Summary of currently available scientific data on antimony trioxide

Background: risk assessment on antimony trioxide

A Risk Assessment on Diantimony Trioxide was carried out in accordance with Council Regulation (EEC) 793/93 on the evaluation and control of the risks of 'existing' substances. The report of this risk assessment was finalised at the end of May 2008 after thorough discussions in the Competent Group of Member State experts with the aim of reaching consensus. Industry closely collaborated with the Swedish Rapporteur, KemI throughout the process.

The major use of antimony trioxide (ATO) is as a flame retardant. However, it does not itself have flame retarding properties; instead, it is a synergist for halogenated flame retardants in plastics, paints, adhesives, sealants, rubber, and textile back-coatings. Other uses of antimony trioxide include: as a polymerisation catalyst in PET resin manufacture and as a clarifying aid in certain glasses, and in pigments. In most final products, antimony trioxide is encapsulated in a matrix, in which it is either physically bound, such as in flame retarded rubbers, plastics and textile back-coatings, or chemically bound in a transformed state such as in PET, glass and pigments. Only by way of wear processes (dry abrasion) is any release as antimony trioxide feasible. In contrast, release processes such as leaching from moist/wet surfaces or into vessels will yield antimony that has been transformed into tri- and pentavalent hydroxo complexed form.

According to the Human Health Risk Assessment Report on Diantimony Trioxide (d.d. 31 May 2008), the risk characterisation for

(I) **workers** results in concerns only for (a) pulmonary toxicity, which requires risk reduction measures, and (b) skin irritation, which indicates the need for classification.

(II) **consumers** results in no concern and conclusion (ii)[1] is reached for all endpoints.

(III) **humans exposed via the environment** results in no concern and conclusion (ii)[1] is reached for all endpoints.

---

[1] There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Combined Exposure: Due to the use of antimony trioxide in the society and the diffuse emissions from products, humans may be exposed from different sources. The total exposure (body burden) is the summary of all the specific exposures. The Swedish Rapporteur states in the Risk Assessment Report that: "The most important sources of human exposure to diantimony trioxide are probably identified. Additions of individual scenarios are not considered to change any of the conclusions, and no calculation on combined exposure has therefore been performed."

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

2

Content

1. Physico-chemical properties

Antimony trioxide is a solid substance at room temperature (melting point is 655°C) and is also most often handled as a solid powder, dry or in wetted form, pellets, or granules. The vapour pressure of solid antimony trioxide is low (1 mm Hg at 574 °C) and it is very slightly soluble in most solvents. The content of antimony in antimony trioxide is 83.5% (w/w).

CAS No: 1309-64-4
EINECS No: 215-175-0
IUPAC Name: Diantimony trioxide
Molecular formula: Sb_2O_3
Molecular weight: 291.52

2. Classification and labelling

Antimony trioxide is classified as a dangerous substance within the meaning of the Dangerous Substance Directive 67/548/EEC and is listed in Annex 1 of this directive, being assigned the following risk and safety phrases:

Xn   Harmful
R40   Limited evidence of a carcinogenic effect
S36/37   Wear suitable protective clothing and gloves
S2   Keep out of reach of children
S22   Do not breathe dust

Due to the review of human health and environmental effects and new scientific knowledge, the abovementioned classification has been revised, adding the following 'new' classification:

R38   Irritating to skin
Xi   Irritant

Explanation why there is no classification for the environment

It is proposed by the TC C&L (agreed by the Rapporteur Member State) not to classify antimony trioxide as dangerous for the environment. This proposal follows the classification strategies for metal compounds (paragraph 9.7.5.3. GHS, 2003 and ECBI/61/95 Add.51 Rev.4).

1. Lowest effect values for aquatic species

The effect assessment reports a 72-h LC_{50} of 1.77 mg Sb/l for the invertebrates *Chlorohydra viridissima* and *Hydra oligactis* as the lowest valid value for acute toxicity. Although these species are no standard test species, this value has been used as the acute reference value for environmental classification of antimony trioxide.

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

4

2. Use of the 'escape clause' and proposal not to classify ATO

In case of an R52-53 classification an escape clause (leading to the removal of the classification) may be used if the dissolved metal ion concentration at the low loading rate after a total period of 28 days is less than or equal to the long-term NOEC (no observed effect concentration).

