MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Antimony (CAS# 7440-36-0)

FROM: Keisha Williams, Air Quality Division, Toxics Unit

DATE: December 1, 2016

SUBJECT: Update of Screening Level

The initial threshold screening level (ITSL) for antimony is 0.2 µg/m^3 (annual averaging time) based on the Michigan Department of Environmental Quality (MDEQ), Air Quality Division (AQD) Rule 336.1229 (2) (b) and 336.1232 (1) (a). The ITSL was originally established with an averaging time set at 24 hours. It is being changed at this time to annual, as allowed per Rule 229 (2), because the original derivation accounted for chronic exposure. Attached is the April 27, 1998 memo describing the derivation of the ITSL value.

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

April 27, 1998

TO: File for Antimony [Sb] (CAS# 7440-36-0)

FROM: Dan O'Brien, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level (ITSL) for antimony

The ITSL for antimony is 0.2 μg/m^3 based on a 24 hour averaging time.

The following 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 (1967 - June 11, 1996), CESARS, Handbook of Environmental Data on Organic Chemicals, Patty's Industrial Hygiene and Toxicology, Merck Index and Condensed Chemical Dictionary.

A summary of the toxicological literature for Sb has been prepared by other AQD staff and documented in the AQD Interim Chemical Evaluation form dated January 6, 1997. In the interest of brevity, that information will not be repeated here, and the interested reader is referred to that document (in the chemical file for Sb), and to other summary references concerning the toxicity of Sb (EPA, 1987; IARC, 1989; ATSDR, 1992; Beliles, 1994) for a complete discussion of the literature. Only points immediately relevant to the final derivation of the screening level will be addressed here.

It should be noted at the outset that some compounds of Sb (specifically Sb trioxide [Sb_2O_3] (CAS # 1309-64-4) and Sb trisulfide [Sb_2S_3] (CAS #1345-04-6)) have been found to be carcinogenic in a small number of laboratory animal studies (Wong et al., 1979; Watt, 1983; Groth et al., 1986)[1]. Other studies (Kanisawa and Schroeder, 1969; Schroeder et al., 1970; Newton et al., 1994) have not found this positive association. As a group, the studies vary widely with respect to quality, study design and route of exposure. The two studies that have produced positive evidence of carcinogenicity have both been inhalation studies, while the negative studies have been by both the oral and inhalation routes of exposure. Sb compounds have been shown to be carcinogenic in only one species (rats). The carcinogenic potential of Sb compounds may be related to the deposition and clearance of Sb from the

[1] It should be noted, when assessing the weight of evidence for carcinogenicity, that Wong et al., 1979 and Groth et al., 1986, though separate publications, report results of studies on the same group of animals. Thus, they jointly represent one positive study rather than two.

respiratory tract; this, in turn, may depend on particle size. ATSDR (1992) speculates at length that smaller Sb particles are deposited deeper in the lung and, being relatively insoluble, are cleared more slowly. Thus, smaller particles may be in contact with pulmonary tissue for longer periods of time, leading to reactive processes typical of pneumoconiosis. So, uncertainties relevant to other substances which induce pneumoconiosis and lung cancer may also be relevant to Sb compounds. It must also be noted that supporting evidence for the positive rat studies from human occupational epidemiological experience is minimal and confounded. The complete body of work has been discussed in detail elsewhere (IARC, 1989; ACGIH, 1991; ATSDR, 1992; Beliles, 1994), and will not be reviewed again here. The International Agency for Research on Cancer (IARC) has concluded that while there is sufficient evidence for the carcinogenicity of Sb_20_3 in experimental animals, there is only limited evidence for the carcinogenicity of Sb_2S_3 in experimental animals, and that there is inadequate evidence for the carcinogenicity of both Sb_20_3 and Sb_2S_3 in humans.

The Inhalation Reference Concentration (RfC) is given first preference as data on which to base an ITSL. This concentration can be used without modification when it has been derived previously by EPA. While no RfC has been developed for metallic Sb (IRIS, 1992), an RfC has been developed for antimony trioxide (IRIS, 1995); it is 0.2 µg/m^3. Beliles has noted that “The toxicity of different Sb compounds varies. The metal is inert. ..“ and that “Sb_20_3 results from the roasting of antimony sulfide ores (and) from the air oxidation of molten Sb metal...” In its Health Effects Assessment for Antimony and Compounds, EPA (1987) has stated that

> Since metallic antimony is oxidized to antimony trioxide during processing, there would be no significant differences in the consequences of exposure to the two substances...

