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OEHHA

Office of Environmental Health Hazard Assessment

Water - Notification Levels for Chemicals in Drinking Water

MEMORANDUM

TO: David P. Spath, Ph.D., P.E., Chief
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FROM: George V. Alexeeff, Ph.D., DABT
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DATE: June 2, 1999

SUBJECT: EXPEDITED EVALUATION OF RISK ASSESSMENT
 FOR TERTIARY BUTYL ALCOHOL IN DRINKING WATER.

In response to your request of May 19, 1999, we have summarized an interim assessment that the Office of Environmental Health Hazard Assessment (OEHHA) staff made last year in connection with our assessment of methyl tertiary butyl ether (MTBE) and based on limited data available at that time. While this is still an interim assessment with preliminary calculations, and by no means represents a full risk assessment, it may be suitable for the purposes stated in your request.

Tertiary butyl alcohol (TBA) has been used as a gasoline octane booster and may be a food contaminant when used in coatings for metallic items that contact food, or as a coating for paperboard food containers. Human exposure can occur via skin contact, inhalation, or ingestion. The Occupational Safety and Health Administration has established a permissible exposure limit of 100 ppm or 300 mg/m³ for TBA. TBA is partially metabolized via demethylation in rats to acetone and formaldehyde. TBA is a metabolite of MTBE and exposure may occur through inhalation of MTBE fumes.

Compared to MTBE, relatively little toxicity data are available for TBA. A bioassay was conducted by the National Toxicology Program (NTP) in Fischer 344 rats and B6C3F1 mice exposed to TBA in drinking water (NTP, 1994; Cirvello et al., 1995). Groups of 60 F-344 rats were administered daily doses via drinking water of approximately 0, 85, 195, and 420 mg/kg-d in males and 0,

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175, 330, and 650 mg/kg-d in females. Ten animals in each group were sacrificed at 15 months for evaluation; the remainder was exposed until the study was terminated at 103 weeks. The high dose groups of both sexes experienced decreased survival. Dose-related decrease in body weight gain was also observed. All treated groups of females showed a dose-related increase in kidney weight at the 15-month evaluation. Males exhibited increased kidney weight at the mid and high doses. Nephropathy was seen in all groups of treated females and caused early mortality in high exposure groups. The study did not identify a NOAEL for chronic TBA toxicity in the rat.

At the 24-month termination of the rat bioassay, the combined incidences of adenomas and carcinoma of the renal tubules were found in 8/50, 13/50, 19/50, and 13/50 of the control, low, mid and high dose male groups, respectively. The increased incidence in the mid dose group was statistically significant ($p = 0.01$) by Fisher's exact test. The increased mortality in the high dose group may have reduced the observed incidence of renal tumors. The incidence of renal tubule hyperplasia was elevated in all treatment groups. Although no renal (or other) tumors were observed in female rats, the incidence of renal hyperplasia was significantly elevated in the high dose group. No renal tubule adenoma or carcinoma was observed in 227 control male rats in the four studies comprising the recent NTP historical control database for drinking water studies indicating the rarity of these neoplasms in male rats. The pathogenesis of proliferative lesions of renal tubule epithelium is thought to proceed from hyperplasia to adenoma to carcinoma (Cirvello et al., 1995). The incidence of renal tubule hyperplasia, adenoma and carcinoma was increased in all treated male groups.

Groups of 60 B6C3F1 mice of each sex were administered TBA in drinking water at doses of approximately 0, 535, 1035, and 2065 mg/kg-d in males and 0, 510, 1015, and 2105 mg/kg-d in females. Reduced survival was observed in the high dose groups. The incidence of thyroid follicular cell hyperplasia was significantly elevated in all treatment groups of males (5/60, 18/59, 15/59, 18/57) and in the mid and high dose groups of females (19/58, 28/60, 33/59, 47/59). Follicular cell adenomas were significantly higher in high dose females (9/59). Chronic urinary bladder inflammation was seen in both sexes at the high dose, but no urinary bladder neoplasias were observed. No NOAEL was identified for chronic TBA toxicity in the mouse.

In conclusion, the increased incidence of renal tubule adenoma or carcinoma, combined, in male rats and of thyroid gland follicular cell adenoma in female mice is evidence of a carcinogenic response to TBA.

