Rev. 4/14/82 Toxicology Branch/HED Review RECEIVED RCB 6/25/82

JUN 25 1982

Caswell No(s).: 470 A Perfetti File petition

To: H. JACOBY P.M. 21

Registration No(s).: 356-685 CFR 180-539

Pesticide Petition No(s).: 2F 2596

Chemical(s): IPRODIONE 209900-0 (ROYRAL)

Requested Action(s): TOLERANCE OF 20 PPM ON CHERRIES, PEACHES AND NECTARINES

Recommendation: The increment in the TMRC, from the previous granted action to this one, is reduced 0.3876 to 0.35 mg/day (1.5 Kg). This action is approved

Inert(s) cleared 180.1001: YES

% of ADI occupied: Existing: 2.58 Resulting: 2.34

Resulting % ~~increase~~ decrease in TMRC: 0.3876 to 0.3508

Data considered in setting the ADI: REFER TO ATTACHED

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

Existing regulatory actions against registration: NONE

RPAR status: NOT IN THE RPAR LIST

New Data: NONE

Data gaps: ACUTE DERMAL, SECOND TERATOLOGY AND MUTAGENICITY OTHER TEST

Comments: PREVIOUS ACTION AND COMPUTER SHEET ATTACHED FOR COMPARISON

Reviewer: [signature] Date: June 24-82

File last updated 6/24/82

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

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Unpublished,Tox Approved 8G2087,0G2402

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Almonds(1)	0.050	0.03	0.00002
Apricots(3)	10.000	0.11	0.01686
Plums,inc prunes(125)	10.000	0.13	0.01993

MPI	THRC	% ADI
15.0000 mg/day(60kg)	0.0413 mg/day(1.5kg)	0.28

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Current Action 2F2596

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Cherries(30)	20.000	0.10	0.03066
Nectarines(100)	20.000	0.03	0.00900
Peaches(114)	20.000	0.90	0.26930

MPI	THRC	% ADI
15.0000 mg/day(60kg)	0.3508 mg/day(1.5kg)	2.34

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537

File last updated: 3/1/82

ACCEPTABLE DAILY INTAKE DATA

RAT, Older NOEL mg/kg	ppm	S.F.	ADI mg/kg/day	TMRC 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

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

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Unpublished, Tox Approved PP# 6G2087, 0G2402

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Almonds(1)	0.050	0.03	0.00002
Apricots(3)	10.000	0.11	0.01686
Cherries(30)	10.000	0.10	0.01533
Nectarines(100)	10.000	0.03	0.00450
Peaches(114)	10.000	0.90	0.13490
Plums, inc prunes(125)	10.000	0.13	0.01993

TMRC	TMRC	% ADI
15.0000 mg/day(60kg)	0.1960 mg/day(1.5kg)	1.31

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Current Action PP# 2F2596 approved.

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Apricots(3)	10.000	0.11	0.01686
Cherries(30)	10.000	0.10	0.01533
Nectarines(100)	10.000	0.03	0.00450
Peaches(114)	10.000	0.90	0.13490
Plums, inc prunes(125)	10.000	0.13	0.01993

TMRC	TMRC	% ADI
15.0000 mg/day(60kg)	0.3676 mg/day(1.5kg)	2.58

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Please add residue of 0.5 ppm onions 82-NJ-18

Section 18

alex

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RHÔNE-POULENC INC.
AGROCHEMICAL DIVISION
P.O. Box 125 - Black Horse Lane - Monmouth Junction, New Jersey 08852 - Telephone: (201) 297-0100 - Telex: 844527

June 3, 1982
DLO/82/083

Henry Jacoby
Product Manager (21)
Environmental Protection Agency
Crystal Mall Bldg. 2
Arlington, VA 22202

Dear Mr. Jacoby:

Subject: Rovral-Stone Fruits
PP# 2F2596

Attached are three copies of a revised Section F for the subject petition. We are now requesting a tolerance of 20 ppm on cherries, peaches and nectarines as per your May 27, 1982 letter.

Also attached are 5 copies of final printed labeling incorporating all of the changes mentioned in your letter of May 27, 1982. In addition to the requested changes, we have changed the warranty statement in order to be consistant with other currently registered Rhone-Poulenc products. We have also added the common name "iprodione" under active ingredient. A letter from ANSI is attached indicating their approval of the name iprodione.

Thank you for your attention to this matter.