A 28-day test (LISEC, 2002) was performed at pH 8 (the initial pH at 0 hours was 8.06 decreasing to 7.91 after 28 days) with a loading of 1 mg ATO/l. After 28 days 0.118 mg Sb/l was measured in the solution. This value should be compared with the NOEC value that has lead to classification, i.e. the NOEC for the hydras. This is however very difficult as no such information is neither available nor any standard test may be employed to generate it.

For this particular case the European Technical Committee for Classification and Labelling (TC C&L) agreed to look at the acute to chronic ratios (ACRs) for available data among the three trophic levels. The ACRs for fish are approximately equal to 6, for *Daphnia* approximately equal to 7 and for *Lemna* above 2. Theoretically, the escape clause would not be applicable to antimony trioxide if the ACR for the hydras would be around or higher than 16. This is however most unlikely. Therefore, the TC C&L agreed not to classify antimony trioxide as dangerous for the environment.

3. Human health

f. Toxicokinetics

Antimony has been detected in blood and urine of workers exposed to antimony trioxide via inhalation, indicating that trivalent antimony can be absorbed from the lungs and excreted via urine (Lüdersdorf *et al.*, 1987).

Dermal: The absorption of antimony trioxide through human skin has been measured in an in vitro percutaneous study. Based on these results a dermal absorption value of 0.24% has been proposed (Roper and Stupart, 2006). Consequently, dermal absorption of antimony trioxide can be considered negligible.

Inhalation: Based on particle size, the deposition of inhaled antimony trioxide in the airways was calculated using the MPPD (Multiple Path Particle Deposition) model. For antimony trioxide deposited in the alveolar region, 100% absorption was assumed even though histopathological investigation reveals alveolar accumulation of inhaled antimony trioxide. This conservative absorption value is chosen in the absence of relevant scientific data regarding alveolar antimony absorption. Antimony trioxide deposited in the upper airways is assumed to be transported via mucociliary transport to the gastrointestinal tract where absorption occurs. Therefore, the Swedish Rapporteur estimated the total absorption via inhalation to be 6.82% (6.0% deposited in the alveolar region + (81.6% deposited in the upper airways corrected by 1% oral absorption)).

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

5

Biomonitoring and autopsy data indicate that antimony is retained in the lungs for long periods of time (the biological elimination half times have been estimated to be 600-1100 days for non-smokers and 1700-3700 days for smokers) and that antimony may accumulate in lung tissue after repeated exposure to antimony trioxide in the air (Garg *et al.*, 2003).

The retention and distribution of antimony trioxide following intratracheal instillation or inhalation exposure has been studied in hamsters (Leffler *et al.*, 1984) and rats (Newton *et al.*, 1994), respectively. The results demonstrate that the extent of deposition and subsequent clearance of antimony trioxide from the lung is primarily dependent on solubility and particle size. The elimination of antimony trioxide from the lung seems to consist of two phases, one early rapid clearance followed by a slower clearance phase. In hamsters the calculated biological half time ($t_{1/2}$) for the initial phase (0-20 h) was 40 hours and for the second phase (20-200 h) it was approximately 20-40 days. The rapid initial phase of elimination from the lungs is considered to be mediated by mucociliary transport.

Oral: After oral exposure of rats to antimony trioxide, absorption of antimony trioxide appears to be slow. The elimination of antimony from blood is also a slow process. As it binds to red blood cells, antimony undergoes significant distribution to most tissues. Highest concentrations have been found in bone marrow and thyroid, followed by spleen, lung, liver, ovaries, heart, kidney, femur and skin (De Bie and Salmon-te Rietstap, 2005). Together with the poor solubility of antimony trioxide, an oral absorption of 1% was proposed for antimony trioxide.

g. Acute toxicity

The assessment of available animal data indicates that antimony trioxide has low acute toxicity by the oral, dermal and inhalation route.

Dermal: There is one valid study on dermal exposure, which indicates no significant local reaction or any apparent sign of systemic toxicity after single application of antimony trioxide. No mortality or other clinical symptoms were reported in this study. Consequently, a $LD_{50} > 8,300$ mg/kg bw can be derived for dermal exposure of rabbits (Gross *et al.*, 1955).