TBA has been reported as negative in the Salmonella typhimurium mutagenicity test, in a chromosome aberrations test in cultured Chinese hamster ovary (CHO) cells, in a sister chromatid exchange test in CHO cells, and in a mutation test in cultured mouse lymphoma cells (Gold and Zeiger, 1997).

Due to the limited data available, the interim assessment for human consumption will be based on the rat cancer bioassay

noted above. Since no mode of carcinogenic action has been established for TBA, and following the U.S. EPA's 1996 Proposed Guidelines for Carcinogen Risk Assessment (FR60: 17960-18011,4/23/96), a low dose linear dose-response approach will be applied to the data for male rat kidney adenoma and carcinoma. The analysis is summarized in Table 1.

Table 1. Dose Response Assessment of Tertiary Butyl Alcohol for Rat Kidney Tumors

| Study | Sex, Species | Doses; Tumor incidences | Dose Response X2, p, k | LMSQ1* (mg/kg-d)-1 | ED10; LED10 mg/kg-d | CSF (mg/kg-d)-1 | C, mg/L |
|----------------------------------|----------------------|--|------------------------|--------------------|---------------------|-----------------|---------|
| NTP, 1994; Cirvello et al., 1995 | Male Fischer 344 Rat | 0, 85, 195, 420 mg/kg-d; 8/50, 13/50, 19/50(p<0.01), 13/50 | 5.12, 0.08, 3 | 3.3E-3 | 75.9;30.4 | 3.0 E-3 | 1.1E-2 |

Note: Dose response assessment performed with Tox_Risk v 3.5 and body weight $\frac{3}{4}$ power scaling to human equivalent.

As can be seen in Table 1, the dose response fit was adequate exceeding the Chi-square fit criterion of $p > 0.05$. The ED10 is the maximum likelihood estimate of the dose giving a 10% tumor response and the LED10 is the 95% lower bound on that dose. The carcinogen slope factor (CSF) is simply the risk 0.1 divided by the LED10 or 3.3E-3 (mg/kg-d)-1. The drinking water interim assessment concentration (C) is calculated as follows:

$$C = 70 \text{ kg} \times 10^{-6} = 0.0117 \text{ mg/L} \\ 3.0 \times 10^{-3} \text{ (mg/kg-d)}^{-1} \times 2\text{L/d}$$

$$C = 0.012 \text{ mg/L (rounded)} = 12 \text{ } \mu\text{g/L}$$

Where: 10^{-6} is the negligible lifetime extra cancer risk criterion;
70 kg in the average human body weight;
 $3.3 \times 10^{-3} \text{ (mg/kg-d)}^{-1}$ is the human carcinogen slope factor (CSF);
2L/d is the average daily human total water consumption.

It should be noted that this calculation addresses exposures to TBA via the oral route only. As noted above, other sources besides water as well as other routes besides oral may be involved in human exposures to TBA.

References:

NTP. (1994). Toxicology and Carcinogenesis Studies of t-Butyl Alcohol (CAS No. 75-65-0) in F344/N Rats and B6C3F1 Mice. National Toxicology Program, Technical Report No. 436, National Institutes of Health, Public Health Service, U.S. Department of Health and Human Services, Research Triangle Park, NC.

Cirvello JD, Radovsky A, Heath JE, Farnell DR, and Lindamood

III C. (1995). Toxicity and carcinogenicity of t-butyl alcohol in rats and mice following chronic exposure in drinking water. *Toxicol Indus Health* 11:151-165.

Gold LS and Zeiger, E eds. (1997). *Handbook of Carcinogenic Potency and Genotoxicity Databases*. CRC Press, Boca Raton, FL.

If you need any additional information about this analysis, please call me at (510) 622-3202.

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MTBE: Regulations and Drinking Water Monitoring Results

Last Update: November 29, 2006

Follow this link for information about the [Drinking Water Treatment and Research Fund \(DWTRF\)](#). The DWTRF addresses MTBE and other oxygenates in drinking water.

MTBE Drinking Water Standards

The gasoline additive methyl tertiary butyl ether (MTBE) is a regulated drinking water contaminant in California. MTBE has:

- a primary MCL of 13 micrograms per liter ($\mu\text{g/L}$), established in 2000, that addresses health concerns. Its 1999 public health goal is 13 $\mu\text{g/L}$, corresponding to the de minimis cancer risk derived from animal studies.
- a secondary MCL of 5 $\mu\text{g/L}$, established in 1999. The secondary MCL addresses taste and odor concerns.
- a detection limit for purposes of reporting (DLR) of 3 $\mu\text{g/L}$. The DLR is the level at which CDPH is confident about the quantity being reported. Results at or above the DLR are required to be reported to CDPH; some laboratories may report results at lower concentrations.

