MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

June 3, 1999

TO: File for Hydroxy Acetic Acid (CAS No. 79-14-1)

FROM: Michael Depa

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level for hydroxy acetic acid is 4 µg/m³ based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL: IRIS, RTECS, ACGIH Threshold Limit Values, NIOSH Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, IARC Monographs, CAS Online (1967 – April 15, 1999), National Library of Medicine, Health Effects Assessment Summary Tables (HEAST), and NTP Status Report. The molecular weight of hydroxy acetic acid is 76.05 g.

In an oral developmental toxicity study, groups of 8 timed-pregnant CD rats were gavaged with 0, 125, 250, 500, or1000 mg/kg/day of hydroxy acetic acid on gestational day 6 through 15 (DuPont, 1995). Technical grade hydroxy acetic acid was used which is 70% hydroxy acetic acid; major impurities include methoxy acetic acid (1.53%), diglycolic acid (0.97%), formic acid (0.32%), sulfates (128 ppm), sodium (3.4 ppm), iron (6.2 ppm), ammonia (80 ppm), chlorides (1 ppm) and water. Maternal toxicity was demonstrated at 500 and 1000 mg/kg/day. At 1000 mg/kg, maternal effects included mortality, significantly reduced maternal body weight, and food consumption. Dose-related increases of the following clinical observations were observed: abnormal gait/mobility, lung noise, salivation, stained and wet fur. At 500 mg/kg/day, similar, yet markedly less severe evidence of maternal toxicity was demonstrated. There was a slight but significant reduction in maternal weight gain. The incidences of lung noise and wet fur were significantly increased as well. Developmental toxicity was evident at 500 and 1000 mg/kg/day. At 1000 mg/kg, mean fetal weight was significantly reduced. Embryolethality was significantly increased and among the surviving fetuses, malformations and variations were significantly increased. At 500 mg/kg, the significant reduction in fetal weight persisted as did the increase in fetal variations. No evidence of either maternal or developmental toxicity was detected at 250 or 125 mg/kg/day. Thus, the maternal and developmental no-observed-adverse-effect-level (NOAEL) was 250 mg/kg.

In a two-week inhalation study, groups of ten CD male rats were exposed to 0, 0.16, 0.51, or 1.4 mg/L hydroxy acetic acid 6 hours/day, 5 days/week for two weeks (Kennedy et al., 1997). These doses were converted to 0, 160, 510 and 1400 µg/m³. There were 5 exposure days, two rest days then 5 more exposure days. Immediately following the 10^{th} exposure, 5 rats were killed; the remaining 5 rats/group were retained for a 14-day non-exposure recovery period. Ninety-five percent of the particle sizes of the aerosols were less than 10µg/m³ (mean between

1.5 and 2 µg/m³). In the 1,400 mg/m³ dose group exposures were discontinued after 8 exposures because most of the rats were in moribund condition. One rat in the 510 mg/m³ dose group was sacrificed in moribund condition 13 days after the last exposure. All rats survived in the control and 160 mg/m³ groups. Body weights were decreased in the 510 and 1,400 mg/m³ at the end of dosing and at day 7 and 14 of recovery ($p<0.05$). No overt unusual clinical signs of response were seen in either the control or 160 mg/m dose groups. In the mid and high dose groups, labored breathing, discharges, and general weakness were observed. Mean corpuscular hemoglobin was decreased compared to controls in all glycolic acid exposed rats. There were increases in selected serum enzyme activities at the 510 and 1,400 mg/m³ ($p<0.05$). Urine volume was decreased at the mid and high dose groups ($p<0.05$). Urine pH was decreased at 1,400 mg/m³. Average relative lung weight was increased significantly ($p<0.05$) compared to control rats in the low and high dose groups. Since the mid-dose lung weight was not statistically different from controls the effect was not considered dose related. Relative testes weight was increased in the mid-dose group at recovery day 14 but not at sacrifice. Relative liver weight was decreased in the mid-dose group on recovery day 14 but not at sacrifice. In the high-dose group, relative heart, lung, kidney, and testes weights were statistically increased compared to control rats ($p<0.05$). Relative thymus weight was decreased in the high-dose group ($p<0.05$). Based on the statistically significant decrease in the mean corpuscular hemoglobin observed in glycolic acid exposed rats, the dose level of 0.16 mg/L (160 mg/m³) was determined to be the lowest-observed-adverse-effect-level (LOAEL).

The hematological endpoint in the inhalation study (Kennedy et al., 1997) was more sensitive than endpoints measured in the oral developmental study (DuPont, 1995). Furthermore, the inhalation study provided a more detailed pathology report, especially concerning hematology, than the oral developmental study. Accordingly, the ITSL was derived pursuant to Rule 232(1)(d) using the LOAEL identified from the Kennedy et al. (1997) study. This rule provides for an uncertainty factor ranging from 1 to 10 when the ITSL is developed from a LOAEL. Since the effect of decreased mean corpuscular hemoglobin was considered a mild effect, an uncertainty factor of 3 was used. The ITSL was calculated as follows:

ITSL = LOAEL/(35 x 100 x UF) x (hours exposed per day)/(24 hours per day)

Where, LOAEL = 160 mg/m³
UF = 3 for mild effects (decreased mean corpuscular hemoglobin)
Hours exposed per day = 6

The ITSL then becomes,

ITSL = 160 mg/m³/(35 x 100 x 3) x 6/24

ITSL = 0.00381 mg/m³

ITSL = 4 µg/m³ (annual averaging time)

The initial threshold screening level (ITSL) for glycolic acid is 4 µg/m³ based on an annual averaging time.

References

DuPont. 1995. Pilot developmental toxicity study of 70% glycolic acid technical solution in rats. Haskell No. 20895. Obtained from the US Environmental Protection Agency, Office of Toxic Substances EPA/OTS Doc# 88-950000185

Kennedy GL, Burgess BA. 1997. Inhalation toxicology of glycolic acid. Inhalation Toxicology. Volume 9, pages 435-447.