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

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~~Firestone~~
File petition

APR 24 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: IR-4 Minor Use Petition for Metolachlor on Chili Peppers
Petition #5E3236; CASWELL No. 188DD

TO: Hoyt Jamerson (43)
Emergency Response and Minor Use Section
Registration Division (TS-767)

FROM: D. Stephen Saunders Jr., Ph.D. DSS 4/19/85 CFC
Toxicologist, Section V
TOX/HED (TS-769)

THRU: Laurence D. Chitlik, DABT LDC 4/19/85
Head, Section V
TOX/HED (TS-769)
and
Theodore M. Farber, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769) [signature] 4/24/85

Action Requested

Expedited review of a request submitted by Interregional Research Project No. 4 for a tolerance of 0.5 ppm for the herbicide Metolachlor and its metabolites 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone in or on the raw agricultural commodity chili peppers.

Recommendations

Metolachlor has been shown to be oncogenic in rats. The risk calculated for the proposed use under the Tolerance Assessment System is 4.2×10^{-9}. The risk for existing and proposed tolerances is 1.592×10^{-6}. The incremental increase in risk from the proposed use is 0.26% (see Discussion for calculations).

Background

The proposed use is requested by IR-4 to control yellow nutsedge and annual grasses in chili pepper fields. There are 17,000 acres of chili peppers under cultivation in the state of New Mexico, and the petitioner estimates that 75-80% of this acreage is infested with yellow nutsedge. An application rate of 2 lbs a.i./acre of Dual 8E (84.6%) emulsifiable concentrate by ground application is proposed. Application will be once per year, with a proposed preharvest interval of 39 days.

Discussion

1) Inerts for the formulation Dual 8E have been cleared under 180.1001.

2) Calculation of Risk: (a) "Old" tolerance system- The existing Theoretical Maximum Residue Contribution (TMRC) is 0.0820 mg/day/1.5 kg diet under the "old" tolerance system. This value is equal to:

0.0820 mg/day/60 kg body weight = 1.37×10^{-3} mg/kg/day.

Risk for existing tolerances = Exposure x Q* = $(1.37 \times 10^{-3}) \times (2.0 \times 10^{-3})$
= 2.74×10^{-6}

Since chili peppers are a minor use, the average value of 0.03% of a 1.5 kg diet is used, which equals:
0.0003 x 1.5 kg = 0.45 g, divided by 60 kg average BW = 0.0075 g/kg

The TMRC of the proposed use =
proposed tolerance x dietary contribution of RAC=
0.5 ppm (ug/g) x 0.0075 g/kg = 0.00375 ug metolachlor/kg BW.

The risk for the proposed use is therefore calculated as:
Exposure x Q* = $(3.75 \times 10^{-6}$ mg/kg BW) x $(2.0 \times 10^{-3}) = 7.5 \times 10^{-9}$

The incremental increase in risk associated with the proposed tolerance is therefore:

$\frac{7.5 \times 10^{-9}}{2.74 \times 10^{-6}} \times 100 = 0.27\%$, which is also the % increase in the TMRC.

Risk for existing and proposed uses = 2.75×10^{-6}.

(b) Risk calculated under the Tolerance Assessment System (TAS): The TAS calculates the TMRC for existing tolerances as 7.94×10^{-4} mg/kg/day. The proposed tolerance of 0.5 ppm on chili peppers results in a TMRC of 2.1×10^{-6} mg/kg/day. The risk for existing tolerances =

Exposure x Q* = $(7.94 \times 10^{-4}) \times (2.0 \times 10^{-3}) = 1.59 \times 10^{-6}$.

Risk for proposed use = $(2.1 \times 10^{-6}) \times (2.0 \times 10^{-3}) = 4.2 \times 10^{-9}$

% increase = $\frac{4.2 \times 10^{-9}}{1.59 \times 10^{-6}} \times 100 = 0.26\%$, which is also the % increase in the TMRC.

Risk for existing and proposed uses = 1.592×10^{-6}.

3) Summary of data: See attached "one-liners". No new data were submitted.

4) Data gaps: Acute inhalation toxicity study for the EC (8 lbs/gal) per Registration Standard.