Sincerely,

RHONE-POULENC INC.
Agrochemical Division

Dave Olson

David L. Olson
Project Leader

DLO/bw
attachments

cc: T. B. Waggoner

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To: Henry Jacoby P M 21

Registration No(s).: 359-685 CFR 180-539

Pesticide Petition No(s).: 2F 2596 Acc. No 070441 070443

Caswell No(s).: 470 A

Chemical(s): Iprodione (Rovral)

RAC(s) - tolerance(s): Request for tolerances of 10 ppm in appricots , nectarines peaches , plums imc. prunes and cherries.

Inert(s) cleared 180.1001: (e) Yes

% of ADI occupied: Existing: 0.03 Resulting: 2.58

Resulting % increase in TMRC: From 0.0045 to 0.3876

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

Existing regulatory actions against registration: None

RPAR status: Is not in the R P A R list

New Data: None Submited / Data required on behalf of this action (next page)

Data considered in setting the ADI: Rat reproduction , 3 generations , study .NOL= 500ppm

Data gaps: The three following study has been classified as supplementary data ; Acute dermal toxicity, second teratology study and mutagenicity other test. The studies classified as supplementary data must be upgraded.

Recommendation: Granting this request will not present a hazard since the ADI is not exceeded

Comments: A one year dog feeding study has been initiated and the report will be submitted within a year. (Info obtained by phone by The PM) The study 3 generation reproduction -rat has been used to find the ADI instead of the 3 month dog feeding study. It will lead to a better appriasal of the toxicity potential of the product

Reviewer: Alex Aasse Date: 3-31-82

Section Head: William M Butler

Data required		Classification
Acute oral -rat	3,700 mg/kg	m
Acute dermal -rabbit	30,000mg/kg male -5,000 mg/kg female	s
Acute inhalation-rat	3.29mg/l/4h	m
Primary eye-skin-rabbit	Not an irritant	m
90 day feeding -dog	NOEL 2,400 ppm - LEL 7,200 ppm	m
Teratology - rat	NOEL 400 mg/kg /day	m
Teratogenicity - rabbit	NOEL 400 mg/kg/day	s
Chronic oncogenicity -rat 24 month feeding	NOEL 1,000 ppm	m
18 months oncogenicity -mouse	NOEL 1,250 ppm	m
Mutagenicity , dominant lethal - mouse	- No evidence of mutagenicity at 1,500 or at 6,000 ppm	m
Three generations reproduction study -rat	NOEL 500 ppm	m

Justification for using the 3 generation reproduction study -rat instead of the 3 month dog feeding study, to find the A D I

The NOEL in the 3 months feeding study -(dog) was found at the 2,400 ppm dose level. The LEL was 7,200 ppm and the symptom observed was muscular atony , no other signs of toxicity were reported

The three generation reproduction study (rat) with a NOEL of 500 ppm and with no toxic signs observed in the parent animals, will give a better indication of the potential toxicity of the material . The only adverse effect observed during the 3 generations study was the post natal pupgrowth for group 1V that was reduced in a minor percent as compared with group 1.

Tox Chem No. 470A Iprodione (Rovral) File Last Updated 2-3-81 Current Date 7-11-81

Study Type	Material	EPA Accession	Results: LD50, LC50, MRL, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Acute oral LD_{50}, mice	TECH	232701	LD_{50} = 3050 mg/kg (2630-3540)	III	Minimum
Acute oral LD_{50}, mice	TECH	232701	LD_{50} = 4.0 (3.3-4.8) g/kg - M 4.4 (3.3-5.9) g/kg - F	III	Minimum
Acute oral LD_{50}, rat	TECH	232701	LD_{50} = 3700 ± 300 mg/kg - M = 4400 (3200-6100) mg/kg -F	III	Minimum
Acute oral LD_{50}, dog	TECH	232701	Atoxic at 2000 mg/kg	III	Supplementary
Acute dermal LD_{50}, rat	TECH	232701	Atoxic at 2.5 g/kg	III	Supplementary
Acute dermal LD_{50}, rabbit	TECH	232701	Atoxic at 1 g/kg LD_{50} > 30,000 mg/kg - M > 5,000 mg/kg - F	IV	Supple-mentary
Primary dermal irritation - rabbit	TECH	232701	Not irritating at 1 g/kg	IV	Supple-mentary
Primary dermal irritation - rabbit	TECH	232701	Not an irritant	IV	Minimum
Primary dermal irritation - rabbit	TECH	232701	Not an irritant (Summary)	IV	Supple-mentary
Primary eye irritation - rabbit	TECH	232701	Not an irritant	IV	Minimum
Acute inhalation LD_{50}, rat	TECH	232701	LC_{50} = > 3.29 mg/L/4 hr.	IV	Minimum
Sensitization dermal - guinea pig	TECH	232701	Negative	IV	Supple-mentary
28-Day Oral - mice	TECH	232701	NOEL = 1,900 ppm		Supple-mentary

