

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

JUNE 8, 1994

TO: File for Acetophenone (CAS No. 98-86-2)
FROM: Marco Bianchi
SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for acetophenone is $490 \mu\text{g}/\text{m}^3$ based on an 8 hr. averaging time.

The following references or databases were searched to identify data to determine the ITSL: IRIS, HEAST, NTP Management Status Report, RTECS, EPB-CCD, EPB library, CAS-online, NLM-online, IARC, NIOSH Pocket Guide, and ACGIH Guide.

The EPA is in the process of reviewing an inhalation RfC assessment for acetophenone (IRIS, 1989). Currently, the HEAST tables note that "The chronic inhalation RfC is considered not verifiable (6/25/92) by the RfD/RfC work group" (HEAST, 1993). In addition, acetophenone is considered a Group D carcinogen; "not classifiable as to human carcinogenicity", based upon no human or animal carcinogenicity data, and limited mutagenicity results which are equivocal.

The EPA has established a chronic oral RfD for acetophenone of 0.1 mg/kg/day, based on a study by Hagen et.al, (1967). In this study, groups of 10 male and 10 female Osborne-Mendel rats were exposed to acetophenone in their diets at levels of 0, 100, 2500, and 10,000 ppm for a period of 17 weeks. There were no observed effects on growth or hematological parameters, nor were there any macroscopic tissue changes in any of the groups. Histological examination revealed no effects even at the high dose (10,000 ppm) level. This concentration was adjusted by a factor of 0.845 to account for loss of the compound from the feed due to volatilization, giving a final NOAEL of 8450 ppm or 423 mg/kg/day (assuming the rats consumed 5% of their body weight per day as food). Dividing the dose by an uncertainty factor of 3000 yields the RfD of 0.4 mg/kg/day. EPA's stated confidence in the RfD is low, due in part to an inadequate sample size, no supporting studies, or doses that did not define a LOAEL. An ITSL derived from this study would yield $350 \mu\text{g}/\text{m}^3$ for a 24 hour averaging time ($630 \mu\text{g}/\text{m}^3$; 8 hr. averaging time).

In 1993, the ACGIH adopted a TLV for acetophenone of $49 \text{mg}/\text{m}^3$ based on a recommendation to reduce eye irritation. Application of acetophenone to the eyes of rabbits as two drops of saturated aqueous solution caused discomfort; however, the effects were limited to a transient optical irregularity of the corneal epithelium, with no opacity, and the eyes returned to normal by the next day. Additionally, one study reported that instillation of 771 mg of undiluted acetophenone into the eyes of rabbits produced moderate irritation and transient corneal injury. Although these studies indicate a low degree of eye irritation, data on long term safety is limited. An ITSL derived from this study would yield $490 \mu\text{g}/\text{m}^3$ for an 8 hr. averaging time.

While data from a RfD study precedes data from an OEL study for ITSL derivation, the above data indicates that the RfD based number may not be protective of eye irritation potential for which the TLV is based. Therefore, data from the ACGIH study will be used to calculate an ITSL for acetophenone.

The ITSL was derived as follows:

ACGIH TLV = 49 mg/m³

49 mg/m³ x 1000 µg/mg = 49,000 µg/m³

ITSL = 1% of the ACGIH

49,000 µg/m³ x 0.01 = 490 µg/m³

The ITSL for acetophenone = 490 µg/m³ based on 8 hr. averaging.

References:

ACGIH, Draft Documentation of Threshold Limit Values for Acetophenone [3/17/94].

ACGIH (1993). Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices, 1993-1994. American Conference of Governmental Industrial Hygienists, Cincinnati, p.12.

IRIS (1989). Acetophenone (98-86-2). Integrated Risk Information System, U.S. Environmental Protection Agency.

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