MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Dibenzofuran (CAS # 132-64-9)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: February 27, 2013

SUBJECT: Screening Level for Dibenzofuran (CAS# 132-64-9)

The initial threshold screening level (ITSL) for dibenzofuran (CAS # 132-64-9) is 4 $\mu g/m^3$ with a 24-hour averaging time. This replaces the previous ITSL of 0.1 $\mu g/m^3$ (annual averaging time) based on the default approach.

Dibenzofuran is a heterocyclic organic compound consisting of two benzene rings fused on either side of one furan ring. It is a pale yellow to white crystalline powder with a molecular weight of 168.19 g/mol. Dibenzofuran is created during the production of coal tar, and is found in coal tar derivatives and creosote; and it is found in the incineration of coal and coal tars, and in cigarette smoke. Dibenzofuran is used: as an insecticide; in the production of PVC, heat-resistant polyarylacetylene, quinoxaline polymers, and photoconductive polymers for electrophotography; as a carrier for dyeing and printing textiles; and in industrial bleaching (Wiki, 2013; EPA, 2013).

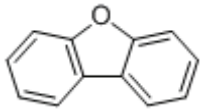

Figure 1. Structure of dibenzofuran

A literature review was conducted to determine an initial threshold screening level (ITSL) for dibenzofuran. The following references and databases were searched to derive the above screening levels: CCD, United States Environmental Protection Agency (US EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH), American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values and Biological Exposure Indices (TLV/BEI) 2012 guide, National Toxicology Program (NTP) Study Database, International Agency for Research on Cancer (IARC), Acute Database, Chemical Abstract Service (CAS) Online (searched 8/2/12), National Library of Medicine (NLM)-

online, EPA Aggregated Computational Toxicology Resource (ACToR) Database, U.S. EPA TSCATS database, and Hazardous Substances Data Bank (HSDB).

Dibenzofurans are listed on the EPA's HAPs list. In the EPA's NATA initiative evaluating the HAP ambient air levels and risks, they did not have a toxicity value to utilize. The current AQD review did not locate sufficient inhalation toxicity data for screening level derivation.

The Environmental Protection Agency does not have a reference concentration or a reference dose for chronic oral exposure (oral RfD), but EPA does have a provisional peer reviewed toxicity values for superfund (PPRTV) with a chronic oral p-RfD at 1E-3 mg/kg per day based on two animal studies. One of the two studies below is on dibenzo-p-dioxin, which is a structural analog of dibenzofuran, and is considered a closer match for risk assessment than any of the chlorinated furans. The toxicity associated with the chlorinated furans involves the ease of interaction of the chlorine atom and therefore dibenzofuran, which lacks any chlorine atoms, should not be assessed like chlorinated furans.

The first animal study cited was on a structural analog of dibenzofuran, dibenzo-p-dioxin, which was performed by NCI (1979) using Osborne-Mendel rats (groups of 35 sex/dose) and B6C3F1 mice (groups of 50 sex/dose) administered either 0, 5,000, or 10,000 ppm in diet for 110 weeks for rats and 87 or 90 weeks for mice. Mean body weights of the dosed male and female rats and mice were only slightly lower than those of the corresponding controls. Except for the male rats, survival at the end of the study was lower in the dosed groups of both female rats and male and female mice. At week 90, 57% of the female rats and 54% of the mice were still alive. "In some male and female rats there was a dose-related increase in the incidence of hepatotoxic alterations characterized by fatty metamorphosis or necrosis. In mice, toxic hepatic lesions including liver degeneration, necrosis, fibrosis and/or cirrhosis were observed in slightly increased numbers in the dosed mice, particularly in the high-dose females. No tumors were induced in rats or mice of either gender at incidences that were significantly higher in the dosed groups than in the corresponding control groups. The authors concluded that unsubstituted dibenzo-p-dioxin exhibited very low toxicity and was noncarcinogenic in Osborne-Mendel rats and B6C3F1 mice, even when the maximum tolerated dose was approached (10,000 ppm diet)" (EPA, 2007).

The second study cited was actually two studies performed by Thomas et. al., (1940); one was a primary 200-day feeding study and a follow-up 78-day study. "In the primary study, groups of five female albino rats (strain not specified), approximately 30 days old, consumed 0, 250, 500, 1,000, 2,000, or 4,000 ppm of dibenzofuran in their food for 200 days. In addition, two female rats consumed 8,000 ppm of dibenzofuran in their diet for a shorter period (approximately 100 days). According to the authors, none of the animals exhibited any abnormal activity or behavior, nor was food intake appreciably altered by dibenzofuran administration, although it was noted that the rats receiving dibenzofuran tended to consume more water than controls. The authors also reported no effect on body weight gain at any dose during the exposure period; however,

decreases in body length and absolute organ weights were observed in all dibenzofuran-exposed groups at necropsy. The authors also reported that the treated animals had unusually large amounts of abdominal fat, which they interpreted as accounting for the lack of effect on body weight gain" (EPA, 2007).

