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DuPont Haskell Laboratory

1999 AUG 31 AM 7:13

8EHQ-0899-13401

August 27, 1999

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Via Federal Express

Document Processing Center (7407)  
Attention: 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
401 M Street SW  
Washington, D.C. 20460-0001

PKC 88950000185



Dear 8(e) Coordinator:

*Glycolic acid (70% technical grade)*



(See 3/29/95 submission for other components of mixture)

8EHQ-95-13401

89990000308

This letter is to inform you of the results of a 90-day subchronic toxicity study by gavage in rats which included an evaluation of immunotoxicity, neurotoxicity, and reproduction function with the above referenced test material.

In the study, CrI:CD®(SD) IGS BR rats (40/sex/dose level) were administered solutions containing the test material at doses of 0, 150, 300, or 600 mg/kg/day. Each dosage group was divided into subchronic-toxicity, immunotoxicity, neurotoxicity, and reproductive-toxicity subsets (10/sex/subset/concentration). Body weight and individual food consumption were determined weekly. Clinical observations were recorded at each weighing and cage-site examinations were performed daily. Ophthalmoscopic examinations were conducted on all rats prior to the start of the study and on surviving subchronic-toxicity rats on test day 86. Clinical pathology evaluations were performed on subchronic-toxicity animals at approximately mid study and near the end of the study. After 28 days of test material administration, humoral immune function was evaluated in animals of the immunotoxicity subset. Rats designated for neurotoxicity evaluation underwent functional observation battery and motor activity assessments once prior to study start, then near the beginning, middle, and end of the study. On test day 97, the animals of the reproductive-toxicity subset were bred within their respective treatment groups, and allowed to deliver and rear their offspring until weaning (postpartum day 21). All rats were given a gross pathological examination. Selected tissues of the subchronic-toxicity, immunotoxicity, and neurotoxicity subset animals were examined microscopically.

The following test material-related changes associated with oxalate crystal formation were observed microscopically in the kidneys of male rats in the 300 mg/kg/day and 600

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mg/kg/day groups of the subchronic toxicity subset. The hyperplasia of the transitional epithelium of the renal pelvis was considered secondary to the mucosal irritation created by passage of oxalate crystals from the kidney.

Dose (mg/kg/day)	0	150	300	600
Number Examined	10	10	10	10
Oxalate Crystal Nephrosis	0	0	6	10
Hydronephrosis, Unilateral	0	0	4	7
Hyperplasia, Transitional Cell	0	0	4	6

Toxicologically important changes in clinical chemistry and urinalysis parameters indicating renal insufficiency correlated with the microscopic observations of oxalate crystal nephropathy in the male rats in the 300 mg/kg/day and 600 mg/kg/day groups of the subchronic toxicity subset. The important clinical chemistry changes were mildly decreased glomerular filtration rate (increased serum urea nitrogen, phosphorus, and creatinine) and decreased urine concentration. There was no evidence of reproductive, neurotoxic or immunologic effects seen at any dose level.

The association of this lesion with the test material administration is well documented in the literature in multiple species. In fact, in the study of kidney stone formation, the test material is often used to induce the creation of calcium oxalate crystals. The gender-specific response in the rat is also well documented. The test material, as reported in the published literature, produces these lesions when administered in the diet of rats, with a no-observed-effect level (NOEL) and lowest-observed-effect level (LOEL) equivalent to approximately 200 mg/kg/day and 500 mg/kg/day, respectively. In the current 90-day study, the NOEL was 150 mg/kg/day and the LOEL was 300 mg/kg/day. We do not believe these differences to be toxicologically different.

Under these experimental conditions, the findings described above appear to be reportable, based upon guidance given in the EPA TSCA Section 8(e) Reporting Guide (June 1991).

Sincerely,



A. Michael Kaplan, Ph.D.  
Director – Regulatory Affairs

AMK/KHK:ras  
(302) 366-5260