MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Molybdenum Trioxide, CAS No. 13 13-27-5

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DATE: June 8, 2009

SUBJECT: Screening Levels for Molybdenum Trioxide, CAS No. 1313-27-5

Molybdenum trioxide is an odorless powder with molecular formula MoO_3, sparingly soluble in water. It is primarily used in the manufacture of steel as an alloying agent. Molybdenum trioxide reacts violently with chlorine trifluoride, lithium, potassium and sodium (NOAA, 2009, CAMEO chemical data sheet). Although molybdenum is a necessary nutrient via oral exposure, its toxicity profile from inhalation exposure is quite different. Short-term exposure may result in irritation of the eyes, nose, throat and skin. Workers with occupational exposure to molybdenum compounds have been found to suffer a variety of respiratory effects.

References checked for the development of a screening level for this chemical included: IRIS, HEAST, RTECS, EPB-CCD, DEQ library, CAS-online, NLM-online, IARC, NIOSH Pocket Guide, and ACGIH Documentation of Threshold Limit Values (TLVs). The U.S. Environmental Protection Agency (USEPA) has not developed a reference dose or reference concentration for MoO3. The American Conference of Governmental Industrial Hygienists (ACGIH) has a threshold limit value (TLV) for molybdenum compounds (separate values for soluble and insoluble compounds). Molybdenum trioxide is included in the ACGIH definition of soluble compounds, with a TLV of 0.5 mg/m^3 and an A3 designation for carcinogenicity. The TLV was used to develop an Initial Threshold Screening Level (ITSL) for soluble and insoluble molybdenum compounds. According to Act 451, Rule 336.1232 (1)(c), the ITSL was derived as follows:

ITSL = OEL divided by 100
ITSL = 0.5 mg/m^3/100 = 0.005 mg/m^3 x 1000 = 5 $\mu g/m^3$ based on an 8 hour averaging time.

For more information on toxicity of molybdenum compounds other than the trioxide form, please refer to AQD tile with CAS #7439-98-7.

The National Toxicology Program published a cancer bioassay on molybdenum trioxide in 1997 (DHHS, 1997). In the study, rats and mice of both sexes were exposed via inhalation for 14 days, 13 weeks or 2 years. In the14-day studies, doses of 0, 3, 10, 30, 100 or 300 mg/m^3 were administered to groups of five animals per sex for 6 hrs/day, 5 days/week. Final mean body weights were reduced at 100 and 300 mg/m^3 in the rats

and at 300 mg/m^3 in the mice. No other clinical findings or chemical related lesions were observed in the14-day study. In the 13-week studies, doses of 0, 1, 3, 10, 30 or 100 mg/m^3 were given to groups of 10 animals per sex for 6.5 hrs/day, 5 days per week. No clinical findings or chemical related lesions were noted in the rats. The only significant finding in the mice was increased liver copper concentrations of females in the30 mg/m^3 group and males as well as females in the100 mg/m^3 group. In the 2-year studies, doses of 0, 10, 30 or 100 mg/m^3 were given to groups of 50 animals per sex, 6hrs/day, 5 days per week. Incidences of chronic alveolar inflammation were seen in the two higher doses at a rate significantly greater than controls. Also, hyaline degeneration in the nasal respiratory epithelium was seen in the rats. There was an increase in alveolar/bronchiolar adenomas or carcinomas (combined) in male rats with a marginally significant positive trend. Mice were found to exhibit metaplasia of the alveolar epithelium of minimal severity. Histiocyte cellular infiltration was seen in all groups of male mice. Mice also exhibited squamous metaplasia of the epithelium of the epiglottis. Hyperplasia of the laryngeal epithelium was also seen in mice. The male and female mice had significantly greater incidences of alveolar/bronchiolar carcinomas than controls and exceeded historical control ranges. The genetic toxicology tests did not yield any positive findings (five strains of S.typhimurium; two tests with Chinese hamster ovary cells) either with or without S9 metabolic activation enzymes. The NTP concluded that there was equivocal evidence of carcinogenic activity of molybdenum trioxide in male F344/N rats; no evidence of carcinogenic activity in the female rats; and some evidence of carcinogenic activity in the male and female mice. All the carcinogenicity findings were based on alveolar/bronchiolar adenomas and/or carcinomas, either separately or combined incidences.

As per Act 451, Part 2. R 336.1231, an initial risk screening level was determined for molybdenum trioxide as follows. Unit risk values (q1*) were determined using both the newer method of using Benchmark Dose Modeling Software (BMDS) and the older method of linearized multistage modeling, Global 82 software for comparison purposes. Model inputs were adjusted to reflect lifetime average daily dose (i.e., doses were multiplied by hours per day and days per week of exposure to obtain an average dose). Using both methods, the highest potency, which met statistical goodness of fit criteria generated was for the female mouse, as shown below:

Sex/species	**Critical Effect/Lesion**	**Model Input Parameters: No. Response per Total at Risk Animals**	**Global 82 q1* animal $(mg/m^3)^{-1}$**	**Benchmark Dose v. 1.4.1 (EPA) Slope Factor $(mg/m^3)^{-1}$**
Female Mice	Alveolar /bronchiolar adenoma or carcinoma	3/10 6/44 8/46 15/44	3.0305E-2	2.876E-2
Male Mice	Bronchiolar adenoma/carcinoma	11/47 27/50 21/48 18/48	1.602E-2 poor fit via Chi^2	Failed Akaike Information Criteria
Male Rat	Alveolar /bronchiolar adenoma or carcinoma	0/26 1/201/27 4/33	1.492E-2	1.42E-2

The Benchmark Dose method was chosen as it represents more current scientific modeling.

Using the unit risk (q*) from the female mice, an IRSL is derived:

IRSL- 1E-6/(human q1* or BMD)
Slope = q1* or Benchmark dose slope factor

Benchmark dose modeling for female mice revealed a slope = 2.876 E -02 $(mg/m^3)^{-1}$

A Regional Deposited Dose Ratio for the tracheobronchial area or $RDDR_{TB}$ is calculated to estimate the ratio of the deposited dose in humans to that of animals in the same region of the lung. It is necessary to calculate the RDDR, which was performed using U.S. EPA, 1994 software. To obtain a human equivalent dose, the risk must be multiplied by the RDDR.

$RDDR_{TB}$ = 3.338

IRSL= 1E-6/ BMD_{animal}

IRSL = 1E-6/2.876 E-02 $(mg/m^3)^{-1}$

IRSL = 3.5E5 X 3.338 = 1.17E4 $(mg/m^3)^{-1}$

Conversion to $\mu g/m^3$ = 1.17E-4 $(mg/m^3)^{-1}$ x 1/(1000 µg/mg) = 1.17E-1 $\mu g/m^3$

IRSL =0.12 $\mu g/m^3$ based on annual averaging.

References

DHHS, 1997. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Molybdenum Trioxide (CAS No. 1313-27-5) in F344/N Rats and B6C3FI Mice (Inhalation Studies). U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, April 1997. NTP TR 462, NIH Publication No. 97-3378

U.S. EPA, 1994, Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry. U.S. Environmental Protection Agency (EPA Doc EPAI600-8-90/066F)