**MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY**

**INTEROFFICE COMMUNICATION**

July 15, 2015

To: File for Hexavalent Chromium (CAS No. 18540-29-9)

From: Michael Depa, Air Quality Division, Toxics Unit

Subject: Screening Level Updates

The Initial Threshold Screening Level (ITSL) for hexavalent chromium mist[1] is 0.008 µg/m³ with annual averaging time.

The ITSL for hexavalent chromium particulate matter[2] is 0.1 µg/m³ with annual averaging time.

The Initial Risk Screening Level (IRSL) for hexavalent chromium mist and particulate matter is 8.3 x $10^{-5}$ µg/m³ with annual averaging time.

The Secondary Risk Screening Level (SRSL) for hexavalent chromium mist and particulate matter is 8.3 x $10^{-4}$ µg/m³ with annual averaging time.

All screening levels are based on U.S. Environmental Protection Agency (EPA, 2015) Integrated Risk Information System (IRIS) values for chromium (VI)(i.e., hexavalent chromium)

## 1) Details on Derivation of Screening Levels

### a) Non-cancer Screening Levels

The EPA (1988) established 2 Inhalation Reference Concentrations (RfCs) for chromium (VI); one for the acid mists and dissolved aerosols and the second for particulates.

The RfC for Cr(VI) mists and dissolved aerosols is based on nasal septum atrophy observed in an occupational study reported by Lindberg and Hedenstierna (1983), where the workers were exposed to Cr(VI) acid mists and dissolved aerosols. The lowest-observed-adverse-effect level (LOAEL) from this study was identified as being 2 µg/$m^3$. The LOAEL(adj) was found to be 0.714 µg/$m^3$. The uncertainty factor (UF) applied to obtain the RfC was 90. The resulting RfC is 0.008 µg/$m^3$. See details in Table 1 below.

Pursuant to Rule 232(1)(a), the ITSL equals the RfC. If an ITSL is derived according to Rule 232, then the averaging time for an RfC derived ITSL is 24-hrs, see Rule 232(1)(a).

[1] Chromic acid mists and dissolved Cr (VI) aerosols
[2] Cr(VI) particulates

However, if an ITSL is derived pursuant to Rule 229(2)(b), the averaging time associated with the ITSL can be what is most appropriate toxicologically. Because EPA used uncertainty factors to account for chronic exposure, it was determined that the RfC specifically protects for long-term effects; therefore, an annual averaging time will be used for the Chromium VI ITSLs.

The following is an excerpt from EPA (1998):

**Table 1. Chromic Acid Mists and Dissolved Cr (VI) Aerosols (EPA, 1988)**

| Critical Effect | Experimental Doses* | UF | MF | RfC |
|---|---|---|---|---|
| Nasal septum atrophy<br><br>Human subchronic occupational study<br>Lindberg and Hedenstierna, 1983 | NOAEL: none<br><br>LOAEL: 2E-3 mg/m$^3$<br>7.14 E-4 mg/m$^3$ (adj.) | 90 | 1 | 8E-6 mg/m$^3$ |

*Conversion Factors and Assumptions — Breathing rate for 8-hour occupational exposure = 10 m$^3$; breathing rate for 24-hour continuous exposure = 20 m$^3$; occupational exposure = 5 days/week; continuous exposure = 7 days/week. RDDR (regional deposited dose ratio for particulates to account for differences between rats and humans) = 2.16

Respiratory symptoms, lung function, and changes in nasal septum were studied in 104 workers (85 males, 19 females) exposed in chrome plating plants. Workers were interviewed using a standard questionnaire for the assessment of nose, throat, and chest symptoms. Nasal inspections and pulmonary function testing were performed as part of the study.

