	10.000	0.03	0.00450

MPI	TMRC	% ADI
15.0000 mg/day(60kg)	0.0045 mg/day(1.5kg)	0.03

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Unpublished,Tox Approved 8G2087,0G2402,2F2596,2F2728,3G2787,3G2801

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Almonds(1)	0.050	0.03	0.00002
Apricots(3)	0.000	0.11	0.00000
Plums,inc prunes(125)	0.000	0.13	0.00000
Cherries(30)	0.000	0.10	0.00000
Nectarines(100)	0.000	0.03	0.00000
Peaches(114)	0.000	0.90	0.00000
Almonds(1)	0.000	0.03	0.00000
Meat, red(90)	0.800	10.81	0.12975
Milk&Dairy Products(93)	0.150	28.62	0.06438
Grapes, not raisins(67)	60.000	0.45	0.40470
Raisins(134)	180.000	0.04	0.11037
Lettuce(84)	7.000	1.31	0.13735

MPI	TMRC	% ADI
15.0000 mg/day(60kg)	0.8511 mg/day(1.5kg)	5.67

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Current Action 3F2810

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Stone Fruits(151)	20.000	1.25	0.37404

MPI	TMRC	% ADI
15.0000 mg/day(60kg)	1.2251 mg/day(1.5kg)	8.17

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Tox Chem No. 470A Glycophene (Iprodione) File Last Updated 6/15/82 Current Date

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Teratology (Oral) - Rabbit, DREB, #730925, 2/5/76	Technical 1% CMC (Carboxymethyl cellulose)	232712	Maternal NOEL = Not determined Maternal LEL = Not determined Terat NOEL = Not determined Terat LEL = 100 mg/kg		Supplementary 000614
Teratology (gastric intubation) - Rat DREB, #731016, 2/5/76	Technical 1% CMC	232712	No mortality = Not determined No raw data for (1) Maternal NOEL, (2) Terat NOEL , and (3) Terat LEL Maternal LEL = 100 mg/kg		Minimum 000614
Acute Oral LD_{50} - Mouse	Technical	232701	LD_{50} = 3050 mg/kg (Male) (2630-3540)	III	Minimum 001519
Acute Oral LD_{50} - Mouse	Technical	232701	LD_{50} = 4 g/kg (Male) (3.3-4.8) LD_{50} = 4.4 g/kg (Female) (3.3-5.9)	III	Minimum 001519
Acute Oral LD_{50} - Rat	Technical	232701	LD_{50} > 2 g/kg (Male & Female)	III	Supplementary 001519
Acute Oral LD_{50} - Dog	Technical	232701	LD_{50} > 2 g/kg (Male & Female)	III	Supplementary 001519
Acute Dermal LD_{50} - Rat	Technical	232701	LD_{50} > 2.5 g/kg (Male & Female)	III	Supplementary 001519
Acute Dermal LD_{50} - Rabbit	Technical	232701	LD_{50} > 1 g/kg (Male & Female)	II	Supplementary 001519
Primary Dermal Irritation Rabbit	Technical	232701	Not an irritant at 1 g/kg (Male & Female)	IV	Supplementary 001519
Primary Dermal Irritation Rabbit	Technical	232701	Not an irritant	IV	Minimum 001519

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Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Primary Dermal Irritation Rabbit	Technical	232701	Not an irritant		Supplementary 001519
Primary Eye Irritant - Rabbit	Technical	232701	Not an irritant		Minimum 001519
Acute Inhalation , LC_{50} - Rat	Technical	232701	LC_{50} > 3.29 g/l/4 hr.	III	Minimum 001519
Dermal Sensitization - Guinea Pig	Technical	232701	No evidence of sensitization		Supplementary 001519
28 Day Oral - Mouse	Technical	232702	NOEL = 1,900 ppm (Male & Female) Strippled liver above 6000 ppm		Supplementary 001519
28 Day Feeding - Mouse	Technical	232702	NOEL = 1,900 ppm, white foci Strippled liver above 6000 ppm		Supplementary 001519
90 Days Feeding - Dog	Technical	232702	NOEL = 2400 ppm LEL = 7200 ppm		Minimum 001519
5 Month Feeding - Rat	Technical	232702	NOEL $\geq$ 1000 ppm (HDT) (Male & Female)		Minimum 001519
24 Month Feeding - Rat	Technical	097201	NOEL $\geq$ 1000 ppm (HDT)		Minimum 001519
18 Month Toxicity and Oncogenicity - Mouse	Technical	097201	NOEL $\geq$ 1250 ppm (HDT) (Male & Female) Not carcinogenic		Minimum 001519
Mutagenicity - Mouse	Technical	232712	No evidence of mutagenicity or adverse effect on fertility at 1500 and 6000 ppm		Minimum 001519

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Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
3 Generation Reproduction Rat	Technical	232712	Reproductive NOEL = 500 ppm Reproductive LEL = 2000 ppm (HDT) decreased fetal weight Systemic NOEL $\geq$ 2000 ppm (HDT)		Minimum 001519
Mutagenicity, Microbiologic	Technical	232712	All tests performed were negative		Supplementary 001519