5) Comments: The Q* used to calculate risk was obtained from an IBT rat chronic feeding study, which although acceptable, was replaced by another rat feeding study submitted by the registrant. A Q* for the most recent study is not available at present, however the oncogenic responses in the two studies were very similar, and therefore the Q* to be obtained from the most recent study is likely to be similar to the previous value.

ROUTINE CHRONIC ANALYSIS: [illegible] LCS BASED ON INDIVIDUALS' 3-DAY AV

*NAME: METOLACHLOR	STUDY	ADI	NOEL	S
*CASWELL NO: 188DD CFR NO: CFR180.368	A	00000.0025	000100.000	00
*CAS NO: 51218-45-2 SHAUGHNESSY NO: 108801	B	00000.0300	000300.000	0C
*STATUS CODES:	C	00000.3600	007200.000	0C

*RDV INFO: The AD value used in this analysis is 0.0005 MG/KG
*FILE INFO: NEW ACTION: No User Modifications APPROVED: Data Used

SUMMARY BY POPULATION SUBGROUP

	TOTAL TMRC ADJUSTED FOR BODY (MG/KG BODY WEIGHT/DAY) PRIOR TMRC (EXCLUDES NEW ACTION)	NEW TMRC (INCLUDES NEW ACTION)	AS
U.S. POP.--48 STATES--ALL SEASONS	0.000684	0.000796	
U.S. POPULATION--SPRING SEASON	0.000655	0.000775	
U.S. POPULATION--SUMMER SEASON	0.000677	0.000783	
U.S. POPULATION--FALL SEASON	0.000700	0.000810	
U.S. POPULATION--WINTER SEASON	0.000694	0.000797	
NORTHEAST REGION	0.000619	0.000734	
NORTH CENTRAL REGION	0.000683	0.000790	
SOUTHERN REGION	0.000753	0.000855	
WESTERN REGION	0.000638	0.000761	
HISPANICS	0.000796	0.000942	
NON-HISPANIC WHITES	0.000662	0.000773	
NON-HISPANIC BLACKS	0.000753	0.000840	
NON HISPANICS OTHER THAN BLACKS & WHITES	0.000665	0.000803	
NURSING INFANTS (<1 YEAR OLD)	0.000491	0.000509	
NON-NURSING INFANTS (<1 YEAR OLD)	0.001251	0.001292	
FEMALES(13+,PREGNANT, NOT NURSING)	0.000476	0.000583	
FEMALES(13+,NURSING)	0.000526	0.000653	
CHILDREN(1-6 YRS)	0.001406	0.001590	
CHILDREN(7-12 YRS)	0.001033	0.001177	
MALES(13-19 YRS)	0.000728	0.000848	
FEMALES(13-19 YRS,NOT PREG. OR NURSING)	0.000588	0.000691	
MALES(20+ YRS)	0.000567	0.000668	
FEMALES(20+ YRS,NOT PREG. OR NURSING)	0.000477	0.000566	
ALASKA	0.000000	0.000000	
HAWAII	0.000000	0.000000	
PUERTO RICO	0.000000	0.000000	
LOW INCOME--48 STATES	0.000000	0.000000	

