

Occupational Exposure to Antimony Trioxide: A Risk Assessment

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Corresponding Authors*SUPPLEMENTARY MATERIALS****Tables S1-S5**

S1: Incidences of tumors in male and female mice by exposure group.

S2: Calculated animal doses.

S3: Female tumor incidences following the Poly3 correction.

S4: BMDS model output for individual female tumors.

S5: European Union antimony trioxide exposure estimates for several occupational settings.

Supplementary Table 1 Incidences [‡] of alveolar/bronchiolar adenoma and carcinoma in all treatment groups among male and female rats and mice reported in the NTP study. Mice were the more sensitive species.				
	Male rats	Female rats	Male mice	Female mice
Alveolar/bronchiolar adenoma				
0 mg/m ³	3/60	0/60	10/60	1/60
3 mg/m ³	4/60	2/60	14/60	10/60
10 mg/m ³	6/60	6/60	11/60	19/60
30 mg/m ³	8/60	6/60	14/60	9/60
Alveolar/bronchiolar carcinoma				
0 mg/m ³	0/60	0/60	4/60	2/60
3 mg/m ³	0/60	0/60	18/60	14/60
10 mg/m ³	2/60	0/60	21/60	11/60
30 mg/m ³	0/60	0/60	29/60	11/60

[‡]Note on the data: The numerator represents the number of tumor-bearing animals and the denominator represents the number of animals on which a necropsy was performed. In the two-year studies, groups of 60 animals per dose group were exposed to antimony trioxide. Ten animals per group were sacrificed at week 53. Some tables reported in the NTP antimony study include only the 50 animals per dose group that were designated to be kept on study for the full 105 weeks. We chose to include the data from the animals in the interim sacrifice groups because treatment-related tumors were observed at interim sacrifice, e.g. alveolar/bronchiolar carcinoma in 2/10 male mice in the 30 mg/m³ dose group.

Supplementary Table 2 Calculated animal doses based on exposure concentrations for male and female mice.		
Sex	Concentration (mg/m ³)	Dose (mg/kg-day)
Female		
	0	0
	3	0.63
	10	2.12
	30	6.35
Male		
	0	0
	3	0.62
	10	2.06
	30	6.19

Supplementary Table 3 Incident tumors and animal sample sizes for female mice alveolar/bronchiolar adenoma/carcinoma and malignant lymphoma per dose group following Poly3 corrections.			
Tumor type	Dose group (mg/kg-day)	Incident tumors	Total animals [‡]
Alveolar/bronchiolar adenoma/carcinoma			
	0	3	47
	0.63	22	46
	2.12	27	44
	6.35	19	44
Malignant lymphoma			
	0	7	46
	0.63	17	46
	2.12	20	43
	6.35	30	48

[‡]Number of animals alive at the time of first occurrence of tumor. Animals in the interim sacrifice groups were included because tumors were observed in interim sacrifice groups.

Supplementary Table 4 Results from the individual site alveolar/bronchiolar adenoma/carcinoma and malignant lymphoma in females. Model outputs include the benchmark dose (BMD), benchmark dose lower (BMDL), and animal cancer slope factor (CSF).

Gender	Tumor type	BMD (mg/kg-day)	BMDL (mg/kg-day)	CSF (mg/kg-day) ⁻¹
Female	Alveolar/bronchiolar adenoma or carcinoma	0.098	0.073	0.68
Female	Malignant lymphoma	0.39	0.27	0.65

Supplementary Table 5 Typical and worst-case exposure estimates for common occupational exposure settings for antimony trioxide. Exposure estimates were estimated by the European Union.[26] Typical exposure concentrations were set as the 50th percentile exposure level and the worst-case exposure concentrations were set as the 90th percentile exposure level.

Industry	Typical-case exposure ($\mu\text{g}/\text{m}^3$)	Worst-case exposure ($\mu\text{g}/\text{m}^3$)
Sb₂O₃ production		
Conversion	27	150
Refining / Refuming	12	47
Product handling	40	110
Flame retardants in rubber		
Formulation	51	220
Processing	64	140
Flame retardants (plastics/textiles), handling/formulation	130	570