Reviewed by : Whang Phang, Ph.D. Whang Phang 7/17/87
Section III, Toxicology Branch (TS-769c)
Secondary Reviewer: Marcia van Gemert, Ph.D. M van Gemert 7/17/87
Section III, Toxicology Branch (TS-769c)

DATA EVALUATION REPORT

STUDY TYPE: Mutagenicity: Reverse Mutation- S. cerevisiae (2 Studies)

MRID NO.: 116490 and 116492

TOX. CHEM. No.: 320

TEST MATERIAL: 2, 4-DP (purity not specified)

SPONSOR: Amchem Products, Inc., Ambler, PA

TESTING FACILITY: Pharmakon Laboratories, Scranton, PA

CITATION: 2 studies

1). Naismith, R.; Matthews, R.; Godek, E. (1979) Summary Data: Reverse Mutation Assay-Saccharomyces cerevisiae: Study No. PH-303-AM-179-2,4- DP, (Unpublished study received Mar 26, 1979 under 264-231; prepared by Pharmakon Laboratories, submitted by Union Carbide agricultural Products Co., Inc., Research Triangle Park, NC; CDL: 237875-R)

2). Naismith, R.; Matthews, R.; Godek, E. (1979) Summary Data: Reverse Mutation Assay-Saccharomyces cerevisiae: Study No. PH-303-AM-19- DP, (Unpublished study received Mar 26, 1979 under 264-231; prepared by Pharmakon Laboratories, submitted by Union Carbide agricultural Products Co., Inc., Research Triangle Park, NC; CDL: 237875-T)

CONCLUSION: These two studies were previously reviewed (Holder: Tox. Doc. No. 001995; Attachment 1): the studies were classified as valid. This reviewer agrees with the conclusions derived by Holder. The test compound, 2,4-DP, caused reverse mutation in Saccharomyces D_7 strain in the abscence of metabolic system in both studies. The original summary data from the submissions are presented in Attachment 2 to supplement the extracted data shown in the previous review of these two studies.

ATTACHMENT 1 001995

§ 6.0 Reverse Mutation Test (Two experiments; Section S of 264-231 EPA No. 237875)

This test measures reversion to the wild type of Saccharmyces cervisiae D_7, a ilv I-92/ilv I-92 homoallelic isoleucine requiring mutant. When an appropiate point mutation is made by the test substance the stain goes isoleu - to isoleu + and no longer requires isoleucine in the media for grow. Plating on isoleucine minus medium selects for the mutants; the number of colonies appearing reflect the number of point mutations reversing the mutant to the isoleucine independent wild type.

The results were:

Exp. # 1

Conc: (mg/ml)	0	.001	.01	0.1	1	10	10^{-6} M NQO
Revertants per 10^7 cells	6.7	7.1	7.0	7.5	6.9	9.9	48.2
% survival	100	89	88	86	77	59	78

Exp. # 2 (Dose/Response Range)

conc: (mg/ml)	0	4	6	8	10	12	10^{-6} M NQO
Revertants per 10^{-6} cells	3.3	4.7	8.6	8.3	9.8	2.0	12.7
Survival (%)	100	83	83	77	66	18	88

In exp. # 1, it can be seen that 10 mg/ml promotes isoleu - to isoleu + revertants, but than ≤ 1 mg/ml was ineffective. In exp. # 2, concentrations of 4, 6, 8, and 10 mg/ml caused a dose response in reverse mutations (p=.001). Conc. of 12 mg/ml was toxic. The NQO acted about 1/4 as well in exp. # 2 as exp. # 1 [for the same effect see §5.0].

6.1 Conclusions: 2,4 DP acid promotes reverse mutations in Saccharomyces D_7 mutant iLv I-92/iLv I-92 at concentrations 4 to 10 mg/ml and is ineffective at 1 mg/ml or lower. No S-9 metabolic activation studies were presented in these studies.

6.2 Classification of Studies: Valid, only for unactivated 2,4 DP

ATTACHMENT 2

Nguyen, cau hue 02-16-83

BEST DOCUMENT AVAILABLE

PHARMAKON LABOR: 'ORIES

Mutagenesis Section

Saccharomices cerevisiae

Reverse Mutation Assay

(DATA TAKE FROM Submission; MRID No: 116490) STUDY No.1

SUMMARY DATA

Client Amchem Products, Inc.

