MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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TO: Selenium and Inorganic Selenium Compounds File (CAS# 7782-49-2)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

SUBJECT: Screening Level for Selenium and Inorganic Selenium Compounds (CAS # 7782-49-2)

DATE: March 12, 2015

This memo is designed to cover selenium and inorganic selenium compounds with ITSLs all based on the selenium TLV for each of those compounds. The ITSL for selenium and inorganic selenium compounds is 2 µg/m^3 based on an 8-hour averaging time. This ITSL is for the following selenium compounds, which includes:

selenic acid (CAS# 13410-01-0)
selenious acid (CAS# 7783-00-8)
selenium dioxide (CAS# 7446-08-4)
selenium disulfide (CAS # 7488-56-4)
selenium sulfide (CAS # 7446-34-6)
sodium selenite (CAS # 10102-18-8)

This screening level does not apply to hydrogen selenide, selenium hexafluoride, and organic forms of selenium.

This memo is an addition to a previous memo (Hultin, 1998; see attachment), which provides the justification for selenium and adequately describes the derivation of 2 ug/m^3 based on an occupational exposure level (OEL) developed by the American Conference of Government and Industrial Hygienists (ACGIH).

References:

ACGIH. 2001. Selenium and compounds. TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices. ACGIH Worldwide Signature Publications.

Act 451 of 1994, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environmental Quality.

Hultin. 1998. Memo to the Files for Selenium; From: Mary Lee Hultin, Toxics Unit, Air Quality Division; Dated: March 25, 1998.

Attachment
DL:lh

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

March 25, 1998

TO: File for Selenium (CAS # 7782-49-2)

FROM: Mary Lee Hultin, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level (ITSL) for Selenium

The ITSL for selenium is 2 µg/m^3 based on an 8 hour averaging time. This screening level does not apply to organic forms of selenium.

The following standard references or databases were searched to identify data to determine the ITSL: AQD chemical files, IRIS, HEAST, ACGIH TLV Booklet, NIOSH Pocket Guide to Chemical Hazards, RTECS, NTP Management Status Report, EPB Library, IARC Monographs, CAS On-line and NLM/Toxline.

Selenium (Se) is a naturally occurring, non-metallic element with a melting point range of 170-217°C (crystals). The element Se may exist as a dark red to bluish-black amorphous solid or a dark red, gray, or black crystal. It is widely, but unevenly, distributed in the earth's crust. Multiple valence states exist which interact with ambient conditions to determine local forms of naturally occurring Se. Selenium may be found in the form of selenium dioxide, as dusts of elemental selenium or as hydrogen selenide (see screening level derivation for hydrogen selenide) when industrial exposure occurs (ATSDR, 1989). When elemental selenium is heated, the oxide is formed (Clayton, 1993). Selenium dioxide is a white, crystalline solid which dissolves in water forming selenious acid. Selenious acid is a strong oxidant and can be reduced *in vitro* to elemental selenium (Koppel et al., 1986).

Selenium is an essential trace element in animals and humans. The United States recommended daily allowance of Se is 0.07 mg/day for men, 0.055 mg/day for women and 0.87 ug/kg/day for children (ATSDR, 1996). Vegetation in various locations with high soil levels can selectively take up selenium, resulting in potentially toxic amounts in feed and foodstuffs. Consequently, a substantial amount of data is available on the oral toxicity of selenium compounds.

Pharmacokinetics/metabolism: Selenium is absorbed following inhalation or ingestion. More information about absorption rates is available on the oral than on the inhalation route of exposure. Different forms of Se are absorbed and metabolized at different rates. For instance, selenious acid was absorbed more rapidly into the blood than elemental Se in dogs and rats after inhaled doses (Medinsky et al., 1981; Weissman et al., 1983). A characteristic "garlic odor" of the mouth after excessive, rapid selenium absorption is caused by

Se are absorbed and metabolized at different rates. For instance, selenious acid was absorbed more rapidly into the blood than elemental Se in dogs and rats after inhaled doses (Medinsky et al., 1981; Weissman et al., 1983). A characteristic "garlic odor" of the mouth after excessive, rapid selenium absorption is caused by dimethylselenide. This metabolite results from the detoxification of inorganic selenium via S-adenosylmethionine primarily in the liver, kidney, and lung. Because Se is a required nutrient, the absorption and subsequent toxicity of an oral dose is dependent upon the nutritional status of the organism. At least in some cases, absorption following oral dosing is greater in the case of selenium deficiency.

A reference concentration (RfC) has not been developed by EPA. However, the EPA has developed a Reference Dose (RfD) for selenium compounds of 0.005 mg/kg/day. As detailed in Integrated Risk Information System (IRIS) (EPA, 1996), EPA's value was based on a NOAEL of 0.015 mg/kg/d from human epidemiologic studies by Yang, et al. (1989) and Longnecker, et al. (1991). Yang studied clinical selenosis in individuals living in areas of China with unusually high environmental levels of Se. Clinical selenosis is characterized in humans by: nail brittleness and loss; alopecia, pruritis of the scalp, dermatitis with hyperemia, edema and eruptive blistering. Also included are: peripheral anesthesia, acroparesthesia and pain in the limbs. The motor dysfunction that may follow is also characteristic in livestock grazed on highly seleniferous pastures, termed "alkali disease" when chronic or acutely as "blind staggers." The following conversions were used by EPA in RfD development: NOAEL (0.853 mg/day) and LOAEL (1.261 mg/day) were calculated from regression analyses based upon the correlation (r=0.962) between dietary selenium intake and blood selenium level for data showing incidence of clinical selenosis in adults based on an average adult body weight of 55 kg (Yang, et al. 1989).

