



The Division of Medical Toxicology at Drexel University College of Medicine appreciates the opportunity to comment on the NTP's Draft Report on Carcinogens Monograph on Antimony Trioxide.

Sections 2.1.1 and 2.1.2 provide a detailed review of the common applications of antimony trioxide and its other major forms. However, there was no mention of antimony use in the synthesis of microelectronics. Antimony may be used as a dopant in the manufacturing of semiconductors and should be included (Biefield 2002, Sundar 2010).

Of note there has been a historical concern of antimony toxicity secondary to application of Kohl, as one of its preparations is made using powdered stibnite. Analysis of global samples of Kohl have demonstrated only trace amounts of antimony. Ultimately we agree with not listing Kohl as a potential use or exposure of antimony as its concentration is negligible and without clinical effects (Parry 1991).

The majority of human studies are based on historical evidence from occupational exposure and patient outcomes. Data is extracted from the National Occupational Exposure Survey (NOES) by the National Institute for Occupational Safety and Health (NIOSH) from 1981 to 1983. As per section 2.3 in this documentation, the highest exposures to antimony (III) trioxide and total antimony take place in the work setting. Common occupations listed included, but are not limited to the production of batteries, lead pipes, ammunition and flame retardant materials. Ammunition production is listed as a possible workplace exposure however workers at gun firing ranges are omitted. Antimony air concentrations may be elevated in indoor firing ranges and elevated soil concentrations in outdoor firing ranges placing exposed workers at risk (Okkenhaug 2016, Martin 2013, Dams 1988).

In Table 4-2, the authors do an excellent job of summarizing the quality of cohort and case-control epidemiological studies in smelter workers. Specific attention is drawn to the three selected cohort studies by Jones (1994), Schnorr et al. (1995) and Jones et al. (2007) which exhibit a relationship between antimony exposure and both lung and stomach cancer, but acknowledge confounding factors such as cigarette smoking and other occupational exposures.

The provided animal studies in mice, rats and hamsters provide good quality methods and reasonable evidence to display a correlation between inhalational exposure and lung parenchyma tumor growth.

Figure 4-1 highlights the risk estimates of lung cancer in workers exposed to antimony. While the RR of 3.25 shown by Jones et al (2007) may indicate antimony exposure as a potential cause, it should be noted that there is wide confidence interval (1.32-21.76).

Many of the studies used in Section 5 investigating cancer in animals due to exposure to antimony describe different types of lesions occurring in rodents based on their sex. Meanwhile, all of the human cancer studies were investigating exposure in males. The report does not highlight whether or not this would be an important consideration or source of bias.

Section 6.1.2 provides a brief listing of non-cancer health outcomes resulting from exposure to antimony. Although the draft clearly states that non-cancer health outcomes are described elsewhere, including an ATSDR systematic review, it does proceed to mention certain non-cancer health outcomes. Dermatitis and ocular irritation following occupational antimony exposures are described in the ATSDR review but omitted from this section. An important non-carcinogenic effect of antimony that worths mentioning is increased spontaneous abortion rate among pregnant workers in an antimony plant.



Prolonged exposure to antimony may cause disturbance in the reproductive system. Rats exposed to antimony prior to and during conception are reported to have decreased number of offsprings (ATSDR 2017). Although the focus of this draft is related to the carcinogenicity of antimony trioxide, we believe if non-cancer health outcomes are going to be listed then a more thorough list may be beneficial to readers. A minor point is the misspelling of "respiratory" as "resepiratory" at the end of this section (pg 83).

We thank you for preparing this comprehensive and well-written report. Utilizing evidence from protracted human epidemiological studies and animal studies, the authors dutifully summarize and conclude that antimony is a carcinogen in mice and rats, but that more research on human carcinogenicity is warranted, and such a relationship may only be reasonably speculated at this time. Again, thank you for allowing us a platform to provide our comments.

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