Material 2-(2,4-Dichlorophenoxy) -propionic acid

Description Tan powder

Date Received July 5, 1978

Date Performed January 11, 1978

Pharmakon Reference 211, pgs. 37-41

	CONTROLS						TEST COMPOUND									
Concentration	Phosphate Buffer		10% DMSO		NOO 10^{-6}M		10 mg/ml		1 mg/ml		0.1 mg/ml		0.01 mg/ml		0.001 mg/ml	
Survival (%)	100		92.6		78.1		59.1		78.9		85.8		88.1		88.9	
Revertants/ Plate	7	14	7	12	50	49	12	6	6	5	6	11	4	2	7	6
	6	9	7	5	54	54	10	5	3	4	7	16	10	8	6	4
	7	5	4	4	43	53	10	7	5	7	8	8	5	4	5	16
	8	5	7	9	34	42	3	11	10	7	7	12	9	8	4	3
	6	5	4	3	51	47	12	12	5	7	8	4	4	3	6	5
	5	6	4	5	44	50	13	15	10	9	6	2	12	10	11	9
	8	4	9	4	47	49	6	9	7	4	9	6	8	9	10	6
	7	6	5	7	52	46	15	14	7	10	4	8	9	7	8	6
	9	6	7	3	47	51	5	15	10	6	5	7	5	8	5	6
	7	4	10	8	47	55	8	10	6	9	5	10	4	9	8	10
Total	134		124		965		198		137		149		139		141	
Revertants/10^7	6.70		6.20		48.25		9.90		6.85		7.45		6.95		7.05	
p value	--		0.6642		34.0490**		3.3157*		0.2128		0.8659		0.3100		0.4159	

*, ** Denotes statistical significance at .01 and .001 level, respectively

Investigator [signature] Date January 11, 1979

Study Director [signature] Date January 11, 1979

2

BEST DOCUMENT AVAILABLE

ATTACHMENT 2 (Continued)

nauyen; call tuul 02-16-83

BEST DOCUMENT AVAILABLE

PHARMAKON LABORATORIES

Mutagenesis Section

Saccharomyces cerevisiae

Reverse Mutation Assay

SUMMARY DATA

(DATA TAKEN FROM MRID# 116492)
STUDY No. 2

Client: Amchem Products, Inc.

Material: 2-(2,4-Dichlorophenoxy)-propionic acid

Description: Tan Powder

Date Received: July 5, 1978

Date Performed: February 5, 1979

Pharmakon Reference: 211, pgs. 43-45

	CONTROLS			TEST COMPOUND				
Concentration	Phosphate Buffer	10% DMSO	NQO 10-6M	12 mg/ml	10 mg/ml	8 mg/ml	6 mg/ml	4 mg/ml
Survival (%)	100	96.3	89.7	18.3	66 2	76.9	83.1	82.6
Revertants/ Plate	4 2	3 1	6 15	1 4	11 15	8 10	7 11	6 5
	2 4	1 2	11 15	2 2	7 11	10 7	6 13	4 3
	0 1	2 2	10 13	1 0	5 11	10 5	5 5	4 4
	3 1	3 2	9 17	1 4	16 7	10 12	11 10	1 3
	2 6	2 3	11 16	3 0	8 6	11 3	9 9	7 0
	2 4	4 8	9 6	2 3	7 17	2 8	7 14	6 4
	5 2	6 5	12 17	2 3	7 13	9 8	6 8	8 3
	5 0	3 5	11 14	1 0	7 5	5 9	7 7	4 5
	6 4	5 7	17 13	0 3	13 11	7 8	13 9	6 5
	7 5	5 3	12 20	4 3	7 12	9 14	3 11	2 3
Total	65	72	254	39	196	165	171	83
Revertants/10^7	3.25	3.60	12.70	1.95	9.80	8.25	8.55	[illegible].15
p value	-	0.5525	*** 9.9056	2.3455	*** 6.9356	*** 6.2996	*** 6.5521	1.4218

*** Denotes statistical significance at the .001 level.

Investigator Edmund G. Grdik Date 2/5/79 Study Director [signature] Date 2/5/79

2

30

4