Inhalation: For acute inhalation toxicity there is one animal study which has been performed according to OECD TG 403 and which shows no signs of acute toxicity or respiratory irritation in rats exposed to a single, nose-only dose of antimony trioxide. Consequently, the LC_{50} for acute inhalation is higher than 5.20 mg/l (5200 mg/m^3) (Leuschner, 2006).

Oral: The animal studies on acute oral exposure are all rather dated, do not comply with today's standards and in most of them mortality was the only parameter investigated. Still, they indicate that the oral LD_{50} is in excess of 20,000 mg/kg bw in rats (Fleming, 1938; Gross *et al.*, 1955; Myers *et al.*, 1978).

h. Irritation

Skin: The only animal study which can be used for assessment of the skin irritation potential of antimony trioxide shows that antimony trioxide is not irritating to rabbit skin. However,

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

6

several human case studies indicate that antimony trioxide may cause dermatitis on skin damp with perspiration and thus the lesions seem to be closely related to sweat ducts. The lack of dermal irritation in rabbits may be explained by the fact that rabbits lack sweat glands (Brewer and Cruise, 1994). In conclusion, antimony trioxide should be regarded as a skin irritant in humans (R38) under conditions that evoke sweating. Antimony trioxide is not considered to be a corrosive agent.

Eye: Only mild conjunctival redness was observed in 2 out of 3 rabbits in an eye irritation study performed according to the OECD guideline and GLP standards (Leuschner, 2005a). Irritation effects were also reported in another rabbit eye irritation study (Wil Research Laboratories, 1979). However, neither of the observed effects fulfil the EU criteria for classification as irritating to eyes. There are three case studies on workers, occupationally exposed to antimony trioxide, where conjunctivitis and irritation of the eyes have been described. However, there is little information concerning exposure in these studies and therefore it is unclear whether antimony trioxide was the causative agent or not. In conclusion, taking account of both animal and human data, antimony trioxide cannot be regarded as irritating to eyes.

Respiratory tract: In an acute inhalation study with antimony trioxide in rats, in which irritation of the respiratory tract was also evaluated, no signs of respiratory tract irritation were found. In five case report studies on workers occupationally exposed to antimony trioxide, effects that could indicate irritation in the respiratory tract have been described. However, there is very little information concerning exposure in these studies and it is unclear whether antimony trioxide was the causative agent. Based on the available data antimony trioxide can be concluded not to be irritating to the respiratory system.

i.   Sensitisation

The skin sensitisation potential of antimony trioxide, 99.93% pure, was investigated in female Dunkin Hartley guinea pigs according to the Magnusson and Kligman method (OECD guideline 406) and GLP. No skin reactions were observed in the test group animals after challenge, neither in animals of the vehicle control group. In conclusion, this study shows that antimony trioxide does not have skin sensitising properties (Leuschner, 2005b).

j.   Repeated dose toxicity

Inhalation: Inhalation studies indicate that antimony trioxide causes inflammatory changes in the lungs of rats (Watt, 1983; Groth *et al.*, 1986; Newton *et al.*, 1994; MPI, 2003). A NOAEC (no observed adverse effect concentration) of 0.51 mg/m^3 was derived from the study by Newton *et al.* (1994) and brought forward to risk characterisation. It is based predominantly on impaired lung clearance observed at 4.50 mg/m^3.

Dermal: No studies on repeated dermal exposure are available.

Oral: Two repeated dose oral toxicity studies exist (Sunagawa, 1981; Hext *et al.*, 1999). In the absence of histological changes or any clinical signs of antimony intoxication, other findings in these studies were regarded as adaptive and incidental to treatment with antimony

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

7

trioxide. A NOAEL (no observed adverse effect level) of 1686 mg/kg/d for repeated dose toxicity was derived from these studies. In the absence of any measured systemic toxicity, no quantitative risk characterisation has been performed for systemic repeated dose toxicity.

k. Mutagenicity

In vitro/in vivo data: Considering the available genotoxicity data, antimony trioxide does not induce gene mutations in vitro, but has been shown in some studies to induce structural chromosome aberrations in cultured mammalian cells in vitro. However, negative in vivo results on chromosome aberrations and micronuclei were obtained in two different species – mouse (Elliot *et al.*, 1998) and rat, involving 21-day repeated oral administration at 1,000 mg/kg bw/d (Whitwell, 2005; Kirkland *et al.*, 2007). An in vivo UDS (unscheduled DNA synthesis) assay in rats was also negative (Elliot *et al.*, 1998). The tests were performed according to GLP and using OECD test protocols. It can be concluded from these studies that antimony trioxide is not genotoxic in vivo after oral administration.

