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

003683

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: R. Taylor (25)/V. Walters
Registration Division (TS-767)

THRU: William Butler Section Head
Section III, Toxicology Branch
Hazard Evaluation Division (TS-769)

William Sr Butler 3/6/84

FROM: W. Thomas Edwards
Toxicology Branch
Hazard Evaluation Division (TS-769)

WTE

SUBJECT: Comments relating to correspondence on DPX-Y6202 from DuPont dated 1-11-84

Additional information and DuPont comments have been considered with the following results.

1. Micronucleus Test

The protocol for this test is not acceptable as presented.

a) Clinical signs of toxicity at the hightest dosage must be reported. Information from a separate test using the same strain might be accepted.

b) Six hours sampling time is not considered to be adequate where the possibility of cell cycle delays occurs. Cytotoxicity in target tissue, bone marrow must be demonstrated.

2. 90-day feeding study in rats

This requirement has been met.

3. Skin sensitization in guinea pigs

This test is accepted as negative for supporting the the intended use.

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TOXICOLOGY BRANCH DATA REVIEW

Study Type: 90-Day Feeding Study in Rats

Accession No.: 250072

MRID No.:

Sponsor: DuPont

Contracting Lab: Nissan Chem. Ind. Ltd.

Date: January, 25, 1982

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxyl]-, ethyl ester

DPX-Y6202, NC302

Protocol: There were 4 treatment groups (including one untreated control), each consisting of 20 males and 20 females. The rats were randomly allocated by computer program to the 4 treatment groups as follows:

Group	Treatment level (NC-302 ppm)	Rat Nos. Male	Female
1	0 (Control)	1-15(16-20)	81-95 (96-100)
2	40	21-35(36-40)	101-110, 116-120(111-115)
3	128	41-55(56-60)	121-135(136-140)
4	1280	61-75(76-80)	141-155(156-160)

Rat Nos. in parentheses were maintained on a 6-week recovery phase following the termination of treatment.

Treatment diet was administered for 13 weeks, then 15 of the 20 rats per groups were killed and examined. 5% of each group were allowed a recovery period of 6 weeks before being killed.

Results:

Liver weight increases (compared to controls) were found in the 1280 ppm dosage group and to a lesser extent in the 128 level but not at the 40 ppm level. Microscopically seen were slight to minimal centrolobular and/or midzonal enlargement. These changes appeared to be reversible. During the recovery period the ratio of animals with liver lesions was reduced to 3 of 5 instead of 14 of 15 found at end of treatment.

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Kidney weight were increased in females at the 1280 and 128 ppm levels but not at 40 ppm.

Tested decreased significantly in 13 of 15 males at the 1280 ppm level and to a lesser extent at the 128 level. Decreased testicular weight was still found after the recovery period ($p<0.01$ for high dosage).

Testicular atrophy and suppression of spermatozoa were also found after the recovery period in 3 of 5 males in the highest doage group.

The treament related testicular atrophy and suppression of spermatozoa found only at the hightest dosage level, 1280 ppm are atributed to excessive-weight loss in the males at this dosage level.

Decreases in pituitary weight for all treated females were considered "marginal" and were statistically significant only at the hightest dosage level.

Conclusions:

NOEL: 40 ppm
LEL: 128 ppm (liver weights and liver lesions)

Core Classification:

Minimum

TOXICOLOGY BRANCH DATA REVIEW

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Study Type: Skin sensitization in guinea pigs

Accession Number: 250554

MRID Number:

Sponsor: DuPont, Haskell Lab No. HLO 182-83

Contracting Lab: Hazleton Labs Project No. 201-591

Date: 5/20/83

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy] propanoic acid,ethyl ester. EC formulation (10.5%) DPX-Y6202-7

Protocol:

48 hours after 10 guinea pigs had been used for a dermal irritation study, they were sensitized by i.d. injection of 0.1 ml of DPX-Y6202-7 (the 10.5% formulation) in the back of each, once a week for 4 injections.

Thirteen days after the last injection 0.05 ml of undiluted test material and 0.05 ml of 10% test material in saline were applied to separate test sites on the backs of each sensitized guinea pig. Ten unsensitized control animals were challenged in the same way. Responses to challenge were compared.

Results:

One animal died after an injection.

Draize scores resulting from challenge are attached.

Conclusions:

Results are negative for dermal sensitization. Induction apears minimal for intended use.

Core Classification: Minimum

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Table 4

Individual Dermal Irritation Scores
Primary Irritation and Sensitization Study in Guinea Pigs
INY 6202-7 (14,809)
Challenge Phase.
Test Animals

Animal Number	Site Number	Dose Level (%)	Observations 24 Hours Erythema	24 Hours Edema	48 Hours Erythema	48 Hours Edema
H04264	1	10	0	0	0	0
	2	100	1	0	1	0
H04265	1	10	0	0	0	0
	2	100	1	1	1	0
H04266	1	10	1	0	0	0
	2	100	1	1	1	0
H04267	1	10	0	0	0	0
	2	100	1	0	1	0
H04269	1	10	1	0	0	0
	2	100	1	1	1	0
H04270	1	10	0	0	0	0
	2	100	1	1	0	0
H04271	1	10	0	0	0	0
	2	100	1	0	0	0
H04272	1	10	0	0	0	0
	2	100	1	1	1	0
H04273	1	10	0	0	0	0
	2	100	1	0	0	0
			9/9	5/9	6/9	0/9

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Table 4 - Continued

Individual Dermal Irritation Scores
Primary Irritation and Sensitization Study in Guinea Pigs
INY 6202-7 (14,809)
Challenge Phase.
Control Animals

Animal Number	Site Number	Dose Level (%)	Observations			
			24 Hours		48 Hours	
			Erythema	Edema	Erythema	Edema
H04294	1	10	0	0	0	0
	2	100	1	1	0	0
H04295	1	10	0	0	0	0
	2	100	1	1	0	0
H04296	1	10	0	0	0	0
	2	100	1	0	0	0
H04297	1	10	0	0	0	0
	2	100	1	0	1	0
H04298	1	10	0	0	0	0
	2	100	1	0	0	0
H04299	1	10	0	0	0	0
	2	100	1	0	0	0
H04300	1	10	0	0	0	0
	2	100	1	0	1	0
H04301	1	10	0	0	0	0
	2	100	1	0	0	0
H4302	1	10	0	0	0	0
		100	1	0	1	0
H4303	1	10	0	0	0	0
	2	100	1	0	0	0
			10/10	2/10	3/10	0/10

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