The median exposure time for the entire group of exposed subjects (104) in the study was 4.5 years (0.1-36 years). A total of 43 subjects exposed almost exclusively to chromic acid experienced a mean exposure time of 2.5 years (0.2-23.6 years). The subjects exposed almost exclusively to chromic acid were divided into a low-exposure group (8-hr TWA below 0.002 mg/m$^3$, N=19) and a high-exposure group (8-hr TWA above 0.002 mg/m$^3$, N=24). Exposure measurements using personal air samplers were performed for 84 subjects in the study on 13 different days. Exposure for the remaining 20 workers was assumed to be similar to that measured for workers in the same area. Nineteen office employees were used as controls for nose and throat symptoms. A group of 119 auto mechanics whose lung function had been evaluated by similar techniques was selected as controls for lung function measurements. Smoking habits of workers were evaluated as part of the study.

At mean exposures below 0.002 mg/m$^3$, 4/19 workers from the low-exposure group of subjective nasal symptoms. Atrophied nasal mucosa were reported in 4/19 subjects from this group and 11/19 had smeary and crusty septal mucosa, which was statistically higher than controls. No one exposed to levels below 0.001 mg/m$^3$ complained of subjective symptoms. At mean concentrations of 0.002 mg/m$^3$ or above, approximately one-third of the subjects had reddened, smeary, or crusty nasal mucosa. Atrophy was seen in 8/24 workers, which was significantly different from controls. Eight subjects had ulcerations in the nasal mucosa and five had perforations of the nasal septum. Atrophied nasal mucosa was not observed in any of the 19 controls, but smeary and crusty septal mucosa occurred in 5/19 controls.

The authors concluded that 8-hour mean exposures to chromic acid above 0.002 mg/m$^3$ may cause a transient decrease in lung function, and that short-term exposures to greater than 0.02 mg/m$^3$ may cause septal ulceration and perforation. Based on the results of this study, a LOAEL of 0.002 mg/m$^3$ can be identified for incidence of nasal septum atrophy following exposure to chromic acid mists in chromeplating facilities. At TWA exposures greater than 0.002 mg/m$^3$, nasal septum ulceration and perforations occurred in addition to the atrophy reported at lower concentrations. The LOAEL is based on an 8-hour TWA occupational exposure. The LOAEL is adjusted to account for continuous exposure according to the following equation:

LOAELc = 0.002 $mg/m^3$ x (MVho/MVh) x 5 days/7 days

where:

LOAELc is the LOAEL for continuous exposure
MVho is the breathing volume for an 8 hour occupational exposure (10 $m^3$)
MVh is the breathing volume for a 24 hour continuous exposure (20 $m^3$)

The LOAEL of 0.002 $mg/m^3$ based on a TWA exposure to chromic acid is converted to a LOAEL for continuous exposure of 7.14 E-4 $mg/m^3$. An uncertainty factor of 3 is applied to the LOAEL to extrapolate from a subchronic to a chronic exposure, an uncertainty factor of 3 is applied to account for extrapolation from a LOAEL to a NOAEL, and an uncertainty factor of 10 is applied to the LOAEL to account for inter-human variation. The total uncertainty factor applied to the LOAEL is 90. Application of the uncertainty factor of 90 to the LOAEL of 7.14E-4 $mg/m^3$ generates an RfC of 8 E-6 $mg/m^3$ for upper respiratory effects caused by chromic acid mists and dissolved hexavalent chromium aerosols.

The EPA also established an RfC for particulate Cr(VI) based on a rat subchronic study reported by Malsch et al 1994. The rats had changes in bronchio-alveolar lavage fluid lactate dehydrogenase, BMD of 16 $\mu g/m^3$. The BMD(adj) was 34 $\mu g/m^3$. An UF of 300 was applied by EPA to obtain the RfC of 0.1 $\mu g/m^3$. The AQD ITSL is being established for Cr(VI) particulates based on the EPA RfC of 0.1 $\mu g/m^3$, using with annual averaging. Details of the RfC derivation are shown below in Table 2, and the following excerpts from EPA (1998):