Human data: In humans, no induction of micronuclei or sister chromatid exchanges could be seen in lymphocytes from workers occupationally exposed to antimony trioxide. The suggested oxidative DNA damage in their lymphocytes occurred at exposures in the range of normal ambient air exposure (i.e. less than 1 $\mu g/m^3$) and the workers were also exposed to various other chemicals. In addition, no monitoring was performed on the control group. Therefore, a correlation between oxidative DNA damage and the concentration of antimony trioxide in the air cannot be established (Cavallo *et al.*, 2002).

To conclude, diantimony trioxide does not cause systemic mutagenicity in vivo after oral, dermal and inhalation administration in rats and mice. No classification has been proposed for mutagenicity.

l. Carcinogenicity

Three chronic inhalation studies in rats are available for assessment of carcinogenicity of antimony trioxide (Watt, 1983; Groth *et al.*, 1986; Newton *et al.*, 1994). Two animal studies indicated neoplastic properties of antimony trioxide, whereas one animal study showed negative results albeit at lower test concentrations. There is also one human study available (Jones, 1994). However, due to lack of exposure data, this human study is regarded inconclusive. The exposure duration in all three animal studies was 12 months and thus all studies deviate from the OECD guideline on chronic toxicity/carcinogenicity, which prescribes an exposure period of 24 months for rats.

In the first animal study (Watt, 1983), inhalation of 5.0 mg Sb_2O_3/m^3 for 12 months resulted in lung neoplasms in 44% of the animals tested (only females were exposed). In the second study (Groth *et al.*, 1986), a single 9-fold higher exposure concentration (45 mg Sb_2O_3/m^3) resulted in pulmonary neoplasms in 32% of the female rats exposed under similar conditions, but none in male rats. It is noted that the female survival rate was significantly higher than that of the male counterparts in the study by Groth *et al*. (1986). The differences in incidence

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

8

between the studies might be explained by the longer observation period (12 months vs 20 weeks) and the use of older animals (8 months vs 14 weeks) in the study by Watt (1983).

The study by Newton *et al*. (1994) showed no antimony trioxide related lung tumours, neither in males nor in females, at any exposure concentration up to 4.5 mg/m^3. This seems to be in contrast with the results from the study conducted by Watt (1983), in which lung neoplasms were observed at an exposure concentration of 5.0 mg Sb_2O_3/m^3. However, thorough comparison of both studies demonstrated that the rats exposed in the Watt study had more lung damage and appeared to have considerably more antimony trioxide deposited in the lungs than those exposed in the Newton *et al.* study. This clearly suggests that the exposure concentrations in the Watt study were much higher (5-fold) than reported.

Due to the deviations from the OECD guidelines and the critical shortcoming in all three studies, US NTP (National Toxicology Program - see http://ntp.niehs.nih.gov) has embarked on a testing programme leading to a new, full 2-year bioassay. A 14d range-finder on rats and mice was already conducted at the end of 2007, with reporting expected in 2008. It is now planned to conduct subchronic and chronic toxicity studies in both rats and mice.

Based on data from all three studies and the absence of systemic mutagenicity, it was concluded by the European Technical Committee for New and Existing Substances (TC NES) that the most likely mechanism for lung carcinogenicity was impaired lung clearance and pulmonary overload, followed by an inflammatory response, fibrosis and tumours. Consequently, antimony trioxide can be regarded as a threshold carcinogen. A NOAEC of 0.51 mg/m^3 was derived from the study by Newton *et al.* (1994) and brought forward to risk characterisation. This NOAEC is based predominantly on impaired lung clearance observed at 4.5 mg/m^3.

Antimony trioxide induces lung tumours in experimental animals and therefore it is currently classified in Annex 1 of Directive 67/548/EEC as Carc. Cat. 3: R40 (Limited evidence of a carcinogenic effect).

