4-27-70

000631

April 27, 1970

File: PP# 0F0960

Dyfonate residue tolerance request:
0.5 ppm asparagus
0.1 ppm leafy vegetables, mint, seed and pod vegetables, strawberries, and sugar cane (negligible)

To: Division of Regulations and Petitions Control (AF-320)

PESTICIDE PETITION No. 0F0-960

Stauffer Chemical Company
1200 South 47th Street
Richmond, California 94804
(AF 17-839)

Toxicity data supporting the safety of established* negligible residue tolerances of 0.1 ppm in root crop vegetables is summarized in PP No. 760 memorandum dated January 2, 1969.

Additional toxicity data provided with this petition included two long term feeding studies and a 3 generation rat reproduction study.

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Two year rat feeding study (Woodard Research Corp., 1968)

Groups of Charles River strain of albino rats, 30 of each sex in each group, were fed 0, 10, 31.6, or 100 ppm Dyfonate diets for two years.

Observations for effects included:

1. Weekly body weights
2. Daily appearance and behavior checks.
3. Hemograms including microhematocrits, total and differential leucocyte counts of 5 of each sex in the 0 and 100 ppm groups at 13, 26, 42 and 51 weeks. Similar numbers from all groups were checked at 19, 78, 92, and 104 weeks.
4. Cholinesterase inhibition tests.
   a. Plasma and rbc of control and 100 ppm groups at 6, 13, 19, 26, 40, 52, 78, 91, and 104 weeks.
   b. Brain of 5 of each sex in each group at termination.

*34 F.R. 1489; Feb. 1, 1969

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5. Necropsy at termination.

   a. Gross examination of tissues and organs for compound related effects.

   b. Heart, liver, kidney, spleen, lung, brain, gonads, adrenal, thyroid, pituitary, prostate, and uterus weighed.

6. Microscopic examination of liver, kidney, heart, spleen, lung, adrenal, thyroid, pituitary, L. node, salivary gland, thymus, gonads, uterus, prostate, G.I. tract, u. bladder, brain, skeletal muscle, mammary gland, bone marrow, skin, and eye from rats sacrificed at termination and from rats dying during the experimental period.

Results:

100 ppm group

Cholinesterase inhibition
Plasma and erythrocyte - marked
Brain-slight in females only
Toxicity signs - tremors and nervous behavior in females

31.6 ppm group

Cholinesterase inhibition
Plasma and erythrocyte - slight

10 ppm - effects not revealed by observations.

Two year dog feeding study (Haskell Research Corp. 1969)

Groups of purebred beagle dogs, 4 of each sex in each group, were fed 0, 8, 60, or 240 ppm Dylox/Trichlorfon diets for two years.

Observations for effects included:

1. Weekly body weights.

2. Daily checks for signs of toxicity. Frequent detailed physical examinations including body temperature, heart rate, respiratory rate, etc.

3. Blood pressure measurements at 0,7,14,20,27,43,56,82,91 and 104 weeks.

4. Opthalmic examination at 7,13,23,57,94 and 104 weeks.

5. Hematology including hematocrits, hemoglobin, sedimentation rate, coagulation rate, thrombocyte counts, total and differential counts, initially and at 6,13,19,26,39,78,91 and 104 weeks.

6. Biochemistry tests at the same intervals included BUN, SAP, blood glucose, SGOT, SGPT, prothrombin time, plasma and rbc cholinesterase, and brain cholinesterase at termination.

7. Electrocardiograms initially and at 7,14,20,37,43,56,82,91 and 104 weeks.

8. Necropsy at termination

   a. Gross examination of tissues and organs for compound related effects.

   b. Heart, liver, kidney, spleen, lung, brain, gonads, adrenal, thyroid, pituitary, uterus and prostate weighed.

9. Microscopic examination of liver, trachea, kidney, heart, spleen, lung, adrenal, thyroid, pituitary, l. node, salivary gland, thymus, gonads, uterus, prostate, G.I. tract, pancreas, brain, spinal cord, bone marrow, skeletal muscle, mammary gland, skin, eye, gall bladder, and urinary bladder.