COMPLETE LISTING OF RELEVANT FOODS FOR U.S. POP.--48 STATES--ALL SEASONS	AVG. DAILY CONSUMPTION (GRAMS/DAY PER KG OF BODY WT.)	
FOOD CODE DESCRIPTION		
15029AA SOYBEANS-SPROUTED SEEDS	0.000001	.
15030AB BEANS-SUCCULENT-HYACINTH(YOUNG PODS)	0.000001	.
15031AA BEANS-DRY-BLACKEYE PEAS(COWPEAS)	0.002473	.
15032AA BEANS-DRY-GARBANZO(CHICK PEA)	0.000526	.
***GROUP TOTALS--LEGUME VEGETABLES(SUCCULENT OR DRIED)		
11003AB CHILI PEPPERS	0.004109	.
15015AA OKRA	0.014635	.
***GROUP TOTALS--FRUITING VEGETABLES(EXCL. CUCURBITS)		
15004AA CORN,POP	0.006771	.
15005AA CORN,SWEET	0.236707	.
24001AA BARLEY	0.057301	0.10
24002EA CORN,GRAIN-ENDOSPERM	0.165401	0.10
24002HA CORN,GRAIN-BRAN	0.000001	0.10
24002SA CORN SUGAR	0.097166	0.10
24003AA OATS	0.082575	0.10
24004AA RICE-ROUGH	0.003060	0.10
24004AB RICE-MILLED	0.155263	0.10
24005AA RYE-ROUGH	0.000001	0.10
24005GA RYE-GERM	0.000274	0.10
24005WA RYE-FLOUR	0.004029	0.10
24006AA SORGHUM (INCLUDING MILO)	0.023769	0.10
24007AA WHEAT-ROUGH	0.140612	0.10
24007GA WHEAT-GERM	0.000805	0.10
24007HA WHEAT-BRAN	0.012157	0.10
24007WA WHEAT-FLOUR	1.257249	0.10
24012AA MILLET	0.000022	0.10
26001AA BUCKWHEAT	0.000988	0.10
27002OA CORN,GRAIN-OIL	0.022800	0.10
***GROUP TOTALS--CEREAL GRAINS		
08015AA DILL	0.000085	.
***GROUP TOTALS--HERBS AND SPICES		
53001BA BEEF-MEAT BYPRODUCTS	0.017662	0.020
53001BB BEEF(ORGAN MEATS)-OTHER	0.006035	0.020
53001DA BEEF-DRIED	0.002533	0.020
53001FA BEEF(BONELESS)-FAT (BEEF TALLOW)	0.372076	0.020
53001KA BEEF(ORGAN MEATS)-KIDNEY	0.000480	0.020

ROUTINE CHRONIC ANALYSIS: ALL STATISTICS BASED ON INDIVIDUALS' 3-DAY AVERA

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*NAME: METOLACHLOR

*CASWELL NO: 188DD CFR NO: CFR180.368

*CAS NO: 51218-45-2 SHAUGHNESSY NO: 108801

*STATUS CODES:

*RDV INFO: The AD value used in this analysis is 0.0005 MG/KG of

STUDY	ADI	NOEL	SF
A	00000.0025	000100.000	00100
B	00000.0300	000300.000	00100
C	00000.3600	007200.000	00100

File last updated 3/25/93

ACCEPTABLE DAILY INTAKE DATA

RAT,Ulcer mg/kg	NOEL ppm	S.F.	DI mg/kg/day	MPI mg/day(60kg)
1.500	30.00	100	0.0150	0.9000

DRAFT

NOEL Change not rec.

Published Tolerances

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Corn,grain(66)	0.100	1.00	0.00150
Soybeans (oil)(148)	0.100	0.92	0.00138
Meat,inc poultry(89)	0.020	13.85	0.00415
M&Dairy Products(93)	0.020	28.62	0.00858
Eggs(54)	0.020	2.77	0.00083
Peanuts(115)	0.100	0.36	0.00054
Sorghum(147)	0.300	0.03	0.00014
Barley(8)	0.100	0.03	0.00005
Buckwheat(21)	0.100	0.03	0.00005
Millet(94)	0.100	0.03	0.00005
Milo(95)	0.100	0.03	0.00005
Oats(102)	0.100	0.36	0.00054
Rice(137)	0.100	0.55	0.00083
Rye(140)	0.100	0.03	0.00005
Wheat(170)	0.100	10.36	0.01554

MPI	TMRC	% ADI
0.9000 mg/day(60kg)	0.0343 mg/day(1.5kg)	3.81

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Unpublished,Tox Approved 9F2203,2416,2495,2506,2521

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Potatoes(127)	0.200	5.43	0.01628
Sunflower(156)	0.300	0.03	0.00014
Seed&Pod Veg(143)	0.300	3.66	0.01646
Corn,pop(39)	0.100	0.08	0.00012
Corn,sweet(40)	0.100	1.43	0.00215
Cottonseed (oil)(41)	0.100	0.15	0.00022

