

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

July 12, 2000

TO: File for Propionic acid (CAS #79-09-4)

FROM: Marco Bianchi, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for propionic acid will remain at 300 micrograms per cubic meter ($\mu\text{g}/\text{m}^3$) based on an eight-hour averaging time. This compound was initially evaluated by Air Quality Division (AQD) staff in 1992, using interim procedures* to derive an impact of 300 $\mu\text{g}/\text{m}^3$ with an eight-hour averaging time. In an effort to finalize all interim chemical screening levels, this chemical was re-reviewed to set a final ITSL.

The following references or databases were searched to identify data to determine the ITSL: Integrated Risk Information System-Online, Health Effects Assessment Summary Table, National Toxicology Program (NTP) Management Status Report-Online, Registry of Toxic Effects of Chemical Substances, Environmental Protection Bureau (EPB)-Chemical Criteria Database, EPB library, Chemical Abstract Service-Online, National Library of Medicine-Online, International Agency for Research on Cancer (IARC)-Online, National Institute for Occupational Safety and Health (NIOSH) Pocket Guide, and American Conference of Governmental Industrial Hygienists Guide (ACGIH).

Propionic acid and the sodium and calcium propionates are used as mold inhibitors, dermatological fungicides, herbicides, and preservatives for grain and wood chips. It is used in emulsifying agents, flavors and perfumes, drugs, electroplating solutions, and in making cellulose propionate plastics. As the sodium salt, it occurs naturally in cheese to 1% by weight, approved for use as a preservative in baked goods, and is on the U.S. Food and Drug Administration's generally recognized as safe (GRAS) list for use in foods.

According to the ACGIH documentation for propionic acid, the oral rat lethal dose 50 (LD_{50}) for this compound is 4.3 grams per kilogram (g/kg), and the skin absorption LD_{50} for rabbits is 500 milligrams per kilogram (mg/kg). An eight-hour inhalation of a saturated atmosphere caused no deaths in rats. In a rabbit skin irritation test, tissue necrosis was observed after application of 10 mg of undiluted propionic acid for 24 hours. The compound is also corrosive to the gastric lining and, upon oral intubation results, in desquamation and hemorrhage.

*Michigan Department of Environmental Quality – AQD Staff Activity Report, "Air Toxic Rules – Implementation Procedures," dated January 20, 1993.

A Toxic Substances Control Act (TSCA) 8(e) submittal by BASF Corporation (1987) described a published study (Bundesgesundheitsblatt 28:322-327, 1985) that showed in addition to lesions found in the forestomach of rats in a long-term feeding study, a dose-dependent increase of focal dysplasia was found in the glandular stomach of rats. However, these lesions were not interpreted as being preneoplastic by the study investigators, because the lesions had not developed into tumors in spite of the extremely long study duration of three years. Additionally, this same study showed that 0.25% and 1% propionic acid in the diet for male and female rats, respectively, resulted in no effects on the forestomach epithelium after 90 days. The proliferative lesions that were observed at higher concentrations of up to 4% have been shown to be mostly reversible after a 90-day and 180-day recovery period. In the feed given to beagle dogs, a concentration of 3% propionic acid over three months resulted in an increase incidence of diffuse hyperplasia of the esophagus epithelium in one of four males and two of four females. With one exception of diffuse hyperplasia of the esophagus in one dose level, only focal hyperplasia occurred in the control animals. The lesions observed in the 1 and 0.3% groups were similar to those found in controls. A recovery of six weeks in animals of the 3% group revealed extensive reversibility. In summary, the TSCA 8(e) submittal concluded by stating that on the basis of the existing experimental work, including numerous genotoxicity studies, the experts consulted by the Bundesgesundheitsamt, among them members of the German Cancer Research Center and of IARC, propionic acid cannot be considered carcinogenic.

Subsequent to the German studies, later investigations have shown that propionic acid has significant irritant activity in rodent forestomachs. Rats receiving 4% propionic acid in a powdered diet developed hyperplasia lesions and tumors of the forestomach. Harrison (1992) found evidence to suggest that repeated or persistent damage to cells of the forestomach epithelium and associated proliferative responses may be a common factor in rodent forestomach tumorigenesis. He concluded by stating that the current evidence suggests that since humans do not have a forestomach, and food retention time is considerably less in the human mouth, pharynx and esophagus; propionic acid cannot be considered a carcinogenic risk to humans. Bueld (1993) found that differences in propionic acid administration in the diet affected the ingested distribution of this compound in the rat forestomach and led to no effects on the forestomach mucosa after 20 weeks of exposure.

In the NTP studies, propionic acid was negative in the Salmonella assay and was withdrawn from testing in the mouse lymphoma assay. The NTP has not conducted other genetic toxicology, other short-term toxicology, or long-term toxicology and carcinogenesis bioassays on propionic acid.

Human studies have shown that acute exposure (concentration unknown) of workers to propionic acid show mild to moderate skin burns, mild eye redness, and a single case of mild cough and asthmatic response. An industrial hygiene survey, with eight-hour time-weighted-average (TWA) levels below 0.25 parts per million (ppm) and with excursions to 2.1 ppm, indicated that no irritation was noted at these concentrations.

Since no other information could be obtained for propionic acid other than the ACGIH documentation, a Threshold Limit Value (TLV) of 30 mg/m³ will be used to derive an ITSL for this compound. The ACGIH recommends this value based on the irritant properties of propionic acid. This value is based on analogy with acetic acid and it is designed to minimize the potential for significant ocular and upper respiratory irritation. The NIOSH also concurs with the TLV by establishing a Recommended Exposure Level (REL) of 30 mg/m³. The ITSL for propionic acid will be derived from the TLV of 30 mg/m³.

The ITSL was determined as follows:

$$\text{ACGIH TLV} = 30 \text{ mg/m}^3$$

$$30 \text{ mg/m}^3 \div 100 = 0.3 \text{ mg/m}^3$$

$$0.3 \text{ mg/m}^3 \times \frac{1000 \text{ } \mu\text{g/m}^3}{1 \text{ mg/m}^3} = 300 \text{ } \mu\text{g/m}^3$$

The ITSL for propionic acid = 300 $\mu\text{g/m}^3$ based on eight-hour averaging.

References:

1. Documentation of Threshold Limit Values and Biological Exposure Indices. 1991. Propionic Acid. American Conference of Governmental Industrial Hygienists (ACGIH), 6th Edition.
2. Bueld JE, et al. 1993. Factors affecting the distribution of ingested propionic acid in the rat forestomach. Food Chemical Toxicology; 31(3). 169-176.
3. Harrison P TC, 1992. Propionic acid and the phenomenon of rodent forestomach tumorigenesis: a review. Food Chemical Toxicology; 30(4). 333-340.
4. Toxic Substance Control Act (TSCA 8(e)) submittal: BASF Corporation; FIFRA registration number 7969-33. EPA-OTS FYI-OTS-1087-0579.

MB:SLB

cc: Cathy Simon, AQD
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