When adequate data for RfC calculation are not available, next preference is given to oral data for calculation of a Reference Dose (RfD) if available data do not indicate that extrapolation from the oral to the inhalation route of exposure is inappropriate. While EPA has published an RfD for Sb (IRIS, 1992), much evidence exists (ACGIH, 1991; ATSDR, 1992; Beliles, 1994) to show that many of the most sensitive and serious effects of inhalation exposure to various antimony compounds occur in the respiratory tract. Moreover, upper respiratory irritation is a prominent clinical sign in workers exposed to antimony compounds. While we did not find description of upper respiratory effects in humans exposed specifically to Sb metal dust or fume, the prominence of such effects in those exposed to other Sb compounds suggests their absence in workers exposed to the metal would probably be unlikely. Thus, the existence of portal of entry effects may make an oral to inhalation extrapolation unwise for Sb, making the RfD inappropriate for use as the basis of the screening level.

Occupational Exposure Limits (OELs) [both the American Conference of Governmental Industrial Hygienists Threshold Limit Value (ACGIH-TLV) and the National Institute for Occupational Safety and Health’s Recommended Exposure Level (NIOSH REL)] are available for Sb and compounds. OELs are specified in Rule 232(1) (c) as being the next most appropriate basis for derivation of the ITSL if an RfC or RfD (or long-term data to derive them) are not available or are not appropriate. The TLV is actually based not on data for the toxicity of Sb per se, but rather on the TLV for hydrochloric acid [HCl] (CAS# 7647-01-O). The link with Sb comes from consideration of the effects of the chlorides of Sb, antimony trichloride [$SbCl_3$] (CAS# 10025-91-9) and antimony pentachloride [$SbCl_5$] (CAS #7647-18-9) . ACGIH (1991), citing Taylor (1966), describes slightly delayed abdominal pain and anorexia (over and above the irritant effects due to HCl) in workers exposed acutely to $SbCl_3$ in an occupational setting. They report similar but more intense effects from $SbCl_5$ exposure. In the absence of better data upon which to base the TLV, ACGIH appears to have determined that approximately 39% of the molar weight of $SbCl_5$ was due to Sb, and the rest (61%) due to Cl. Since the previously determined TLV for HCl was 7.5 mg/m^3, they simply scaled that TLV up to cover the remaining 39% of the molar weight of $SbCl_5$, making the TLV for $SbCl_5$ = 12.3 mg/m^3. Subtracting from that concentration the portion due to Cl (7.5 mg/m^3) left a TLV of ≈5 mg/m^3 for the Sb component. "Because the reported effects appear to be greater than those of hydrochloric acid alone...," ACGIH appears to have then divided 5 mg/m^3 by a ten-fold uncertainty factor to obtain the final Sb TLV of 0.5 mg/m^3 on a time-weighted average. One cannot help but commend ACGIH's resourcefulness in deriving a TLV for Sb and compounds in the absence of specific Sb toxicity data.

Nonetheless, given the previously mentioned fact that processing would likely oxidize metallic Sb to Sb_20_3 prior to human exposure via ambient air, the RfC for Sb_20_3 arguably provides a more scientifically-valid basis for the derivation of a screening level for Sb than does the TLV for Sb and compounds, which is based on HCl. Consequently, that RfC will be used as the basis of the ITSL.

Derivation of the ITSL: Applying Rule 232(1) (a) of Article II, Chapter 1, Part 55 of Act 451, the ITSL for Sb equals the inhalation RfC for Sb_2O_3. Therefore:

$$\boldsymbol{ITSL} = RfC = 0.002\frac{mg}{m^3}\ x\,\frac{1000\ \mu g}{1\ mg} = \mathbf{0.2}\,\frac{\boldsymbol{\mu g}}{\boldsymbol{m^3}}$$

and per Rule 232(2) (b), a **24 hour averaging** time applies.

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DO: SLB
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