In the Thomas et. al., (1940) study, "Histological examination of the liver, kidney, spleen, heart, and adrenals were performed in rats exposed to dibenzofuran at 500 ppm and higher, and in the control animals" (EPA, 2007). The low dose group (250 ppm) was not examined histopathologically. "In the kidney, histological examination of rats exposed to concentrations of 500 ppm and higher revealed fine, brown-pigmented granules in the epithelial cells of proximal convoluted tubules in the deeper parts of the renal cortex. This effect was noted among all rats receiving dibenzofuran, and both the amount of pigmented material within cells and the frequency of occurrence among cells increased with dose of dibenzofuran. In addition, the two rats fed diet containing 8,000 ppm dibenzofuran exhibited prominent, irregular dilatation of the collecting tubules with coagulated material resembling protein; other tubules in these two rats were slightly dilated and contained more granular and amorphous material than controls" (EPA, 2007).

The Thomas et. al. (1940) study showed some (frequency not specified) of the kidneys from rats receiving 4,000 ppm showed similar, but less severe, changes. "These lesions were not reported among rats fed the lower doses of dibenzofuran…In the spleen, slight hyperplasia of the Malpighian bodies was reported among several rats (frequency not given) in the 4,000 and 8,000 ppm groups. No alterations, other than reduced organ weight, were noted in the liver, heart, or adrenals of the treated rats." (EPA, 2007).

In the follow-up study performed by Thomas et. al. (1940) to determine whether dietary dibenzofuran affected the water balance, it was noted that there was an increase in water consumption in female rats receiving dibenzofuran in their food. Groups of five male rats (average initial body weight 255 grams) were given either 0 or 5,000 ppm dibenzofuran in their diet for 78 days. "Treated rats exhibited greater water consumption and urine output than controls, suggesting that dibenzofuran alters water balance. The excess urine output was greater than the excess in water consumption in the treated group, suggesting a slight degradation of tissues. The authors reported that no alterations in hematological parameters were observed (hemoglobin and erythrocyte, leukocyte, and reticulocyte counts)" (EPA, 2007).

The Thomas et. al. (1940) study may have been well-executed for the time period, but it is not detailed enough for proper risk analysis. Nevertheless, this study can be used when also considering the NCI (1979) study on the structurally similar dibenzo-p-dioxin, which reported hepatic lesions, slight reductions in weight gain, and nephropathy (in male rats). EPA (2007) used the Thomas et. al. (1940) study to determine a point-of-departure of 250 ppm (12.3 mg/kg/day) in the determination of a screening chronic oral provisional RfD of 1 µg dibenzofuran/kg-day. The EPA derived this value using an uncertainty factor of 10,000 (10 for variability in human susceptibility; 10 for animal-to-human extrapolation; 3 for extrapolating from a 200-day rat data to a chronic screening

value; 3 for using a minimal LOAEL instead of a NOAEL; and 10 for database deficiencies).

Data are not available to indicate that oral route to inhalation route extrapolation is inappropriate. According to Rule 232(1)(b), an ITSL can be derived from an oral RfD using the following equation:

$$ITSL = Oral\ RfD \times \frac{70\ kg}{20\ m^3} = 1\ \frac{\mu g}{kg/day} \times \frac{70\ kg}{20\ m^3} = 3.5\ \frac{\mu g}{m^3}$$

Rounded to one significant figure, the ITSL is 4 µg/m^3. Rule 232(2)(b) sets the averaging time at 24 hours. Therefore, the initial threshold screening level (ITSL) for dibenzofuran (CAS # 132-64-9) is 4 µg/m^3 with a 24-hour averaging time.

References:

APCR. 2013. Air Pollution Control Rules, Promulgated pursuant to Part 55, Air Pollution Control, of the Natural Resources and Environmental Protection Act, Michigan Department of Environmental Quality. 1994, Act 451, as amended (NREPA).

EPA. 2007. Provisional Peer Reviewed Toxicity Values for Dibenzofuran (CASRN. 132-64-9). 6-11-2007. Superfund Health Risk Technical Support Center. National Center for Environmental Assessment. Office of Research and Development. U.S. Environmental Protection Agency. Cincinnati, OH 45268.

EPA. 2013. Dibenzofuran. Technology Transfer Network Air Toxics Web Site. Available online at: http://www.epa.gov/ttnatw01/hlthef/di-furan.html

NCI (National Cancer Institute). 1979. Bioassay for Dibenzo-p-Dioxin for Possible Carcinogenicity (CAS No. 262-12-4). Technical Report Series No. 122; NIH Publ. No. 79-1377, Research Triangle Park, NC. P. 1-122. http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr122.pdf

Thomas, J.O., Wilson, R.H., and Eddy, C.W. 1940. Effects of continued feeding of diphenyl oxide. Food Res. 5:23-30.

Wikipedia. 2013. Dibenzofuran. Available online at: http://en.wikipedia.org/wiki/Dibenzofuran

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