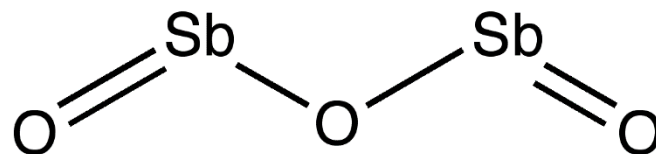


## Overall Cancer Evaluation



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## Summary of NTP's preliminary conclusions

- **A significant number of people living in the United States are or were exposed to antimony trioxide**
- **Studies in humans are inadequate for evaluating the relationship between human cancer and exposure to antimony trioxide and other antimony compounds**
- **Sufficient evidence of carcinogenicity for antimony trioxide from cancer studies in experimental animals**
  - **Multiple tissue sites in multiple species**
- **Supporting mechanistic information**
- **Biologically plausible in humans**



## Human exposure

- **A significant number of people in the United States are exposed to antimony(III) trioxide**
- **Highest levels of exposure to antimony(III) trioxide occur in the workplace**
- **The general population is exposed to antimony**
  - From some consumer products
  - From primary (i.e., pollutant is antimony(III) trioxide) and secondary (i.e., pollutant is transformed from other antimony species into antimony(III) trioxide) environmental releases



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## **Inadequate human evidence for determining carcinogenicity**

### **Limited by:**

- Number of studies with small sample sizes for stomach and lung cancers.**
- Potential confounding due to smoking and occupational co-exposures.**



# Sufficient animal evidence for antimony trioxide carcinogenicity

Increased incidences of malignant tumors and combined incidences of malignant and benign tumors at multiple tissue sites in multiple species.



## Mice had increased incidences of

### lung tumors

Benign	Alveolar/bronchiolar adenoma (F)
Malignant	Alveolar/bronchiolar carcinoma (M and F)
Combined	Alveolar/bronchiolar adenoma or carcinoma (F)

### skin tumors

Benign	Fibrous histiocytoma (M)
Combined	Fibrous histiocytoma or fibrosarcoma (M)

### lymphoma

Malignant	Lymphoma (F)
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## Rats had increased incidences of

### lung tumors

Benign	Alveolar/bronchiolar adenoma (M* & F)	NTP 2017
Combined	Alveolar/bronchiolar adenoma or carcinoma (M*)	
Benign	Bronchiolar/alveolar adenoma (F)	Groth et al. 1986
Malignant	Squamous-cell carcinoma (F)	
Malignant	Scirrhous carcinoma (F)	Watt 1983
Malignant	Scirrhous carcinoma (F)	

### adrenal gland tumors

Benign	Pheochromocytoma (M & F)	
Combined	Pheochromocytoma (F)	NTP 2017



Newton et al. 1994 reported no increase in tumors.



# Supporting mechanistic information

- Electrophilicity ●
- Affinity to vicinal thiol groups

Interact with

- Peptides (e.g., GSH)
- Proteins/ enzymes (including zinc finger)

Increase oxidative stress



Decrease DNA damage repair capacity



Cause receptor-mediated effects



e.g., Prevent cell differentiation →  
Preserve proliferation potential



Genotoxicity



- DNA damage
- Chromosomal aberrations
- Sister chromatid exchange



## Cancer Evaluation: Integration of Animal, Human, and Mechanistic Data

- Comment on the overall cancer evaluation (Section 7: Overall Cancer Evaluation and Preliminary Listing Recommendation) and whether the available mechanistic data provide support for the relevance of the cancer studies in experimental animals to human carcinogenicity.
  - Provide any scientific criticism of the NTP's overall assessment and integration of the human cancer, experimental animal, and mechanistic data.