The following parameters were however not considered during the discussions:
- the fractional deposition in the respiratory tract is driven by the particle size distribution, so that -deposition rates under occupational settings are likely to differ from those in laboratory animal studies.
- obvious differences in the morphology between the lungs of rats and humans were not considered, so that the question whether this effect in rat lungs is of relevance to humans was not addressed.

m. Toxicity for reproduction

<u>Effects on fertility</u>: A gavage study indicated that repetitive gavage administration of antimony trioxide to rats (3 days/week) and mice (5 days/week) at a dose of 1200 mg/kg bw for 4 weeks was not toxic to testes. The concentration of antimony in testes was not stated. An oral NOAEL > 1200 mg/kg bw for testicular toxicity has been suggested (Omura *et al.*, 2002).

A 90-day oral feeding study with antimony trioxide in male and female rats reported no effects on reproductive organs at doses up to 1686 mg/kg bw in males and 1879 mg/kg bw in females. (Hext *et al.*, 1999). Together with toxicokinetic data, it was concluded that reproductive organs are not a target tissue for ATO.

Developmental toxicity: For developmental toxicity there is only one acceptable animal study available (MPI, 2003). This inhalation study, with exposure 6 hours/day throughout gestation, showed no statistically significant developmental toxicity at 2.6, 4.4 or 6.3 mg ATO/m^3. The NOAEC for developmental toxicity suggested based on this study is 6.3 mg/m^3, the highest exposure level evaluated.

Based on the abovementioned studies there is no concern for reproductive toxicity and thus no quantitative risk characterisation was therefore performed for fertility and developmental toxicity.

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

10

n. Summary of human health effect data

Toxicity endpoints	Outcome of the effects assessment
Acute toxicity	ATO has low acute toxicity Oral LD_{50} rat > 20,000 mg/kg bw Dermal LD_{50} rabbit > 8,300 mg/kg bw Inhalation LC_{50} rat > 5,200 mg/m³
Irritation	ATO is skin irritating, therefore classified as Irritating (Xi), R38 ATO is not a skin corrosive agent ATO is not irritating to eyes ATO is not irritating to the respiratory system
Sensitisation	not skin sensitising
Repeated dose toxicity	$NOAEC_{inhalation}$ = 0.51 mg/m³ $NOAEL_{oral}$ = 1,686 mg/kg/day
Mutagenicity	ATO is not genotoxic in vivo after oral administration No classification is proposed
Carcinogenicity	ATO induces lung tumours in experimental animals (female rats) at high exposure levels and is therefore classified as carcinogenic category 3 (Xn), R40
Toxicity for reproduction	No concern for reproductive toxicity and thus no quantitative risk characterisation has been performed for fertility and developmental toxicity

o. Risk characterisation for consumer exposure

There is no known direct private use of antimony trioxide as such. However, antimony trioxide is used in several products, some of which are available to consumers. Due to wear and tear of the antimony trioxide containing materials, the material will partly be abraded into small particles. These particles will become part of the in-house dust. Consequently, exposure of consumers to antimony trioxide may occur via inhalation and dermal contact.

The use of antimony trioxide in consumer end products such as electrical and electronic equipment as well as other flame retarded items (such as textiles, carpets, etc.) was explicitly addressed in the Risk Assessment Report. A wide-spread monitoring study on antimony content in house dust in the UK (a country which operates an active flame retardant policy), overall reported very low antimony levels in indoor air, resulting in the conclusion that exposure to antimony trioxide resulting from these applications is minimal.

Overall, the EU Risk Assessment Report on Diantimony Trioxide evaluated four scenarios for products which were considered to cause the highest level of consumer exposure:

Scenario No. 1 – PET-bottles: The reasonable worst case *oral* exposure is 0.035 µg/kg bw/day for an *adult* drinking from a PET bottle.

Scenario No. 2 – Fabrics: The worst case *dermal* exposure is 1.8 µg/kg bw/day for an *adult* sitting on upholstery fabric.

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

11

Scenario No. 3 – Cuddly toys: For a *child* sucking on cuddly toys the reasonable worst case *oral* exposure is 0.25 µg/kg bw/day.

Scenario No. 4 – Indoor air: The reasonable worst case exposure level in *indoor air* is $3.15 \cdot 10^{-6}$ mg/m^3.

