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UNITED STATES GOVERNMENT

Memorandum

001842

TO : Mr. William Stokes
Petitions Control Branch

DATE: July 6, 1967

FROM : Dr. M. L. Quaife *M. L. Quaife signed by odf*
Division of Toxicological Evaluation
Petitions Review Branch

SUBJECT: Dodine, tolerance at 5 ppm in or on peaches.

PESTICIDE PETITION No. 7FO 577

American Cyanamid Company
Princeton, New Jersey
(AF 14-731)

Dodine (n-dodecylguanidine acetate, Cyprex, or n-C₁₂H₂₅-N-C-NH₂·CH₃COOH) is to be used to control certain fungus diseases. N NH

TOXICITY:

New toxicity data consist only of a reproduction study.

The test material was a composite of five production lots of technical dodine, 97.9% pure.

Reproduction--mice

On mice, CF₁ strain, a "standard" three-generation, six-litter reproduction study was carried out with dodine. Sixteen females and 8 males were used for each mating at each dietary level, with few exceptions where numbers of females were slightly smaller.

Slight differences from "standard" design are: (1) Litters larger than 10 were not reduced in size at day 5, and (2) Pups of 3a (instead of 3b) litter were autopsied and studied microscopically.

Food intake of F₀ generation (only) prior to mating was measured and found unaffected by dodine intake.

In Table 1 are shown the usual Oser indices and mean weights at weaning of male and female pups, separately for each litter.

Results (Table 1) show deleterious effect of 800 ppm dodine on both viability and lactation, as well as (in F_{3a} and F_{3b} pups of both sexes) on weaning weights.



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Below are summarized total numbers of pups born alive and weaned by dietary groups.

Dietary level (ppm)	Pups per litter	
	Born alive	Weaned
0	10.8	7.7
400	10.3	6.3
800	9.5	3.6

We consider the slight differences between the three groups in numbers per litter of pups born alive as incidental. Obviously, the mean number weaned is severely decreased at 800 ppm dodine and slightly, but of questionable significance, at 400 ppm.

Numbers of stillborn, whether of whole litters or of individuals in a litter, seem to have been relatively few in number and randomly scattered throughout various dietary groups and litters.

All pups of the F_{3a} generation were autopsied except where autolysis prevented. From each F_{3a} litter one female and one male pup were subjected to microscopic study of major tissues and another pair to skeletal examination via alizarin staining.

No abnormalities of any kind were found in the F_{3a} pups which could consistently be related to dodine.

Only one tumor was found (in an adult female at 800 ppm) in the study.

DISCUSSION:

This reproduction study shows 400 ppm dodine to be no-effect (except for possibly a very slight lessening of mean numbers weaned per litter) and 800 ppm to be an effect level in mice; since, at 800 ppm, both viability and lactation and, possibly, weaning weights were adversely affected.

No-effect level of dodine is 200 ppm in the rat and at least 50 ppm in the dog (DTE memo of March 4, 1964, PP No. 416).

Acceptable daily human intake of dodine, therefore, is at least 0.5 ppm, whole-diet basis.

Present tolerances for dodine on apples, pears, sweet and sour cherries, and strawberries are 5 ppm and in meat and milk zero ppm.

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One on peaches at 5 ppm will not cause maximum content of daily diet with respect to dodine to exceed the acceptable intake (0.5 ppm, above). The requested tolerance is safe.

CONCLUSION:

Based on chronic studies in rat and dog and a six-litter, three-generation reproduction study in mice, dodine at 5 ppm in or on peaches will provide a safe tolerance.

TABLE 1

Indices and weaning weights in mouse reproduction study on dodine.

Litter	ppm dodine	F.I. (%)	G.I. (%)	V.I. (%)	L.I. (%)	Mean wt at weaning (g)	
						M	F
F _{1a}	0	100	100	91	89	8.4	8.3
	400	100	100	78	87	7.6	6.8
	800	100	100	44	77	8.1	8.3
F _{1b}	0	100	100	85	81	5.9	5.8
	400	100	100	82	74	5.5	5.5
	800	100	100	47	64	7.1	6.9
F _{2a}	0	94	100	75	85	6.6	6.4
	400	94	93	73	81	6.0	6.2
	800	94	100	68	60	6.5	6.7
F _{2b}	0	94	100	67	87	7.3	7.2
	400	100	100	75	89	6.0	5.8
	800	94	93	48	56	6.4	7.1
F _{3a}	0	100	100	89	87	7.0	7.0
	400	94	94	69	78	6.7	6.5
	800	94	100	71	55	5.9	6.0
F _{3b}	0	100	100	86	88	6.8	6.9
	400	94	100	64	87	7.1	6.9
	800	87	100	77	74	6.2	6.0

F.I. = (Pregnancies/Matings) x 100.

G.I. = (Litters born alive/Pregnancies) x 100.

V.I. = (Pups Surviving at 5 days/Pups born alive) x 100.

L.I. = (Pups weaned/Pups at 5 days) x 100.

cc: FSA, BVM, DTE,

Dr. Jacobson, PPs 7F0577 & 416

MLQuaife:mtt 7/6/67

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