CHAPTER 2. HEALTH EFFECTS

2.1 INTRODUCTION

The primary purpose of this chapter is to provide public health officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective on the toxicology of antimony. It contains descriptions and evaluations of toxicological studies and epidemiological investigations and provides conclusions, where possible, on the relevance of toxicity and toxicokinetic data to public health. When available, mechanisms of action are discussed along with the health effects data; toxicokinetic mechanistic data are discussed in Section 3.1.

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile.

To help public health professionals and others address the needs of persons living or working near hazardous waste sites, the information in this section is organized by health effect. These data are discussed in terms of route of exposure (inhalation, oral, and dermal) and three exposure periods: acute (≤14 days), intermediate (15–364 days), and chronic (≥365 days).

As discussed in Appendix B, a literature search was conducted to identify relevant studies examining health effect endpoints. Figure 2-1 provides an overview of the database of studies in humans or experimental animals included in this chapter of the profile. These studies evaluate the potential health effects associated with inhalation, oral, or dermal exposure to antimony, but may not be inclusive of the entire body of literature. A systematic review of the scientific evidence of the health effects associated with exposure to antimony was also conducted; the results of this review are presented in Appendix C.

Summaries of the human observational studies are presented in Tables 2-1 and 2-2. Animal inhalation studies are presented in Table 2-3 and Figure 2-2, animal oral studies are presented in Table 2-4 and Figure 2-3, and animal dermal studies are presented in Table 2-5.

Levels of significant exposure (LSEs) for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. "Serious" effects are those that evoke failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress

or death). "Less serious" effects are those that are not expected to cause significant dysfunction or death, or those whose significance to the organism is not entirely clear. ATSDR acknowledges that a considerable amount of judgment may be required in establishing whether an endpoint should be classified as a NOAEL, "less serious" LOAEL, or "serious" LOAEL, and that in some cases, there will be insufficient data to decide whether the effect is indicative of significant dysfunction. However, the Agency has established guidelines and policies that are used to classify these endpoints. ATSDR believes that there is sufficient merit in this approach to warrant an attempt at distinguishing between "less serious" and "serious" effects. The distinction between "less serious" effects and "serious" effects is considered to be important because it helps the users of the profiles to identify levels of exposure at which major health effects start to appear. LOAELs or NOAELs should also help in determining whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health. Levels of exposure associated with cancer (Cancer Effect Levels, CELs) of antimony are indicated in Table 2-3 and Figure 2-2.

A User's Guide has been provided at the end of this profile (see Appendix D). This guide should aid in the interpretation of the tables and figures for LSEs and MRLs.

The health effects of antimony (Sb) have been evaluated in epidemiological and laboratory animal studies following inhalation, oral, or dermal exposure. As summarized in Figure 2-1, 48% of these studies involved oral exposure, 37% involved inhalation exposure, and the remaining 15% were dermal and ocular exposure studies. Most of the studies involved intermediate- or chronic-duration exposure, and body weight, respiratory tract, and cardiovascular systems were the most studied endpoints. In addition to these studies, there are numerous studies in humans and animals involving parenteral administration of antimony compounds.

Trivalent and pentavalent antimony compounds have been used for the treatment of parasitic diseases, particularly leishmaniasis and schistosomiasis, for over 100 years. Although trivalent antimony in the form of potassium or sodium antimony tartrate was first used, it was later discontinued due to the side effects. Pentavalent organic antimony compounds have been used for the last 60 years. The two predominant forms are sodium antimony gluconate (sodium stibogluconate) and meglumine antimoniate (*N*-methyl-D-glucamine or Glucantime) (Haldar et al. 2011). In the treatment of parasitic diseases, the patient receives multiple injections of the antimony compounds. Numerous investigators have reported adverse effects associated with these treatments. These studies provide useful information for identifying potential targets of antimony toxicity, although the relevance to environmental exposure is not known

given the poor absorption of antimony compounds following inhalation, oral, or dermal exposure (see Section 3.1.1). The primary targets of toxicity appear to the heart (alterations in EKG readings), gastrointestinal tract (nausea, abdominal pain, vomiting, diarrhea, anorexia), musculoskeletal system (myalgia, arthralgia), liver (increases in alanine and aspartate aminotransferases), pancreas (increases in serum amylase levels), and nervous system (headache, dizziness) (Andersen et al. 2005; Dancaster et al. 1966; Lawn et al. 2006; Neves et al. 2009; Palacios et al. 2001; Sundar et al. 1998; Thakur 1998; Zaki et al. 1964).

Health effects data for all antimony compounds are discussed together in this chapter. There is some evidence of compound-specific differences in toxicity that are likely reflective of toxicokinetic differences, particularly differences in the relative absorption of the compounds. When relevant, these differences are discussed. Concentrations and doses in the tables and text have been calculated from the investigated compound to the elemental antimony in order to facilitate comparisons between studies.