Given the very low exposure involved, the risk characterisation for consumers resulted in **no concern**, and **conclusion (ii)** was reached for all endpoints.

4. Environment

a. General information

The toxicity of antimony is expected to be exerted through its dissolved ions. Antimony prevails as Sb(III) and Sb(V) in the environment. Both Sb(III) and Sb(V) ions hydrolyse easily: Sb(III) is present as the neutral species $Sb(OH)_3$ and Sb(V) is present as the anion $Sb(OH)_6^-$. According to thermodynamic calculations, antimony should almost exclusively be present as Sb(V) in oxic systems, and as Sb(III) in anoxic systems. Even though the dominant species in oxic waters is Sb(V), Sb(III) has been detected in concentrations much above what is predicted, and the reverse is true for Sb(V) in anoxic systems.

Because environmental conditions (e.g. pH and redox potential) control the speciation of dissolved antimony in water, sediment and soil, regardless of the antimony compound added, toxicity data for all antimony compounds were considered useful for deriving toxicity thresholds for Sb_2O_3. However, when using an antimony compound other than Sb_2O_3 as a source of antimony in toxicity testing, an increase in counter ions and protons will occur which may influence the interpretation of the observed responses. How much protons are produced, and whether this will affect the pH or not, depends on the conditions in the test system, the type of antimony compound used, and the amount of the antimony compound added. The effect of counter ions and pH, and hence the relevance of the toxicity data for Sb_2O_3 was evaluated on a case-by-case basis.

The majority of the available toxicity data are for Sb(III) compounds and only a few data for Sb(V) compounds are available. There are however at present no toxicity studies available which also include redox speciation measurements. Since the results of toxicity studies using a trivalent antimony compound are probably due to exposure to a mixture of trivalent and pentavalent antimony ions, and since there is no conclusive evidence supporting a significant difference in toxicity between the two valences, it is decided not to differentiate between relevant and reliable results originating from toxicity studies with tri- or pentavalent antimony compounds.

b. Aquatic toxicity

i. Fish

A total of 18 studies with 15 different species were found. However, most of these studies could not be used since they were not considered valid due to reasons of reliability (e.g., test concentrations above solubility of test compound, nominal concentrations only, lack of information on test protocol). Only 5 acute and 2 chronic toxicity studies were considered reliable.

The lowest valid values for acute and long-term toxicity to freshwater fish as well as the value for acute toxicity to a marine fish are given in the table below. There are no valid long-term toxicity data for marine species.

Organism	Water	Exposure period	Endpoint	LC_{50} or NOEC	Value (mg Sb/l)	Reference
Pimephales promelas	Fresh	4 d	Mortality	LC_{50}	14.4	Brooke *et al.*, 1986
Pimephales promelas	Fresh	28 d	Growth (length)	NOEC	1.13	Kimball, 1978
Pargus major	Marine	4 d	Mortality	LC_{50}	6.9	Takayanagi, 2001

ii. Aquatic invertebrates

A total of 12 studies with 8 different species were found. Several studies could not be used since they were not considered valid due to reasons of reliability. Overall, 9 reliable LC_{50} values and 2 reliable NOEC values could be retained.

The lowest valid LC_{50} for acute toxicity is 1.77 mg Sb/l (for the hydra *Chlorohydra viridissimus*). The lowest valid NOEC for chronic toxicity is 1.74 mg Sb/l (for *Daphnia magna*). The NOEC was calculated for the endpoint reproduction.

There are no valid acute toxicity data and no data on long-term toxicity of antimony to marine species.

Organism	Water	Exposure period	Endpoint	LC50 LOEC NOEC	Value (mg Sb/l)	Reference
Chlorohydra viridissimus	Fresh	4 d	Mortality	LC_{50}	1.77	TAI Environmental Sciences, 1990
Daphnia magna	Fresh	21 d	Reproduction	LOEC	3.13	Heijerick and Vangheluwe, 2003
Daphnia magna	Fresh	21 d	Reproduction	NOEC	1.74	Heijerick and Vangheluwe, 2003

iii. Algae

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

13

A total of 8 studies with 8 different species were found. Only 3 of these studies were considered reliable.

The lowest reliable effect concentration is the growth rate-based EC_3 of 2.11 mg Sb/l for the unicellular green alga *Raphidocelis subcapitata* (previously *Selenastrum capricornutum*) resulting from tests performed by Heijerick and Vangheluwe (2004).

