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REPLY TO:
AIR QUALITY DIVISION
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March 29, 1996

TO: File for n-butyl propionate (NBP) (CAS# 590-01-2)

FROM: Robert Sills

SUBJECT: Screening Level Development

For screening level development for NBP, a search of the available literature was conducted including the on-line databases CAS, NLM-Toxline, and NLM-Toxline 65. The available toxicological literature is sparse, and there is no available occupational exposure limit, RfD or RfC.

There are unpublished reports on the acute oral and inhalation toxicity of NBP. Union Carbide (1988) exposed a group of 5/sex Sprague-Dawley albino rats to "substantially saturated vapor" for 6 hours. The vapor (unmeasured concentration) was produced by enclosing approximately 100 g of NBP in a sealed animal chamber for 18 hours under static conditions. Following exposure, body weight and signs of toxicity were monitored over 14 days, and animals were examined for gross pathology. A control group was not discussed. Exposure did not result in any signs of toxicity, and necropsy revealed no gross lesions. However, in a later report fron Union Carbide (1993), it is stated that this study did cause a loss of coordination and anesthesia-like effects in animals during exposure.

Union Carbide (1988) also reported results of $LD_{50}$ studies in male and female Sprague-Dawley albino rats dosed via gavage. The reported $LD_{50}$s with 95% confidence limits were 14.1 (12.1 to 16.4) ml/kg for males, and 12.6 (10.7 to 14.8) ml/kg for females. Using a density reported as 0.87 g/ml, these $LD_{50}$s are equivalent to 12.3 and 11.0 g/kg to males and females respectively. NIOSH (1988; RTECS) reports an oral rat $LD_{50}$ of 5 gm/kg, from a 1980 publication ( Food and Cosmetics Toxicology Vol. 18, p. 661) which is not readily available for review.

In a nine-day vapor inhalation study, Union Carbide (1993) exposed four groups of Fischer 344 rats to NBP for 6 hours/day for 9 exposures over an 11-day period. Group sizes were 10/sex. Target exposure concentrations were 0, 800, 1600, and 3200 ppm. Animals were exposed on 5 consecutive days, followed by 2 days without exposure, followed by 4 consecutive days of exposure. All animals were sacrificed after the last exposure, except an additional 10 animals/sex in the control and highest concentration groups were given a 26-day recovery period before sacrifice. Measured mean NBP concentrations for each group were 0, 802, 1600, and 3051 ppm. Exposures resulted in no mortality, clinical signs, or any effects during ophthalmic and neurobehavioral evaluations. Several dose-related changes were found in clinical chemistry and hematology, which were attributed to body weight loss, decreased food consumption, and changes in water balance in the animals. At necropsy, there were no treatment-related gross lesions, and the only histopathological finding involved changes in the nasal olfactory epithelium. These included vacuolization and occasional atrophy in both males and females from all exposure groups, and more frequent and severe atrophy and intraepithelial cysts or glands in males and females from the 1600 and 3200 ppm groups. These changes were also found in the recovery group animals (3200 ppm exposure). The magnitude of the body weight gain depression in the 800 ppm group at the end of the exposure regimen was 18% in males (not statistically significant) and 20% in females (significantly lower than controls, $p < 0.01$, on days 2, 8, and 9 of the study). The authors reported that a NOEL was not determined, due to decreases in body weight and microscopic changes in the anterior olfactory mucosa of the nasal cavity at the lowest concentration. Thus, the LOAEL for slight effects is 802 ppm, which is equivalent to 4271 $mg/m^3$ based on a MW = 130.2 (Union Carbide, 1988).

The ITSL is most appropriately derived from the algorithm in Rule 232 (1) (d) for a 7-day inhalation NOAEL, with an additional uncertainty factor for the presence of slight adverse effects rather than a NOAEL. A risk assessment by Strohm (1996) also selected this key study/concentration and algorithm for ITSL derivation. Strohm (1996) further recommended that it would be more appropriate to not adjust for the LOAEL than to use a 10-fold UF, given the anticipated ease of metabolism of NBP and comparing the resulting ITSL to the ITSL and OEL for a similar compound (n-butyl acetate). In the present assessment, an intermediate UF of 3 is employed for LOAEL-to-NOAEL adjustment.

The ITSL calculation is as follows.

$$ITSL = \frac{NOAEL}{35 \times 100} \times \frac{\text{hours exposed per day}}{24 \text{ hours per day}}$$

$$= \frac{4271 \text{ mg/m}^3 \text{(LOAEL)}}{35 \times 100 \times 3} \times \frac{6 \text{ hrs.}}{24 \text{ hrs.}}$$

$$= 0.102 \text{ mg/m}^3$$

$$= 102 \text{ ug/m}^3 \text{ (annual averaging time)}$$

REFERENCES:

NIOSH. 1996. Registry of Toxic Effects of Chemical Substances (RTECS database).

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Union Carbide. 1988. UCAR N-Butyl Propionate ; Acute Toxicity and Primary Irritatancy Studies. Bushy Run Research Center. Project report 51-68.

Union Carbide. 1993. N-Butyl Propionate: Nine-Day Vapor Inhalation Study in Rats. Bushy Run Research Center. Laboratory Project ID # 91U0091.

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