MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Benzoin [CAS# 119-53-9]

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: February 7, 2017

SUBJECT: Benzoin [CAS# 119-53-9] ITSL change in the averaging time from 24 hours to annual

The initial threshold screening level (ITSL) for benzoin is 32 µg/m^3 based on an annual averaging time. The ITSL was originally established on 2/9/1999 and was based on a NTP (1980) 104 week feeding study in male and female rats. The critical effect of benzoin is a dose-related increase in chronic nephritis in both male and female rats. As the key study used to derive the ITSL is a 104 week feeding study, the averaging time is appropriately set at annual. Therefore, the averaging time is being changed from 24 hours to annual.

References:

Act 451 of 1994, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environmental Quality.

NTP. 1980. Bioassay of Benzoin for Possible Carcinogenicity. Carcinogenesis Testing Program; National Cancer Institute; National Toxicology Program. U.S. Department of Heatlh and Human Services. NIH Publication No. 80-1760. [NTP-80-9; NCI-CG-TR-204].

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

February 9, 1999

TO: File for benzoin (119-53-9)

FROM: Marco Bianchi, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The Initial Threshold Screening Level (ITSL) for benzoin is 32 ug/m^3 based on a 24 hr. averaging time. The following references or databases were searched to identify data to determine the ITSL/IRSL: IRIS, HEAST, NTP Management Status Report, RTECS, EPB-CCD, EPB library, CAS-online, NLM-online, IARC, NIOSH Pocket Guide, and ACGIH Guide.

A complete reference check was conducted for benzoin, but only limited information was available. In an acute rat toxicity summary report submitted to the Research Institute for Fragrance Materials, Inc., three groups of six male rats were orally dosed with 2500, 5000, or 10,000 mg/kg of benzoin. The suspending agent was 40% ethyl alcohol. No dose-related symptoms or adverse effects were noticed at any time during a seven-day observation period. The LD_{50} value for benzoin was determined to be >10,000 mg/kg.

In a dietary bioassay to determine possible carcinogenicity effects, benzoin was incorporated into the diets of F344 rats and B6C3F1 mice. Specifically, groups of 50 male rats were fed diets containing 125 or 150 ppm benzoin for 104 weeks, and similar groups of female rats received feed containing 250 or 500 ppm. Groups of 50 mice of each sex were fed diets containing 2500 or 5000 ppm benzoin for 104 weeks. Groups of untreated rats and mice of each sex were used as matched controls. Mean body weights and clinical signs of low-dose, high-dose, and control male and female rats and male mice were comparable throughout the study. After week 44, mean body weights of dosed female mice were slightly lower (10% or less) than those of the controls.

An increase incidence of lymphomas or leukemia occurred in dosed male rats, but the observed dose-related trend was not statistically significant. Likewise, the incidences of lymphomas that occurred in male mice varied with each dose but were not statistically significant when compared with those of the match controls. Lymphomas or leukemias occurred in low-dose female mice at an incidence that was significant when compared with the matched controls. However, because the incidence of lymphomas or leukemias in the high-dose female mice was not significant, the occurrence of these tumors was not clearly related to administration of the test compounds. Under the conditions of this bioassay, benzoin was not carcinogenic for F344 rats or B6C3F1 mice.

For non-carcinogenic adverse effects, other degenerative, proliferative, and inflammatory lesions were of the usual number and kind observed in aged F344 rats and B6C3F1 mice. These lesions occurred with essentially comparable incidence in control and treated mice, except for a dose-related increased incidence of chronic nephritis observed in both sexes of treated rats. This chronic inflammation didn't appear to be related to the α2u-globulin-associated nephropathy, a condition occurring only in male F344 rats whereby hyaline droplets containing α2u-globulin in the kidney leads to the production of renal tumors. Therefore, because chronic nephritis occurred in both sexes, and no mention was made of hyaline droplets or renal tumors, a lowest-observed-adverse-effect level (LOAEL) was determined based on the increased incidence of chronic nephritis in rats. Since male rats were dosed at a lower dose level than female rats, a LOAEL of 125 ppm will be used to establish an ITSL. Data from this dietary bioassay was sufficient to justify developing an ITSL using the oral reference dose (RfD) methodology according to Rule 232(1)(b).

The ITSL was determined as follows:

LOAEL = 125 ppm in diet
Actual concentration in feed = 119 ppm in diet
Fischer 344 food consumption = 0.078 kg/kg body wt.

Dietary Dose Conversion

$$\frac{\text{level in feed (ppm)} \times \text{(kg) feed eaten}}{\text{body wt. (kg)}} = \text{mg/kg body wt.}$$

119 ppm x 0.078 kg/kg body wt. = 9.28 mg/kg

Uncertainty Factors

10 - specie to specie
10 - sensitive sub-populations
10 - LOAEL to NOAEL

$$\frac{9.28 \text{ mg/kg}}{10 \times 10 \times 10} \times 0.00928 \text{ mg/kg}$$

Conversion from mg/kg to *ug/kg*

$$0.00928 \text{ mg/kg} \times \frac{1000 \text{ ug}}{1 \text{ mg}} = 9.28 \text{ ug/kg}$$

Conversion from *ug/kg* to *ug/m*^{3}

$$9.28 \text{ ug/kg} \times \frac{70 \text{ kg}}{20 \text{ m}^3} = 32.48 \text{ ug/m}^3$$

The ITSL for benzoin = 32 $\mu g/m^3$ based on a 24 hr averaging time.

References:

1. Margolin, S. 1970. Oral LD50 Test - Rats. Report to: Research Institute for Fragrance Materials, Inc.

2. U.S. Department of Health and Human Services. 1980. Bioassay of Benzoin for Possible Carcinogenicity. Carcinogenesis Testing Program; National Cancer Institute; National Toxicology Program. NIH Publication No. 80-1760. [NTP-80-9; NCI-CG-TR-204].

MB:SLB
cc: Mary Lee Hultin, AQD