

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

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INTEROFFICE COMMUNICATION

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April 27, 1998

TO: File for Antimony Trichloride [SbCl<sub>3</sub>] (CAS # 10025-91-9)

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

SUBJECT: Initial Threshold Screening Level (ITSL) for antimony trichloride

**The ITSL for antimony trichloride is 5 µg/m<sup>3</sup> 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 - August, 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 SbCl<sub>3</sub> 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 SbCl<sub>3</sub>), 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<sub>2</sub>O<sub>3</sub>] (CAS #1309-64-4) and Sb trisulfide [Sb<sub>2</sub>S<sub>3</sub>] (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)<sup>1</sup>. 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 that smaller Sb particles are deposited

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<sup>1</sup> 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.

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  $\text{Sb}_2\text{O}_3$  in experimental animals, there is only limited evidence for the carcinogenicity of  $\text{Sb}_2\text{S}_3$  in experimental animals, and that there is inadequate evidence for the carcinogenicity of both  $\text{Sb}_2\text{O}_3$  and  $\text{Sb}_2\text{S}_3$  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  $\text{SbCl}_3$ . Moreover, no adequate long term human or animal inhalation toxicity data were located 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 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.

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 antimony 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 # 7647-01-0). The link with Sb comes from consideration of the effects of the chlorides of Sb,  $\text{SbCl}_3$  and antimony pentachloride [ $\text{SbCl}_5$ ] (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  $\text{SbCl}_3$  in an occupational setting. They report similar but more intense effects from  $\text{SbCl}_5$  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  $\text{SbCl}_5$  was due to Sb, and the rest (61%) due to Cl. Since the previously determined TLV for HCl was  $7.5 \text{ mg/m}^3$ , they simply scaled that TLV up to cover the remaining 39% of the molar weight of  $\text{SbCl}_5$ , making the TLV for  $\text{SbCl}_5 = 12.3 \text{ mg/m}^3$ . Subtracting from that concentration the portion due to Cl ( $7.5 \text{ mg/m}^3$ ) left a TLV of  $\sim 5 \text{ mg/m}^3$  for the Sb component. "Because the reported effects appear to be greater than those of hydrochloric acid alone..." ACGIH appears to have

then divided  $5 \text{ mg/m}^3$  by a ten-fold uncertainty factor to obtain the final Sb TLV of  $0.5 \text{ mg/m}^3$  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.

Since the available toxicity data for  $\text{SbCl}_3$  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. While the method used to calculate the TLV is perhaps unconventional, the TLV is nonetheless based on the observation of health effects in humans specifically as a result of  $\text{SbCl}_3$  exposure. Moreover, it is essentially the only usable inhalation-based toxicity data available.

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

$$ITSL = OEL \times \frac{1}{100} = 0.5 \frac{\text{mg}}{\text{m}^3} \times \frac{1}{100} = 0.005 \frac{\text{mg}}{\text{m}^3} \times \frac{1000 \mu\text{g}}{1 \text{ mg}} = 5 \frac{\mu\text{g}}{\text{m}^3}$$

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  $\text{SbCl}_3$  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 tenfold 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.

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