The inhalation, oral, and dermal exposure studies in humans and animals suggest several sensitive targets of antimony toxicity:

- **Respiratory Endpoints:** Antimony is presumed to cause respiratory effects following inhalation exposure based on low evidence in workers exposed to antimony oxides and a high level of evidence in several animal species exposed to antimony trioxide, antimony trisulfide, and antimony ore. The respiratory effects include irritation of epiglottis epithelium, increases in the number of alveolar/bronchiolar macrophages, decreases in lung clearance, and lung interstitial fibrosis.

- **Cardiovascular Endpoints:** Antimony is suspected to cause myocardial damage and EKG alterations based on inadequate evidence in an inhalation occupational exposure study and low evidence in inhalation and oral exposure studies in animals. This hazard identification conclusion is supported by numerous reports of cardiovascular effects in patients administered antimony compounds for the treatment of leishmaniasis and injection studies in animals.

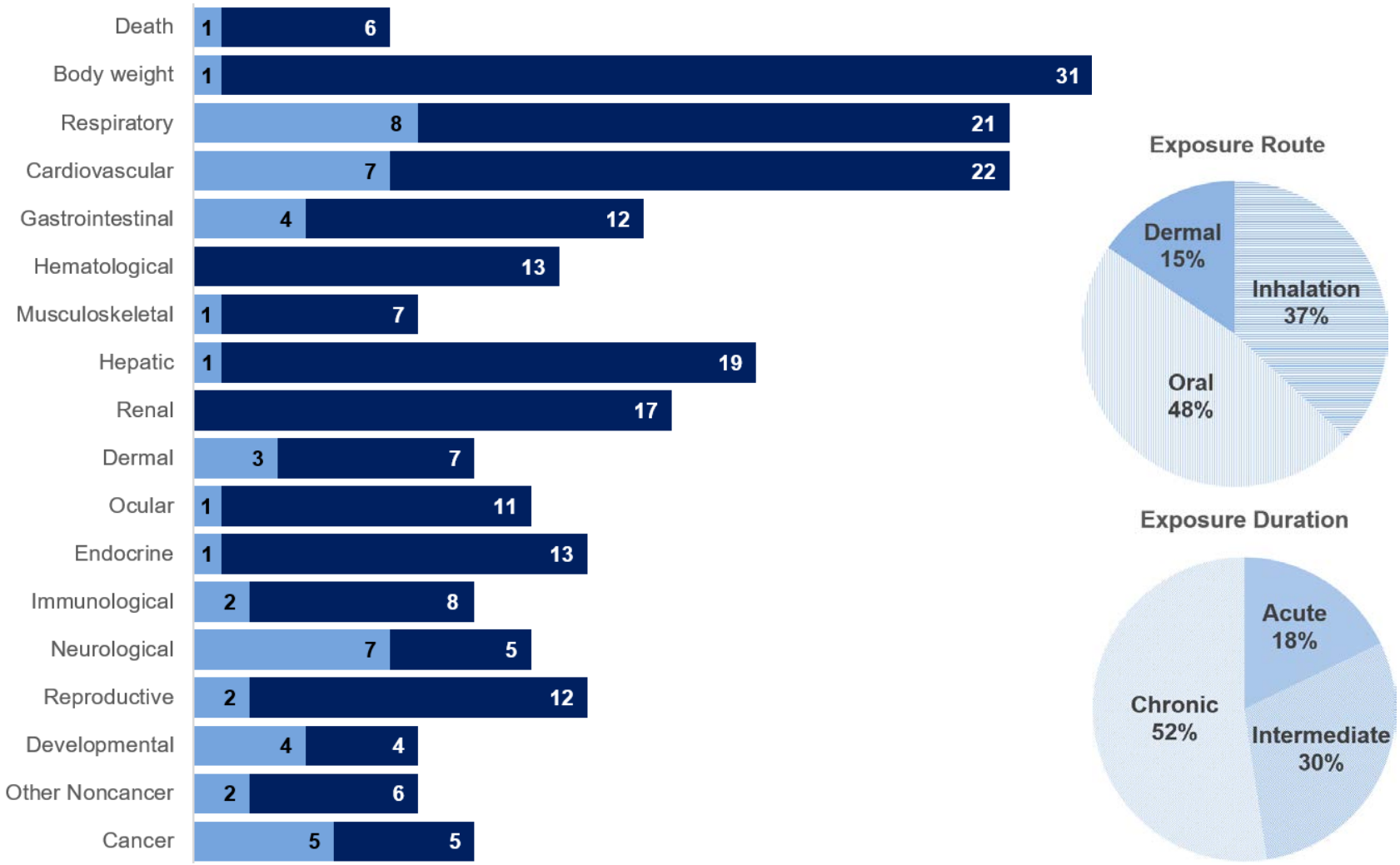
- **Gastrointestinal Endpoints:** Antimony is presumed to cause gastrointestinal tract irritation based on inadequate evidence in human studies and high evidence in animal studies. Observed gastrointestinal effects include nausea and vomiting and forestomach ulceration.

- **Serum Glucose Endpoints:** Antimony is suspected to cause decreases in serum glucose levels based on high evidence from two animal oral exposure studies, supported by an animal intramuscular exposure study; human data are lacking.

