MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: Butyric acid file (CAS # 107-92-6)

FROM: Gary Butterfield

SUBJECT: Screening level development for butyric acid

DATE: February 8, 2007

Butyric acid is also known as butanoic acid. This is liquid at ambient temperatures. The melting point is -7C. The boiling point is 164C. The vapor pressure is 0.43 mmHg at 20C. The molecular formula is $C_4H_8O_2$, with a molecular weight of 88 g/mol. It is used as a food artificial flavoring substance, and is found naturally in some dairy products at concentrations up to 5%. Industrially, it is used in varnishes, perfumes, pharmaceuticals, and as a disinfectant. The FDA considers butyric acid to be a generally recognized as safe (GRAS) material when in normal low concentrations in foods.

The following references or databases were searched to identify data to determine the screening level: U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH) Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), Michigan Department of Environmental Quality (DEQ) library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1968 - January 2007), National Library of Medicine (NLM) - Toxline, and National Toxicology Program (NTP) Status Report.

The CAS and NLM literature on-line searches were conducted on January 31, 2007. The published toxicity information on butyric acid is not very plentiful. There are no inhalation toxicity studies available.

There is some concern due to butyric acids being an acid and fairly reactive, the point of contact (respiratory tract from inhalation) will likely receive the largest impact. This point of contact effect is also evident in oral dosing studies with butyric acid where there is evidence of stomach lining inflammation.

There are some published articles, including Barton et al (2000), that look at chemical family hazard and PBPK models. One of the commonly used families is the butyl acetate (123-86-4) family, including the subsequent metabolites in the chain butanol (71-36-3), butyraldehyde (123-72-8), and the final metabolite butyric acid. The authors talk about the

rapid and efficient de-estrification of butyl acetate by esterase to butanol. The next metabolite in the chain is butyraldehyde, which comes from butanol by the action of alcohol dehydrogenase. The last step in this chain is the metabolism of butyraldehyde to butyric acid by the action of alcohol dehydrogenase. The authors claim that exposure to one of the chemicals in this family also results in exposure to the subsequent metabolites in the chain. There is an ITSL established for butyraldehyde of 7 ug/m^3 with 24-hour averaging, that was based on a 14-week inhalation study LOAEL of 125 ppm for nasal cavity degeneration pathology – a point of contact effect.

The best available data upon which the ITSL for butyric acid will be based is the rat oral LD50 reported by Smyth et al (1951) of 2.94 g/kg with a 95% confidence interval of 2.01 to 4.29 g/kg. The ITSL can be calculated from the equation in R232(1)(h) as follows.

$$\text{ITSL} = \frac{2.94\ \text{g/kg}}{500 \times 40 \times 100 \times 0.167} \times \frac{1\ \text{kg}}{0.9\ \text{m}^3} = 10\ \text{ug/m}^3 \quad \text{annual average}$$

The default rat inhalation rate of 0.9 m^3 per kg body weight was used in the above calculation.

Note that this ITSL of 10 ug/m3 for butyric acid is very similar to the ITSL for butyraldehyde. However, this ITSL, based on an LD50, may need to be up dated if and when inhalation toxicity studies are located for butyric acid.

References:

Barton et al. 2000. Family approach for estimating reference concentrations/doses for a series of related organic chemicals. Toxicol Sci 54:251-61.

Smyth et al. 1951. Range - finding toxicity data: List IV. AMA Arch. Indus. Hyg. Occup. Med. 4:119-122.

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