12-5-86
RCB

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DEC 5 1986

MEMORANDUM

SUBJECT: Request to Amend the Registration of Iprodione to Include Tolerances on Rice, Rice Hulls, and Rice straw

TO: Lois Rossi, PM 21
Registration Division
(TS-767)

FROM: Margaret L. Jones 11/19/86
Review Section III
Toxicology Branch, HED
(TS-769)

THROUGH: Marcia Van Gemert, Ph.D., Head 11/20/86
Review Section III
Toxicology Branch

and Theodore M. Farber, Ph.D., Chief 12/1/86
Toxicology Branch

Compound: Iprodione; Rovral; Glycophene Tox. Chem No: 470A

Registration No: 178651, 178652 Tox. Project No: 2328

Petitioner: Rhone Poulenc

Accession No: N/A Petition No: 6F3443, 6H5507

Action Requested: Amend the registration of Iprodione to include tolerances on rice, rice straw, and rice hulls.

Data Considered:

Reproduction in the rat (undated)
Chronic/oncogenicity in the mouse (3/6/78)
Subchronic dog (undated)
Developmental toxicity in the rabbit (12/12/85)

Data Currently Lacking on Iprodione: Toxicology data requirements were published in the Federal Register (Vol.49 No.207, 10/24/84, pp.42892 - 42893). According to these requirements, the following data for the technical chemical are lacking:

Acute Dermal LD_{50}

Dermal sensitization
Developmental Toxicity in a species other than the rabbit
General Metabolism

Actions Under Way to Obtain Missing Data: No known action is presently under way to obtain these data.

Published Tolerances for Iprodione: Tolerances exist for Iprodione in or on raw agricultural commodities as published in 40 CFR 180.399, 21 CFR 193.251 and 21 CFR 561.263.

Effect of Proposed Tolerances on Acceptable Daily Intake (ADI): The present request for tolerances of Iprodione in or on rice at 10.0 ppm was analyzed using the Toxicology Branch acceptable daily intake (ADI) program. The ADI program cannot analyse the effect of tolerances on rice hulls or rice straw as these are not human foods. The secondary residues expected to occur in meat and/or milk as a result of this additional use will be considered by Residue Chemistry Branch and Toxicology Branch will then analyse the impact on the acceptable daily intake.

The present analysis used the ADI based on the three generation reproduction study in rats with a no observed effects level (NOEL) of 500 ppm (25 mg/kg/day). The cumulative percent of the ADI used from the existing and proposed actions is 13.56 for the US population. (Please note the previous analysis using the Tolerance Assessment System (TAS) indicated a slightly higher percent ADI. The difference reflects slightly different consumption information for each raw agricultural commodity.)

Acceptable Daily Intake, Maximum Permissible Intake, and Theoretical Maximum Residue Contribution: The ADI is based on the results of the three generation reproduction study discussed above.

ADI = 0.25 mg/kg/day
MPI = 15 mg/day (60 kg)
TMRC = 0.034 mg/kg/day
NOEL = 500 ppm (25 mg/kg/day)
Safety Factor (SF) = 100

Recommendation: Toxicology Branch recommends acceptance of the proposed tolerances for Iprodione in or on rice at 10.0 ppm. If, as expected, this use results in added residues in meat and/or milk from the use of rice straw and rice hulls as feed, a revised petition should be submitted to the Agency reflecting the new levels in those commodities.

It is further recommended that steps be taken to obtain the currently lacking toxicity data on Iprodione.

No known regulatory actions are pending against the registration of Iprodione.

TOXICOLOGY BRANCH ADI PRINTOUT Date: 11/13/86

Glycophene (Iprodione)
Caswell #470A NOEL = 0.0000 mg/kg ADI = 0.250000 mg/kg/day
CFR No. 180.399 LEL = 0.0000 mg/kg Safety Factor = 100
Status: ADI NOT VERIFIED BY TOX ADI COMMITTEE OR AGENCY RFD COMMITTEE.
WHO last reviewed 1977.

DRAFT

RESIDUE CONTRIBUTION OF PUBLISHED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
1	Almonds	0.050		0.03	0.000023
54	Eggs	0.800		2.77	0.033240
61	Garlic	0.100		0.03	0.000045
67	Grapes, not including raisins	60.000		0.45	0.405000
84	Lettuce	15.000		1.31	0.294750
90	Meat, red	0.400		10.81	0.064860
93	Milk and dairy products	0.300		28.62	0.128790
128	Poultry	2.000		2.94	0.088200
134	Raisins	300.000		0.04	0.180000
151	Stone fruits	20.000		1.25	0.375000
203	Kidney	3.000		0.03	0.001350
204	Kiwi fruit	10.000		0.03	0.004500
211	Liver	3.000		0.03	0.001350

TMRC
0.026285 mg/kg/day (60kg BW, 1.5kg diet)

%ADI
10.514050

RESIDUE CONTRIBUTION OF TOX-APPROVED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
1	Almonds	0.250	5F3241	0.03	0.000112500
10	Beans, dry edible	4.000	4F3150	0.31	0.018600000
11	Beans, lima	2.000	4F3150	0.19	0.005700000
12	Beans, snap	2.000	4F3150	0.98	0.029400000
17	Boysenberries	15.000	4F3129	0.03	0.006750000
18	Blueberries	15.000	5E3214	0.03	0.006750000
19	Broccoli	25.000	6F3305	0.10	0.037500000
48	Currants	15.000	5E3214	0.03	0.006750000
90	Meat, red	0.200	4F3129	10.81	0.032430000
93	Milk and dairy products	0.400	4F3129	28.62	0.171720000
105	Onions	0.500	4F3111	0.83	0.006225000
115	Peanuts	0.100	4G3037	0.36	0.000540000
115	Peanuts	0.400	4F3129	0.36	0.002160000
127	Potatoes	0.500	6F3366	5.43	0.040725000

RESIDUE CONTRIBUTION OF TOX-APPROVED TOLERANCES

CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
135 Raspberries	15.000	5E3214	0.03	0.006750000
223 Ginseng	4.000	6E3426	0.03	0.001800000

TMRC
0.032517 mg/kg/day (60kg BW, 1.5kg diet)

%ADI
13.006800

RESIDUE CONTRIBUTION OF NEW (PENDING) TOLERANCES

CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
137 Rice	10.000	6F3443	0.55	0.082500000

TMRC
0.033892 mg/kg/day (60kg BW, 1.5kg diet)

%ADI
13.556800
