MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

April 27, 1998

TO: File for Stibine [SbH_3] (CAS #7803-52-3)

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

SUBJECT: Initial Threshold Screening Level (ITSL) for stibine

The ITSL for stibine is 5 µg/m^3 based on an 8 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 - September, 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 SbH_3 has been prepared by other AQD staff and documented in the AQD Interim Chemical Evaluation form. 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 SbH_3), 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 respiratory tract; this, in turn, may depend on particle size. ATSDR (1992) speculates at length

[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.

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_2O_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_2O_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. No RfC has been developed for SbH_3. Moreover, no adequate long term human or animal inhalation toxicity data are currently available which could be used in the derivation of an RfC-based ITSL.

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 metallic antimony [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 SbH_3 and other antimony compounds. 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 for SbH_3.

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 SbH_3. 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 for SbH_3 (ACGIH, 1992) is based on the TLV for arsine [AsH_3] (7784-42-1), which it greatly resembles with respect to physiological action (ACGIH, 1991; Beliles, 1994). Both gases cause severe hemolysis in exposed humans, with acute renal failure as a sequela. ACGIH considers SbH_3 to be less bioavailable, and so less toxic than, AsH_3. Thus it has set the TLV for SbH_3 at twice the TLV for AsH_3, 0.1 ppm (0.51 mg/m^3). This opinion is at variance with that of at least one older reference located in our searches (Webster, 1946), which considered the two compounds to be "of the same order of toxicity".

However, recent opinion (Beliles, 1994) appears to concur with ACGIH's assessment. Beliles notes that SbH_3 is less readily formed and less stable than AsH_3, perhaps accounting for its apparently lower toxicity, although he also speculates that this instability may cause some cases of SbH_3 toxicity to go unrecognized.

Since the available toxicity data for SbH_3 are inadequate for derivation of an RfC-based ITSL, and the use of oral data to derive an RfD-based ITSL would be inappropriate, the ACGIH TLV is used here to derive the screening level. Given the fact that only acute animal inhalation data exist, the TLV remains the most defensible basis for the ITSL, despite the fact that the TLV is perhaps less desirable because it is based on the toxicity of arsine (rather than that of stibine itself).

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

$$\textbf{ITSL} = \text{OEL} \times \frac{1}{100} = 0.51\ \text{mg/m}^3 \times \frac{1}{100} = 0.005\ \text{mg/m}^3 \times \frac{1000\ \mu\text{g}}{1\ \text{mg}} \cong \mathbf{5\ \mu g/m^3}$$

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 SbH_3; 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 time-weighted average exposure, an **8 hour averaging** time applies to this ITSL.

REFERENCES

ACGIH (1991). Arsine (7784-42-1). *In*: Documentation of Threshold Limit Values and Biological Exposure Indices, American Conference of Governmental Industrial Hygienists, Cincinnati, pp. 87-88.

ACGIH (1992). Stibine (7803-52-3). *In*: Documentation of Threshold Limit Values and Biological Exposure Indices, American Conference of Governmental Industrial Hygienists, Cincinnati, pp. 1426-1427.

ATSDR (1992). Toxicological Profile for Antimony. Prepared by Syracuse Research Corporation under subcontract to Clement

International Corporation, for the Agency for Toxic Substances and Disease Registry, Public Health Service, U.S. Department of Health and Human Services. Doc. # TP-91/02.

Beliles, R.P. (1994). Antimony. *In*: Patty's Industrial Hygiene and Toxicology, 4th Ed. (Clayton, G.D and Clayton F.E., Eds.), Volume II, Part C, Chapter Twenty-seven: The Metals. John Wiley and Sons, Inc., New York, pp. 1902-1912.

Groth, D.H., Stettler, L.E., Burg, J.R., Busey, W.M., Grant, G.C. and Wong, L. (1986). Carcinogenic effects of antimony trioxide and antimony ore concentrate in rats. *J Toxicol Environ Health* **18**:607-626.

IARC (1989). *Some Organic Solvents, Resin Monomers and Related Compounds, Pigments and Occupational Exposures in Paint Manufacture and Painting.* Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Vol. 47, pp. 291-305. International Agency for Research on Cancer, Lyon.

Kanisawa, M. and Schroeder, H.A. (1969). Life term studies on the effect of trace elements on spontaneous tumors in mice and rats. *Cancer Res* **29**:892-895.

Newton, P.E., Bolte, H.F., Daly, I.W., *et al.* (1994). Subchronic and chronic inhalation toxicity of antimony trioxide in the rat. *Fund Appl Toxicol* **22**:561-576.

Schroeder, H.A., Mitchener, M. and Nason, A.P. (1970). Zirconium, niobium, antimony, vanadium and lead in rats: Life term studies. *J Nutrit* **100**:59-68.

Taylor, P.J. (1966). Acute intoxication from antimony trichloride. *Br J Indus Med* **23**:318-321.

Watt, W.D. (1983). Chronic Inhalation Toxicity of Antimony Trioxide: Validation of the Threshold Limit Value. Detroit: Wayne State University, Ph.D. Dissertation.

Webster, S.H. (1946). Volatile hydrides of toxicological importance. *J Indus Hyg Toxicol* **28**(5):167-182.

Wong, L.C.K., Winston, J.M., Hagensen, J., *et al.* (1979). Study of carcinogenicity and toxicity of inhaled antimony trioxide, antimony ore concentrate and thallic oxide in rats. Prepared for National Institute for Occupational Safety and Health, Centers for Disease Control, U.S. Department of Health and Human Services. Cincinnati, OH: U.S. Department of Health and Human Services.

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