Monitoring Results

After detections of MTBE in some drinking water sources in the early and mid-1990s, CDHS (the California Department of Health Services, now CDPH) adopted a 1997 regulation that included MTBE as an unregulated chemical for which monitoring was required to be done by certain public water systems. Subsequently, required monitoring has been associated with compliance with MTBE's MCLs.

As of November 1, 2006, the CDHS database includes MTBE analytical results reported for 14,351 sources, where "sources" may include both raw and treated drinking water wells and surface water sources, distribution systems, blending reservoirs, and other sampled entities. Active, standby, inactive, and abandoned or destroyed sources are included.

Nearly all of the results are non-detects. However, 89 sources have reported MTBE detections greater than the DLR. The sources are in 32 counties, as shown in Table 1, which also shows 32 sources with a peak detection greater than MTBE's primary MCL, and 28 sources with a peak level greater than the secondary MCL but lower than the primary MCL.

The highest values reported were 610 $\mu\text{g/L}$ in Los Angeles County in 1996; 500 $\mu\text{g/L}$ in San Francisco in 1990; 400 $\mu\text{g/L}$ in Monterey County in 2004; 234 $\mu\text{g/L}$ in Yuba County in 1999; and 112 $\mu\text{g/L}$ in San Diego County in 2004.

| County | >13 $\mu\text{g/L}$ | 5.5-13 $\mu\text{g/L}$ | 3-5 $\mu\text{g/L}$ | Total No. Sources | Peak Finding ($\mu\text{g/L}$) |
|---------------|---------------------|------------------------|---------------------|-------------------|----------------------------------|
| Los Angeles | 6 | 8 | 3 | 17 | 610 |
| San Diego | 5 | 3 | 3 | 11 | 112 |
| Kern | 5 | 2 | 1 | 8 | 49.2 |
| Monterey | 3 | 1 | . | 4 | 400 |
| San Francisco | 2 | 1 | . | 3 | 500 |

| | | | | | |
|-----------------|-----------|-----------|-----------|-----------|-----------|
| Riverside | 2 | . | . | 2 | 24 |
| Sacramento | 2 | . | . | 2 | 28 |
| San Mateo | 1 | 2 | 1 | 4 | 35 |
| Madera | 1 | 1 | . | 2 | 33 |
| El Dorado | 1 | . | 4 | 5 | 68 |
| Orange | 1 | . | 2 | 3 | 40.9 |
| Yuba | 1 | . | 1 | 2 | 234 |
| San Benito | 1 | . | . | 1 | 25 |
| Siskiyou | 1 | . | . | 1 | 17 |
| Lake | . | 1 | 1 | 2 | 13 |
| San Luis Obispo | . | 1 | 1 | 2 | 13 |
| Tulare | . | 1 | 1 | 2 | 13 |
| Tuolumne | . | 1 | 1 | 2 | 11 |
| Merced | . | 1 | 1 | 2 | 6.4 |
| Alameda | . | 1 | 1 | 2 | 5.5 |
| San Bernardino | . | 1 | . | 1 | 11 |
| Fresno | . | 1 | . | 1 | 9.2 |
| Mono | . | 1 | . | 1 | 9 |
| Shasta | . | 1 | . | 1 | 6.9 |
| Calaveras | . | . | 1 | 1 | 5.3 |
| Mendocino | . | . | 1 | 1 | 4.9 |
| Lassen | . | . | 1 | 1 | 4.3 |
| Ventura | . | . | 1 | 1 | 4 |
| Santa Barbara | . | . | 1 | 1 | 3.6 |
| Solano | . | . | 1 | 1 | 3.5 |
| Butte | . | . | 1 | 1 | 3.2 |
| Sonoma | . | . | 1 | 1 | 3 |
| TOTAL | 32 | 28 | 29 | 89 | -- |

¹Numbers of sources should be considered draft, since they may change with subsequent updates. Data are from sources with two or more reported MTBE detections at any concentration.

Go to Drinking Water Treatment and Research Fund (DWTRF)
(The DWTRF addresses oxygenates such as MTBE in drinking water)