**Table 2. Cr(VI) Particulates**

| Critical Effect | Experimental Doses* | UF | MF | RfC |
|---|---|---|---|---|
| Lactate dehydrogenase in bronchioalveolar lavage fluid<br><br>Rat subchronic study<br><br>Glaser et al., 1990<br>Malsch et al., 1994 | BMC: 0.016 $mg/m^3$<br>0.034 $mg/m^3$ (adj.) | 300 | 1 | 1E-4 $mg/m^3$ |

$$RfC = BMC/(UF_A \times UF_F \times UF_H) \times RDDR$$

Where,

- **BMC** is the benchmark concentration (lower 95% confidence limit on the dose corresponding to a 10% relative change in the endpoint compared to the control)
- **RDDR** is the regional deposited dose ratio to account for pharmacokinetic differences between species
- $\mathbf{UF_A}$ is a threefold uncertainty factor to account for pharmacodynamic differences not addressed by the RDDR
- $\mathbf{UF_F}$ is a threefold uncertainty factor to account for extrapolating from subchronic to chronic exposures; and
- $\mathbf{UF_H}$ is a 10-fold uncertainty factor to account for the variation in sensitivity among members of the human population

The RDDR factor is incorporated to account for differences in the deposition pattern of inhaled hexavalent chromium dusts in the respiratory tract of humans and the Wistar rat test animals. The RDDR of 2.1576 was determined based on the mass median aerodynamic diameter (0.28 µm for dose levels of 0.05-0.1 mg/m3 and 0.39 for dose levels of 0.1-0.4 mg/m3) and the geometric standard deviation (1.63 for dose levels of 0.05-0.1 mg/m3 and 1.72 for dose levels of 0.1-0.4 mg/m3) of the particulates reported in Glaser et al. (1990). A 3.16-fold uncertainty factor (midpoint between 1 and 10 on a log scale) was incorporated to account for the pharmacodynamic differences not accounted for by the RDDR. An additional 3.16-fold uncertainty factor was incorporated to account for the less-than-lifetime exposure in Glaser et al. (1990), and a 10-fold uncertainty factor was applied to account for variation in the human population. A total uncertainty factor of 100 was applied to the BMC in addition to the RDDR.

### b) Screening Level for Carcinogenic Potential of Chromium VI

The EPA performed a quantitative estimate of carcinogenic risk from occupational inhalation exposure. Using a linearized multistage model the EPA derived a unit risk for chromium VI of $1.2 \times 10^{-2}$ per (µg/m$^3$). The unit risk for Cr(VI) is for both "acid mists and dissolved aerosols" and particulates. The details of the occupational study are shown below:

**(Excerpts from EPA, 1998):**

Tumor type -- lung cancer
Test subjects — human
Route — inhalation, occupational exposure
Source -- Mancuso, 1975

Table 3. Dose-Response Data from Mancuso, 1975

| Subject age (years) | Exposure Level midrange (µg/m$^3$) | Deaths From Lung Cancer | Person-Years |
|---|---|---|---|
| 50 | 5.66 | 3 | 1,345 |
| | 25.27 | 6 | 931 |
| | 46.83 | 6 | 299 |
| 60 | 4.68 | 4 | 1,063 |
| | 20.79 | 5 | 712 |
| | 39.08 | 5 | 211 |
| 70 | 4.41 | 2 | 401 |
| | 21.29 | 4 | 345 |

(EPA, 1998)

Based on this unit risk value, the concentration of chromium VI in the air that would result in an increased risk of cancer of one in a million ($1 \times 10^{-6}$) and one in 100,000 ($1 \times 10^{-5}$) are calculated below:

| Initial Threshold Screening Level (IRSL) | Secondary Threshold Screening Level (SRSL) |
|---|---|
| IRSL = $(1 \times 10^{-6})$/unit risk | SRSL = $(1 \times 10^{-5})$/unit risk |
| IRSL = $(1 \times 10^{-6})/[1.2 \times 10^{-2}\ \mu g/m^3)^{-1}]$ | SRSL = $(1 \times 10^{-5})/[1.2 \times 10^{-2}\ \mu g/m^3)^{-1}]$ |
| IRSL = 0.000083 µg/m$^3$ | SRSL = 0.00083 µg/m$^3$ |

The averaging times for the IRSL and SRSL are annual.

**References**

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