Notes from a mtg discussing whether to require chronic data for 2,4-DP.

UNDATED

2,4-DP Acid

Summary of Toxicology Data

	Remarks	
Acute Studies		
Acute oral- rat	LD_{50} = 700 mg/kg (male) = 500 mg/kg (female) Tox. Category III	Minimum
Acute oral-mouse	LD_{50} = 500 mg/kg (males) = 620 mg/kg (female) Tox. Category III	Minimum
Subchronic Studies		
90-Day feeding-rat	Doses tested: 100, 500, & 2,500 ppm LOEL = 100 ppm (LTD) increased incidence of kidney and liver lesions. NOEL could not be established.	Supplementary
4-Week feeding-dog	Doses tested: 8, 20, & 32 mg/kg Used only 1 dog/sex/dose.	Supplementary
Chronic Studies		
Chronic feeding-rat (Fischer 344)	NOEL = 100 ppm LOEL = 300 ppm (decrease in urinary specific gravity/protein) Doses tested: 100, 300, 1000, & 3000 ppm.	Minimum
Oncogenicity-rat (oral)	Doses tested= 25, 50, & 200/150 mg/kg (change occurred at 60 wks) Numerous deficiencies.	Invalid
Mouse oncogenicity (oral)	Doses tested = 25, 100, & 300 mg/kg LOEL = 25 mg/kg (LTD) (Increased incidence of hepatic regeneration) No NOEL could be established No increase in tumor incidence	Supplementary
Teratology-rat	Doses tested = 150, 450, & 1500 ppm Numerous deficiencies	Invalid

Chronic Studies (cont'd)

	Remarks	
Teratology - rabbit	Dose-range finding study doses tested = 25 & 100 mg/kg	Supplementary
3-Generation Repro. rat	Doses tested = 125, 500, 2000/1000 ppm Parental NOEL = 1000 ppm Parental LOEL = 2000 ppm (decreased body weight & food concumption) NOEL for developmental tox. = 1000 ppm LOEL for developmental tox. = 2000 ppm (increased offspring mortality)	Supplementary

Mutagenicity Studies

Ames assays (Salmonella)	Negative	Unacceptable
Primary DNA damage assay-E. coli	Positive (with metabolic activation	Unacceptable
Mitotic crossing over (DNA damage) S. cerevisiae	Negative (without activation)	Unacceptable
Chromosomal Aberration (CHO cells) (DNA damage)	Positive (with activation) (Review is almost completed) acid	Acceptable
Reverse mutation (S. cerevisiae)	Positive (without activation)	Acceptable
Reverse mutation (S. cerevisiae)	Positive (without activation)	Acceptable
Mitotic gene conv.- (S. cerevisiae) (2 Studies)	Positive (without activation)	Acceptable

3 positive studies w/ 2,4-DP acid

Metabolism

Single oral dose-metablism (rat)	Compound was rapidly absorbed. Within 96 hr., majority of the administered dose was eliminated in the urine	Unacceptable

	Remarks	
Metablism-analysis of urinary metabolites	Intact 2,4-DP was found to be the major component in the urine (75% of the administered dose)	Unacceptable
Metablism-tissue distribution	Only fat retained a small amount of radioactivity.	Unacceptable