Tox Chem No. 470A

File Last Updated 2-3-81

Current Date 7-11-81

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD50, LC50, RIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Mutagenicity dominant lethal - mice	TECH	232712	No evidence of mutagenicity or adverse effects on fertility at 1500 or 6000 ppm dose males		Minimum
Mutagenicity - microbiologic	TECH	232712	Negative		Supplementary
3-Generation reproduction - rat	TECH	232712	NOEL = 500 ppm		Minimum

Tox Chem No. 470A

File Last Updated 2-3-81

Current Date 7-11-81

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LDso, LCso, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
[illegible]	Tech	232701	NOEL = 1,000 ppm		Supplementary
90-Day feeding, dog	TECH	232701	NOEL = 2,400 ppm LEL = 7,200 ppm		Minimum
5-Month feeding, rat	TECH	232701	NOEL $\geq$ 1,000 ppm (highest dose tested)		Minimum
24-Month feeding, rat	TECH	097201	NOEL $\geq$ 1,000 ppm (highest dose tested)		Minimum
18-Month feeding - oncogenicity, mice	TECH	097201	NOEL $\geq$ 1,250 ppm (highest dose tested) Not carcinogenic.		Minimum
Teratogenic - rat	TECH	232712	Teratogenic NOEL $\geq$ 400 mg/kg/day (highest level tested) Fetotoxic NOEL = 200 mg/kg/day Fetotoxic LEL = 400 mg/kg/day (decrease in mean number of implantation sites) Maternal NOEL = 200 mg/kg/day Maternal LEL = 400 mg/kg/day (decrease in conception rate and food consumption)		Minimum
Teratogenic - rabbit	TECH	232712	Teratogenic NOEL $\geq$ 400 mg/kg/day (highest level tested) Fetotoxic NOEL = undetermined Maternal LEL = undetermined		Supplementary 000614

ACCEPTABLE DAILY INTAKE DATA

RfD, Older NOEL		S.F.	ADI	TMRL
mg/kg	ppm		mg/kg/day	mg/day(60kg)
25.000	5000.00	100	0.2500	15.0000

Published Tolerances

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

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

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Unpublished, Tox Approved Pet# 8G2037,0G2402

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Almonds(1)	0.050	0.03	0.00002
Apricots(3)	10.000	0.11	0.01686
Cherries(30)	10.000	0.10	0.01533
Nectarines(100)	10.000	0.03	0.00450
Peaches(114)	10.000	0.90	0.13490
Plums,inc prunes(125)	10.000	0.13	0.01993

RfD	TMRC	% ADI
15.0000 mg/day(60kg)	0.1960 mg/day(1.5kg)	1.31

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Current Action Pet# 2F2596

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Apricots(3)	10.000	0.11	0.01686
Cherries(30)	10.000	0.10	0.01533
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Peaches(114)	10.000	0.90	0.13490
Plums,inc prunes(125)	10.000	0.13	0.01993

RfD	TMRC	% ADI
15.0000 mg/day(60kg)	0.3876 mg/day(1.5kg)	2.58

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SECTION F

PROPOSED PERMANENT TOLERANCES FOR RESIDUES OF THE FUNGICIDE IPRODIONE, ITS ISOMER AND METABOLITE IN OR ON THE RAW AGRICULTURAL COMMODITY STONE FRUITS INCLUDING FRESH AND PROCESSED FRUITS

Stone Fruits

It is hereby proposed a tolerance for the combined residues of iprodione [3-(3,5-dichlorophenyl)-N-(1-methyl ethyl)-2,4-dioxo-1-imidazolidinecarboxamide], its isomer [3-(1-methyl ethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide], and its metabolite [3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidine-carboxamide] in and/or on:

apricot, cherries (sour and sweet), nectarines, peaches, plums (fresh prunes)	10 ppm

Animal Products

It is hereby proposed a modified use to restrict grazing livestock in treated orchard and to restrict the feeding of cover crops, therefore, no tolerances for residues in meat, milk, poultry and eggs would be needed. Section 180.6 (a) (3).

RHÔNE POULENC