

Wang

Office of Environmental Health Hazard Assessment

Joan E. Denton, Ph.D., Director

Headquarters • 301 Capitol Mall, Rm. 205 • Sacramento, California 95814-4308

Oakland Office • Mailing Address: 1515 Clay Street, 16th Floor • Oakland, California 94612



Winston H. Hickox
Secretary for
Environmental
Protection



Gray Davis
Governor

MEMORANDUM

TO: David P. Spath, Ph.D., Chief
Division of Drinking Water and Environmental Management Branch
Department of Health Services
601 North 7th Street, Mail Stop 92
P.O. Box 942732
Sacramento, California 94234-7320

FROM: George V. Alexeeff, Ph.D., DABT *George Alexeeff*
Deputy Director for Scientific Affairs

DATE: December 29, 1999

SUBJECT: PROPOSED ACTION LEVEL FOR METHYL ISOBUTYL KETONE

Staff of the Office of Environmental Health Hazard Assessment (OEHHA) have reviewed your Department's proposed action level of 170 µg/L for Methyl Isobutyl Ketone (MIBK) based on a no-observable-adverse-effect-level (NOAEL) taken from the U.S. Environmental Protection Agency's (U.S. EPA) Health Effects Assessment Summary Tables (HEAST) document (U.S. EPA, 1997). OEHHA does not concur with this proposed action level for MIBK. By checking the U.S. EPA report cited in the HEAST Tables, we have found that the NOAEL given in the HEAST Tables (250 mg/kg-day) is actually a misprint. The real NOAEL reported by U.S. EPA (1987) is 50 mg/kg-day. This NOAEL is based on a subchronic (13-week) gavage study in Sprague-Dawley rats performed by Microbiological Associates (1986). No adverse effects were observed at this dose, but higher doses (250 mg/kg-day and 1,000 mg/kg-day) resulted in increased relative kidney and liver weights and general nephropathy.

The HEAST Tables mention a combined uncertainty factor (UF) of 3,000 used to calculate a chronic reference dose (RfD) of 8×10^{-2} mg/kg-day. This combined UF is not mentioned in the U.S. EPA (1987) report. The source of this combined UF is unclear, but it may have come from an earlier U.S. EPA evaluation (perhaps unpublished). We can reasonably estimate, based on conventional approaches, that the combined uncertainty factor may have been derived in the following manner:

ten for animal to human extrapolation,
ten for intrahuman variability,
ten for extrapolating from subchronic to chronic exposure,
three for limited database.

California Environmental Protection Agency



Printed on Recycled Paper

David P. Spath, Chief
December 29, 1999
Page 2

In the later U.S. EPA report (1987) the factor of three has been omitted and only a combined UF of 1,000 is used.

A computer search of the literature did not reveal new studies of MIBK by the oral route that could be used in place of the one discussed above. Using the correct NOAEL of 50 mg/kg-day and the same UFs listed above, an action level for chronic exposure can be calculated as follows.

$$\begin{aligned} C &= \frac{\text{NOAEL} \times \text{BW} \times \text{RSC}}{\text{UF} \times \text{DWC}} = \frac{50 \text{ mg/kg-day} \times 70 \text{ kg} \times 0.2}{3,000 \times 2 \text{ L/day}} \\ &= 0.12 \text{ mg/L} \\ &= 120 \text{ } \mu\text{g/L} \end{aligned}$$

Where:

NOAEL = No-Observed-Adverse-Effect-Level
BW = body weight
RSC = relative source contribution
UF = uncertainty factor (3,000 – from HEAST, adopted by OEHHA)
DWC = drinking water consumption

The value we have calculated is 120 $\mu\text{g/L}$, compared with your proposal of 170 $\mu\text{g/L}$. The difference is due to using the correct NOAEL, and using adult body weight and adult water consumption. This calculation is for oral exposure only. MIBK has a vapor pressure of 15 mm Hg, so there may be some potential for exposure by inhalation, as well as by the dermal route. This new calculation is provided only as a proposed action level.

If you have questions on this review, please contact me at (510) 622-3150 or Dr. Anna Fan at (510) 622-3170.

References

Microbiological Associates (1986). Subchronic toxicity of methyl isobutyl ketone in Sprague-Dawley Rats. Performed for Research Triangle Institute, Research Triangle Park, North Carolina. Final Report. Study No. 522104.

David P. Spath, Chief
December 29, 1999
Page 3

U.S. EPA (1987). Health Effects Assessment for Methyl Isobutyl Ketone. Environmental Criteria and Assessment Office; Office of Health and Environmental Assessment; Office of Research and Development; U.S. Environmental Protection Agency. Cincinnati, Ohio. EPA/600/8-88/045.

U.S. EPA (1997). Health Effects Assessment Summary Tables (HEAST) FY 1997 Update. Office of Research and Development; Office of Emergency and Remedial Response, U.S. Environmental Protection Agency, Washington, DC. EPA 540/R-97-036-PB97-921199.