OPP-2004-0239

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES
WASHINGTON, D.C. 20460

October 6, 2004

MEMORANDUM

SUBJECT: **4-Chloro-2-Methylphenoxy Acetic acid (MCPA):**

Reviews of :

- Rat *In Vivo* Dermal Absorption (MRID Nos. 46327601; DP Barcode: D303672; DER for this only is attached)
- MCPA and CCPA: Repeated dose toxicity study in rats administration in the diet over 4 weeks (MRID 46276101; DP Barcode: D303677; PC Code: 630501);
- A Dermal Penetration Study Protocol (DP Barcode: 305042);
- Summary document entitled "MCPA and Testicular Toxicity" (MRID 45889301; DP Barcode: 289856)

PC Code: 030501 **TXR No.: 0052752**
PC Code: 630501

From: Paul Chin, Ph.D.
Reregistration Branch I
Health Effects Division 7509C

Through: Whang Phang, Ph.D., Branch Senior Scientist
Reregistration Branch I
Health Effect Division 7509C

To: Kelly White/Susan Lewis
Reregistration Branch I
Special Review and Reregistration Division (7508C)

The registrant, MCPA Task Force Three, submitted a study concerning Dermal Absorption of MCPA in rats. This study was reviewed by Robert Zendzian, HED, OPP. The DER for this

1/5

study is attached, and the citation and conclusion are presented below.

CITATION: Beimborn, D.B. and Leibold, E. (2003) 14 C-MCPA- Study of the dermal absorption in rats. Experimental Toxicology and ecology BASF, Project No. 01B0209/026003. March 13, 2003. MRID 46327601 Unpublished

EXECUTIVE SUMMARY:

In a dermal penetration study (MRID 46327601) 14 C-MCPA(99.3 % a.i., batch/lot #1313A-6-1, 4-Chloro-2-methyl-phenoxyacetic acid-[ring-U-^{14}C]) was administered as the dimethyl amine salt (DMA) to 4 male Charles River CrlGlxBdHan:WI rats/dose exposure to a 10 cm^2 area on the back, in the formulation vehicle (high dose) and a water dilution thereof (low dose) at dose levels of 0.09 mg/cm^2 and 7.5 mg/cm^2. Doses, exposures and percent absorbed are presented in the table.

Dose Level	Mean Percentage of Dose Absorbed			
	4 hours	10 hours	24 hours*	96 hours*
0.09 mg/cm^2	5.19	7.09	6.75	9.40
7.5 mg/cm^2	1.67	22.09	14.59	12.87

* Washed at 10 hours.

Over all recovery was good ranging from 90.35% to 95.46% for the low dose and 94.43% to 96.85 % for the high dose. For the low dose the majority of absorbed dose was excreted in the urine with the second highest portion in the carcass. For the high dose the absorbed test compound build up in the carcass with the highest portion at 10 hours (22.08%). At 96 hours 12.86% remained in the carcass and 12.28% was excreted in the urine. This pattern indicates saturation of excretion at the high dose.

The over all pattern of absorption, increased percent absorbed with increasing dose, is typical of a chemical which directly damages the skin. MCPA is reported to be a caustic chemical based on dermal irritation studies. In performing a risk assessment with MCPA this effect must be considered a direct toxic effect on the skin

This study in the rat is acceptable and satisfies the guideline requirement for a dermal penetration study (870.7600) in rats.

The registrant, MCPA Task Force Three, also submitted following 3 documents (MRID Nos. 46276101 and 45889301; DP Barcode: 305042). Each document was reviewed and the following conclusions were made:

- *MCPA and CCPA: Repeated dose toxicity study in rats administration in the diet over 4 weeks (MRID 46276101; DP Barcode: D303677).* This study compared relative toxicity of MCPA to CCPA (2-Carboxy-4-chlorophenoxyacetic acid), a plant metabolite of MCPA. Brief review of data presented in MRID 46276101 appeared to indicate that MCPA is more toxic than CCPA. The report indicated the kidney was a target organ for both MCPA and CCPA. At 2,000 ppm MCPA, observed changes were reduced food consumption and body weights, reduced food efficiency, increased water consumption, decreased plasma glucose, increased plasma creatinine, and increased incidence of urinary transitional epithelial cells and epithelial casts.

  Changes observed at 12, 000 ppm CCPA were decreased urinary volume, decreased serum protein and albumin, increased urinary specific gravity, increased urinary urobilinogen, higher incidence of basophilic tubules in the kidneys, and increased severity of calcification at transition outer/inner medulla. No test substance-related changes were observed at 2,000 ppm CCPA.

- *A Dermal Penetration Study Protocol (DP Barcode: 305042).* This protocol was submitted to PMRA, Health Canada to fulfill PMRA's requirement. However, this protocol was not reviewed because it was sent to us for our information only.

- *Summary document entitled "MCPA and Testicular Toxicity" ((MRID 45889301 DP Barcode: 289856).* Based on the brief review of this summary document, we concur with the conclusions that testicular changes associated with MCPA treatment has been seen at doses where the threshold of effect in other organs (i.e. kidneys and livers) and the threshold of renal excretion are clearly exceeded.