Results:

240 ppm group:

Deaths - suggestive related to compound - one at 6 weeks and another at 76 weeks.

Toxicity signs; tremors, and increased lacrimal, nasal, and salivary secretions. Hair loss.

Erythrocyte cholinesterase completely inhibited; plasma 50% inhibited.

SAP values slightly increased.

Liver weights slightly increased.

Tissue reactions (microscopically) in small intestine and liver.

60 ppm

Moderate inhibition of blood cholinesterase

Liver weights slightly increased in some dogs.

Toxic reactions in one dog - tremors and hair loss

3 ppm - compound related effects not revealed by observations.

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Three generation rat reproduction study (Woodard Research Corp. 1969)

Groups of SD (CR) albino rats, 20-24 of each sex in each group were fed 0, 10, or 31.6 ppm Dyfonate diets during the production of three generations. Two litters were produced from each female in each generation.

Observations for effects included:

1. Birth, 4 day, and weaning weights.
2. Physical examination of newborn.
3. Visceral and skeletal examination of newborn for anomalies.
4. Implantation sites counted in selected females (non bearers and those have but one litter) and in F_0 and F_2 parent females.
5. F_{3b} weanling examination.
   a. Liver, kidney, and heart weights of 2 pups of each sex from each litter.
   b. Microscopic examination of liver, kidney, heart, spleen, adrenal and gonads, and bone marrow of 1 of each sex from each litter.

Litter Statistics

Generations

Diet Level	Litter	Litters born/group			Total live born		
		1st	2nd	3rd	1st	2nd	3rd
0	a	16/22	18/23	14/19	182	171	154
0	b	20/22	16/22	17/19	190	149	166
10	a	15/22	16/21	16/21	158	172	173
10	b	16/22	16/21	16/19	177	154	152
31.6	a	17/21	17/23	13/19	168	185	192
31.6	b	18/21	22/23	16/17	156	216	179

		Mean Litter size			Still births		
0	a	11.4	9.5	11.0	7	3	9
0	b	10.0	9.3	10.9	16	3	15
10	a	10.5	10.7	10.3	9	1	6
10	b	11.8	9.9	11.4	2	1	15
31.6	a	9.9	10.9	10.7	6	7	6
31.6	b	10.0	9.[illegible]	11.[illegible]	14	14	10

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Litter Statistics (Cont.)

Generations

Diet Level	Litter	Live pups/4 days			Live pups/weaning		
		1st	2nd	3rd	1st	2nd	3rd
0	a	--	151	142	140	140	103
0	b	152	135	137	115	121	104
10	a	--	136	129	121	121	89
10	b	164	143	131	124	129	72
31.6	a	--	161	163	146	146	163
31.6	b	150	194	146	116	154	103
		Mean birth weight			Mean weaning weight		
0	a	5.5	5.6	6.6	--	42.5	39.9
0	b	6.3	6.7	6.2	39.5	35.2	34.9
10	a	5.4	5.2	6.5	--	39.1	36.7
10	b	6.5	6.0	5.9	38.5	41.4	34.4
31.6	a	5.5	5.2	6.5	--	41.4	35.6
31.6	b	6.2	7.3	6.1	41.0	39.9	33.2

Results: Compound related effects were not revealed by the observations.

Toxicity data summary:

2 year dog no effect

ChE 3 ppm
Systemic 3 ppm

2 year rat no effect

ChE 10 ppm
Systemic 31.1 ppm

3 generation rat reproduction study

31.3 ppm

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CONCLUSION:

Provided toxicity data support the safety of the requested residue tolerances of this petition.

G. E. Whitmore, D.V.M.
Division of Toxicology
Petitions Review Branch (RF-148)

INIT: EBlumenthal

cc:
RF-148
RF-148
RF-216
RF-218
WH-108
PP No. 0F0-960

GEWhitmore:mmc 4/27/70

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