

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Fluorene (CAS # 86-73-7)

FROM: Robert Sills, AQD Toxics Unit Supervisor

SUBJECT: Fluorene ITSL change in the averaging time from 24 hrs to annual

DATE: December 27, 2016

The current ITSL for Fluorene is 140 ug/m^3 , with annual averaging time (AT).

Previously, the ITSL was established on July 19, 1993 at 140 ug/m^3 with 24 hr averaging time (attached). The averaging time (AT) assigned to the ITSL at that time was 24 hours, as per the default methodology at that time (Rule 232(2)(b)). The ITSL was based on an EPA (1990) Reference Dose (RfD) of 0.06 mg/kg-d, which EPA derived from a subchronic (13 week) mouse gavage bioassay. The critical effects were decreased RBCs, packed cell volume, and hemoglobin. EPA (1990) applied a total uncertainty factor (UF) = 3000, which consisted of a UF = 10 for each interspecies extrapolation, intraspecies variability, and subchronic-to-chronic conversion, and, $\text{UF}_{\text{db}} = 3$ for lack of adequate data in a second species and reproductive/developmental data. The current review notes that in utilizing this oral study for ITSL derivation, AQD also has route-to-route (oral to inhalation) conversion uncertainty which is also addressed with this UF_{db} . The current file review concludes that the AT for the ITSL may appropriately be set at annual, based on the nature and duration of the key study and the ITSL value derivation, as allowed under Rule 229(2)(b).

References:

EPA. 1990. Integrated Risk Information System (IRIS database). Chemical file for Fluorene. Oral RfD assessment last revised 11/1/90. Retrieved on 12/27/16.

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

July 19, 1993

TO: File for Fluorene, CAS #86-73-7

FROM: Dennis Bush, Surface Water Quality Division

SUBJECT: ITSL Derivation

Inhalation exposure to mixtures containing polyaromatic hydrocarbons has been associated with the development of cancer in humans (ATSDR, 1990). However, studies of fluorene for complete carcinogenic activity, initiating activity or cocarcinogenicity in mouse skin painting studies are either negative or inconclusive (EPA, 1993). Because there is insufficient data available to classify fluorene as a human carcinogen, it is classified as a Class D carcinogen in IRIS (EPA, 1993).

The ITSL for fluorene is based on the RfD listed in IRIS (EPA, 1993) because there is no RfC available. The RfD of 0.04 mg/kg/d is based on a subchronic mouse study conducted by EPA (1989). In this study, male and female CD-1 mice (25/sex/group) were administered 0, 125, 250, or 500 mg/kg/d fluorene by gavage for 13 weeks. Body weight, clinical observations, hematology, serum chemistry and histopathology were examined. A significant decrease in RBC count and packed cell volume were observed in females treated with 250 mg/kg/d and in males and females treated with 500 mg/kg/d. Decreased hemoglobin concentrations and increased serum bilirubin levels were also observed in the 500 mg/kg/d group. An increase in absolute liver weight occurred in mice treated at the higher two doses. A significant increase in absolute kidney and spleen weight was observed in both sexes exposed to 500 mg/kg/d and males exposed to 250 mg/kg/d. Histopathology revealed changes in the spleen and liver. An uncertainty factor of 3000 was used by EPA to derive the RfD. The uncertainty factor consisted of 10x for each interspecies, intraspecies and subchronic-to-chronic extrapolation. An additional 3x uncertainty factor was used because there were insufficient data on reproduction/development and there was insufficient data in a second species.

A review of the Toxicological Profile for Polycyclic Aromatic Hydrocarbons (ATSDR, 1990) revealed no inhalation studies which used fluorene. No occupational exposure levels (OELs) were available either. A CAS search conducted in June 1993, covering the period since 1988 also failed to reveal any useful studies. It was considered appropriate to use an RfD to derive an ITSL.

ITSL Derivation:

$$\text{ITSL} = \text{RfD} \times \frac{70 \text{ kg}}{20 \text{ m}^3}$$

$$\text{ITSL} = 0.04 \text{ mg/kg/d} \times \frac{70 \text{ kg}}{20 \text{ m}^3}$$

$$\text{ITSL} = 0.14 \text{ mg/m}^3 \quad 24 \text{ hour averaging time}$$

REFERENCES

ATSDR. 1990. Toxicological Profile for Polycyclic Aromatic Hydrocarbons.

U.S. EPA. 1989. Mouse Oral Subchronic Toxicity Study. Prepared by Toxicity Research Laboratories. As cited in IRIS.

U.S. EPA, 1993. Integrated Risk Information System (IRIS database). Chemical file for Fluorene (86-73-7). RfD verification date 11/15/89. Carcinogenicity verification date 2/7/90.

DB:ma