MPI	TMRC	% ADI
0.9000 mg/day(60kg)	0.0696 mg/day(1.5kg)	7.74

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Current Action 85-MI-02

Current Action not recorded

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Onions(105)	1.000	0.83	0.01242

MPI	TMRC	% ADI
0.9000 mg/day(60kg)	0.0820 mg/day(1.5kg)	9.12

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Tox Chem No. 188DD Metolachlor File Last Updated 1/8/85

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Teratology - rat; Ciba Geigy;# 227625; 6/21/76	CGA 24705 technical		Teratogenic NOEL>360 mg/kg/day(HDT) Fetotoxic NOEL > 360 mg/kg/day Maternal NOEL > 360 mg/kg/day Levels tested by gavage in Sprague - Dawley strain - 0, 60, 180 and 360 mg/kg/day		Minimum 000434
Teratology - rabbit; Argus Research Labs; #203-001; 7/25/80	Metolachlor (Technical) in hydroxymethyl cellulose	099630	Fetotoxic NOEL > 360 mg/kg/day Teratogenic NOEL > 360 mg/kg Maternal NOEL = 120 mg/kg		Minimum 001051
3 Generation reproduction-rat; IBT; #622-07928; 1/4/78	CGA 24705 technical		NOEL > 1000 ppm (HDT) IBT Supplementary (1/31/80) Levels tested: 0,30, 300 & 1000 ppm.		Minimum 000434 Supplementary 000438 Supplementary 002265 Supplementary 003197
2-Generation reproduction - rat;Toxigenics, Inc.; # 450-0272; 08/31/81	TECH	245959 245960 245961	Reproductive NOEL = 300 ppm Reproductive LEL = 1000 ppm (reduced pup weights and reduced parental food consumption).		Guideline 001374
6 Month feeding - dog; IRDC;#382-054; 11/2/79	CGA 24705 technical		NOEL =100 ppm LEL = 300 ppm SAP levels increased Levels tested = 0, 100, 300 and 1000 ppm		000432
90 Day feeding - rat; Oncins Research & Breeding Center;3/1/74	Metolachlor technical	112841	NOEL = 1000 ppm		Supplementary 000434 000436 000437 000438

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
90 Day feeding - dog; Oncins Research & Breeding Center; 1974	CGA 24705 technical		NOEL = 500ppm		Minimum 000438 000436 000434
Oncogenic - mice; IBT; #622-07925; 12/15/77	CGA 24705 technical		Oncogenic NOEL = > 3000 ppm (HDT) IBT Valid (audited by Ciba-Geigy) Levels tested: 0,30,1000 & 3000 ppm.		Minimum 000434
2-Year feeding/onco-rat; Hazleton Raltech; #80030; 5/2/83	Technical FL-800362	250369 250370 250371 250372 250373 250374 250375 245957 245958	Oncogenic NOEL - not established due to conflicting reports. Increased incidence of neoplastic nodules/hepatocellular carcinomas Systemic NOEL = 30 ppm Systemic LEL = 300 ppm (testicular atrophy) Levels tested = 0, 30, 300, and 3000 ppm in CD-CRL: CD(SD)BR rats		Supplementary 001374 Supplementary 002488 Supplementary 003435 Minimum 004199 Minimum 004200
2 Year feeeding/onco-genic - rat; IBT; #622-07926; 2/9/79	Tech	244166 099628 099626 070048	Systemic NOEL < 30 ppm (LDT) (decreased spleen wt) Oncogenic NOEL - Dosage levels tested in Charles River strain - 0, 30, 300, 1000 and 3000 ppm IBT - validated		Supplementary 001051
2 year feeding/oncogenic - mice; Hazleton Raltech; no. 79020; 8/13/82	Technical	248722	Oncogenic NOEL > 3000ppm (HDT) Systemic NOEL = 1000 ppm Systemic LEL = 3000 ppm (decreased weight gain, decreased survival of females). Levels tested: 0, 300, 1000, and 3000 ppm		Minimum 003885
Mutagenic - dominant lethal-mice; Ciba Geigy; 9/8/76	CGA 24705 technical		Negative mutagen		minimum 000434