There are no useful data available on the toxicity of antimony to marine species.

Organism	Water	Exposure period	Endpoint	EC_{50}/NOEC	Value (mg Sb/l)	Reference
Raphidocelis subcapitata	Fresh	3 d	Growth rate	EC_{50}	> 36.6	Heijerick and Vangheluwe, 2004
Raphidocelis subcapitata	Fresh	3 d	Growth rate	NOEC	2.11	Heijerick and Vangheluwe, 2004

iv. Microorganisms

There is only one study on microorganisms available that is considered relevant and reliable (EPAS, 2005). A NOEC of 2.55 mg Sb/l and an EC_{50} of 27 mg Sb/l (based on measured concentrations) were derived from this study.

v. Sediment organisms

Three reliable and relevant chronic sediment toxicity tests with different species are available. The test species all have different exposure routes, feeding habits and ecological niches: (1) the bottom-dwelling *Hyalella azteca* (crustacean) is a surface deposit and filter feeder; (2) *Chironomus riparius* (insect) burrows within the sediment with a combined surface and sub-surface feeding behaviour; and (3) *Lumbriculus variegatus* (oligochaete) is a head-down deposit feeder that feeds well below the sediment-water interface. The lowest NOEC (78 mg Sb/kg ww or 112 mg Sb/kg dw) has been derived for the midge *Chironomus riparius* and the oligochaete *Lumbriculus variegatus* (Heijerick and Vangheluwe, 2005a,b).

c. Terrestrial compartment

It was agreed at TC NES I ´07 that the preferred exposure regime for terrestrial toxicity studies is in sufficiently aged soils spiked with Sb_2O_3. Two toxicity studies, which are both considered valid and performed in the same sufficiently aged soil (31 weeks), generated toxicity data for invertebrates, plants and microorganisms.

Organism	Exposure period	Endpoint	NOEC (mg Sb/kg dw)	Reference
Hordeum vulgare	5 d	Root elongation	999	Smolders *et al.*, 2007
Folsomia	28 d	Reproduction	999	Moser, 2007

candida				
Native microorganisms	7 d	Potential nitrification rate	2930	Smolders *et al.*, 2007

i. Plants

There are four studies available on the toxicity of antimony to plants, but only the study by Smolders *et al*. (2007), which results in a bounded NOEC of 999 mg Sb/kg dw, complies with the preferred exposure regime as given above.

ii. Invertebrates

There are seven studies available on the toxicity of antimony to invertebrates, but only the study by Moser (2007), which results in a bounded NOEC of 999 mg Sb/kg dw, complies with the preferred exposure regime as given above.

iii. Microorganisms

There are four studies available on the toxicity of antimony to soil microorganisms, but only the study by Smolders *et al*. (2007), which results in a bounded NOEC of 2930 mg Sb/kg dw, complies with the preferred exposure regime as given above.

iv. Bioavailability correction

It was demonstrated that 31 weeks of ageing in the field was sufficient in order to have fully equilibrated soils at high exposure levels, but not at low exposure levels. For example, based on the known distribution coefficient for antimony in the soil used in the abovementioned studies, an antimony pore water concentration of 26 mg Sb/l is predicted at 999 mg Sb/kg dw, whereas the observed concentration was only 9.7 mg Sb/l.

Since not all Sb_2O_3 had dissolved during the ageing period, the NOECs derived from these studies were corrected for the fraction of Sb_2O_3 not yet transformed to soluble antimony. The correction was based on the measured pore water antimony concentration (9.7 mg Sb/L) at the lowest NOEC (999 mg Sb/kg dw) and the equilibrium solid:liquid distribution coefficient for antimony in the soil used in these studies (K_d = 38 l/kg, observed for Sb_2O_3 amended soil aged for five years and for soluble $SbCl_3$ added to the same soil, Oorts *et al.*, 2005). The measured pore water antimony concentration at the lowest NOEC value corresponds to a total antimony concentration in soil of 370 mg Sb/kg at complete dissolution.