Inhalation toxicity data for selenium is available from occupational exposure reports and from rodent studies. The threshold limit value-time weighted average (TLV-TWA) is 0.2 mg/m^3 (measured as Se). This value is based on the fact that there have been no reports of disabling chronic disease or death from industrial exposures to selenium. This value is recommended to prevent systemic toxicity and minimize the potential for ocular and upper respiratory tract irritation (ACGIH, 1991).

Very few human studies exist that describe the inhalation toxicity of Se. In occupational studies, the respiratory tract is the primary site of injury after inhalation of selenium dust or compounds. However, gastrointestinal, cardiovascular, dermal and neurological effects have also been noted. The most comprehensive reports are from Glover, (1967, 1970) in which 200-300 selenium rectifier plant workers were examined. Symptoms similar to chronic selenosis were noted at

concern in the neonate. Inorganic and organic selenium compounds cross the placenta in rodents, cats, sheep, and nonhuman primates.

The International Agency for Research on Cancer (IARC) evaluated selenium for carcinogenicity in 1975 and concluded that there was insufficient evidence for carcinogenicity. Since then, however, a study by the National Cancer Institute (NCI) in 1980 showed an increased incidence of hepatocellular carcinomas in male and female rats (F344) and mice (B6C3F1) treated by oral gavage with selenium sulfide (3 or 15 mg/kg) 7 days/week for 103 weeks. Female mice in this study also showed invasive alveolar/bronchiolar carcinomas and adenomas. Based on this study NCI concluded that selenium sulfide is carcinogenic in rats and female mice and noncarcinogenic in male mice. Selenium has been assigned to Group 2 (reasonably anticipated to be a carcinogen) by the National Toxicology Program (NTP) based on this NCI study as well (ACGIH, 1991). The carcinogenicity evidence for selenium compounds in animals and mutagenicity data is conflicting and difficult to interpret. Selenium sulfide has sufficient data to be classified as a B2 carcinogen (probable human carcinogen). However, the EPA has classified Se as a class D (not classifiable) carcinogen (IRIS, 1996). This is based on inadequate human data and inadequate evidence of carcinogenicity in animals. In contrast, epidemiologic data have demonstrated an increased risk of malignant morbidity and mortality associated with reduced selenium concentrations. No Initial Risk Screening Level will be derived for Se, based on inadequacy of data for quantitative assessment.

In choosing data for screening level development, preference is generally given to human epidemiologic data or chronic laboratory animal inhalation studies which can be used to derive a RfC. Such data were not found in our searches. When adequate data for RfC calculation are not available, next preference is given to oral data. The oral data is then used for calculation of a RfD, if available studies do not indicate that extrapolation from the oral to the inhalation route of exposure is inappropriate. The limited amount of data on the pharmacokinetics of inhaled Se makes this determination difficult. However, the inhalation route will be used preferentially for the following reasons: occupational data indicate that primary effects from inhalation exposure target the respiratory system; elimination of excess Se can be partially accomplished via exhalation after an inhaled dose, but exhalation of Se metabolites only occurs after extremely large oral doses and; the nutritional status impacts the toxicity of ingested Se, whereas no information of this type is available on an inhaled dose. Extrapolation from oral to inhalation dosing is, therefore, deemed inappropriate at this time.

The next order of preference is given to data from an occupational exposure level (OEL) developed by NIOSH or ACGIH. Both NIOSH and ACGIH have OELs = 0.2 mg/m3. Consistent with Rule 232(1)(c), the ACGIH TLV will be used.

ITSL Derivation: Per Rule 232(1)(c), Part 55, of Act 451:

$$\textbf{ITSL} = \text{OEL} \times \frac{1}{100} = 0.2\ \text{mg/m}^3 \times \frac{1}{100} = 0.002\ \text{mg/m}^3 \times \frac{1000\ \mu\text{g}}{1\ \text{mg}} = 2\ \mu\text{g/m}^3$$

where the factor of 1/100 is a safety factor to account for: 1) differences in susceptibility between the healthy, adult worker population as compared to the general population which may include individuals or subpopulations more sensitive to the effects of exposure to Se and, 2) the difference in exposure duration for the worker population as opposed to the general population. The factor is derived as follows:

$$\text{Safety factor} = \frac{40 \text{ hours}}{168 \text{ hours}} \times \frac{30 \text{ years}}{70 \text{ years}} \times \frac{1}{10} = \frac{1}{100}$$

The first term adjusts for the difference between a 40 hour work week and the total hours in a week; the second factor adjusts for the difference between an assumed working life of 30 years and an assumed total lifespan of 70 years; and the third factor is a standard ten-fold uncertainty factor to extrapolate from the healthy worker to sensitive individuals in the general population.

Per Rule 232(2)(a), since the screening level is based on an OEL with a TWA exposure, an **8 hour averaging** time applies to this ITSL.

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