d. Summary of PNECs

$PNEC_{surface\ water}$ 0.113 mg Sb/l
$PNEC_{microorganism}$ 2.55 mg/Sb/l

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

15

PNEC$_{sediment}$ 11.2 mg Sb/kg dw (7.8 mg Sb/kg ww)
PNEC$_{marine\ water}$ 11.3 µg Sb/l
PNEC$_{marine\ sediment}$ 2.24 mg Sb/kg dw (1.6 mg Sb/kg ww).
PNEC$_{soil}$ 37 mg Sb/kg dw.

e. Risk characterisation for the environment

In the EU Risk Assessment Report on Diantimony Trioxide all the main stages during which antimony may be released into the environment due to production, use and waste disposal of antimony trioxide have been considered. The regional background concentrations were based on measured reasonable worst case ambient levels in Europe.

Three possible conclusions may result from risk characterisation:

Conclusion (i)   There is a need for further information and/or testing.

Conclusion (ii)   There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (iii)   There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Water

All risk characterization ratios are below 1, indicating that the risk to surface water is low both from regional and local sources, leading to conclusion (ii) for all scenarios.

Sediment

Conclusion (iii) applies to the generic scenarios for formulation and application of flame retardant textile back-coating and to one production site.

Conclusion (ii) applies to all other scenarios, including 19 sites using antimony trioxide in textile applications and 3 production sites, all of which reported releases.

Waste water treatment plant

All risk characterisation ratios are below 1, which indicates that the risk to sewage treatment plants is low, leading to conclusion (ii) for all scenarios.

Terrestrial compartment

All risk characterisation ratios are below 1, which indicates that the risk to soil is low, leading to conclusion (ii) for all scenarios.

Atmosphere

No PNEC could be derived for atmosphere hence only a qualitative assessment could be made for this compartment. Neither biotic nor abiotic effects are considered likely due to the atmospheric release of antimony resulting from production and use of products containing antimony trioxide, nor are any effects considered likely due to releases of antimony from unintentional sources. All this indicates that the risk to atmosphere is low, leading to conclusion (ii) for all scenarios.

Secondary poisoning

A $PNEC_{oral}$ was derived based on the results from two repeated dose oral studies (with rats) which indicate that antimony trioxide may be toxic to the liver. Although no real histological changes were observed in the liver and it can be discussed whether or not the effects are relevant on a population level, it was decided to use the results from these studies for $PNEC_{oral}$ derivation. The $PNEC_{oral}$ has been calculated to be 374.8 mg Sb/kg food. All risk characterisation ratios are below 1, which indicates that the risk for secondary poisoning from the use of antimony trioxide is low, leading to conclusion (ii) for all scenarios.

Marine water

The PNEC for marine surface water was estimated to be 11.3 μg Sb/l based on the lowest available NOEC for freshwater fish (1.13 mg Sb/l) and an assessment factor of 100 according to the TGD (Technical Guidance Document). For the generic site for application of textile back-coating (for which emissions were calculated using default emission factors) the PEC/PNEC ratio is higher than 1. However, since there are no sites located by the sea, conclusion (ii) applies to <u>all</u> scenarios.

Marine sediment

An assessment factor of 50 has been used to derive a PNEC of 1.56 mg Sb/kg ww. For the generic site for formulation and application of textile back-coating (for which emissions were calculated using default emission factors) the PEC/PNEC ratio is higher than 1. However, since there are no sites located by the sea, conclusion (ii) applies to <u>all</u> scenarios.

PBT assessment

There is currently no agreed approach to perform a PBT (Persistent/Bioaccumulative/Toxic) assessment for a metal. Therefore, no PBT assessment was performed in the risk assessment.

International Antimony Association VZW – Av. De Broqueville 12 – 1150 Brussels – Belgium
Tel: +32 (0) 3 297 60 92 Fax: +32 (0) 3 297 60 92 WWW.IAOIA.ORG VAT : BE 0894.536.176

17

Summary

All scenarios lead to conclusion (ii) for the continental and regional level: no risk identified. Most scenarios lead to conclusion (ii) on a local level as well: no need for further information, testing or risk reduction. Conclusion (iii) is reached for sediment, but only for one production site and for the generic site for formulation and application as flame retardant in textile and textile back-coating. No risk for sediment is identified for the textile companies that provided emission data. Risk reduction measures will be proposed for the sites for which a PEC/PNEC ratio > 1 is obtained for sediment.