- **Developmental Endpoints:** Antimony is suspected to cause developmental effects based on inadequate evidence in humans and high evidence in a small number of animal studies. Developmental effects observed in laboratory animals included decreases in pup growth and alterations in vasomotor reactivity in pups.

Figure 2-1. Overview of the Number of Studies Examining Antimony Health Effects

Most studies examined the potential body weight, respiratory, and cardiovascular effects of antimony
Fewer studies evaluated health effects in **humans** than **animals** (counts represent studies examining endpoint)



*Includes studies discussed in Chapter 2. A total of 53 studies (including those finding no effect) have examined toxicity; most studies examined multiple endpoints.

Table 2-1. Health Effects in Humans Exposed to Antimony Dusts

Reference	Study population	Exposure	Outcomes
Belyaeva 1967	Female workers at an antimony metallurgical facility; some of the women worked in a more dusty section of the facility. A control group was also examined; however, no information was provided whether the controls were matched to the exposed group or whether they had similar jobs without antimony exposure. The number of subjects was not reported; antimony levels were measured in 308 and 115 blood samples from workers and controls, respectively.	**Exposure:** Workers were exposed to metallic antimony, antimony trioxide, and antimony pentasulfide. The antimony levels in the blood and urine were 0.5–20.2 and 0.5–18.2 mg/dL, respectively, in the workers in the dusty section of the facility and 0.5–18.2 mg/L and 0.5–16.2 mg/dL, respectively, in the less dusty section. The blood antimony level in the control group ranged from 0 to 3.3 mg/dL. **Confounding exposure:** Co-exposure to other chemicals was likely but not discussed.	**Reproductive effects:** Reproductive disturbances were reported in 77.5% of the workers and 56% of controls. Increases in the occurrence of disturbances in the menstrual cycle were found (61.2% in workers and 35.7% in controls). Increases in spontaneous abortion (12.5%) were found in the workers, as compared to controls (4.1%). **Developmental effects:** Decreases in infant body weight gain among infants born to workers were observed beginning at 6 months of age. By 12 months of age, infants of workers weighed 8.96 kg compared to 10.05 kg in the controls.
Brieger et al. 1954	112 workers involved in the production of grinding wheels. Workers were employed for 8 months to 2 years. No control group was used.	**Exposure:** Antimony trisulfide levels ranged from 0.42 to 3.9 mg Sb/m^3, with the majority of the findings >2.2 mg Sb/m^3. **Confounding exposure:** Workers were also exposed to phenol formaldehyde resin.	**Respiratory effects:** No signs of respiratory irritation were reported. **Cardiovascular effects:** Altered EKG readings (mostly T waves) were found in 37/75 workers. Increased blood pressure was observed in 14/112 workers and low blood pressure was observed in 24/112 workers; significance of these findings are not known since there was no control group. **Gastrointestinal effects:** A higher incidence of ulcers were found in the antimony exposed workers (63 per 1,000) compared to the total plant population (15 in 1,000).
Cooper et al. 1968	28 antimony process workers involved in extraction of antimony ore to antimony trioxide. Workers employed for 1–15 years. No control group was used.	**Exposure:** Antimony trioxide levels ranged from 0.081 to 138 mg Sb/m^3 at 47 locations within the facility. **Confounding exposure:** Co-exposure to other chemicals was likely but not discussed	**Respiratory effects:** No consistent alterations in lung function (only 14 subjects were examined). Pneumoconiosis was confirmed in three workers and suspected in five other workers.

Table 2-1. Health Effects in Humans Exposed to Antimony Dusts

Reference	Study population	Exposure	Outcomes
Jones 1994	Retrospective cohort mortality study of 192 workers involved in the production of antimony metal, antimony alloys, and antimony trioxide. Workers were employed for at least 3 months. Cause of death of maintenance workers and zircon plant worker, and office workers at the same facility was examined as a comparison group.	**Exposure:** No monitoring data were provided. **Confounding exposure:** Investigators noted that the workers were likely exposed to arsenic in the antimony ore. Smoking status was not included as a potential confounding variable.	**Respiratory effects:** No significant increases in deaths from respiratory effects. **Cancer:** Increase in lung cancer deaths in antimony workers and maintenance workers. Only significant in workers hired prior to 1940 and between 1946 and 1950. Workers with latency period of >20 years had the highest increase in lung cancer deaths.
Kim et al. 1999	Study of 12 workers (mean age of 35 years) exposed to antimony trioxide at a manufacturing facility for an average of 30 months. Another group of 22 workers (mean age of 33 years) at the facility not near the antimony sources was also examined. A second control group of 33 volunteers (mean age of 50 years) without occupational exposure to antimony was also examined.	**Exposure:** The mean serum antimony concentration in the exposed workers was 0.766 mg/m^3. Geometric mean urine antimony concentrations were 410.8, 112.5, and 27.8 µg/g creatinine in the exposed workers, control workers, and volunteer controls, respectively. **Confounding exposure:** Co-exposure to other chemicals was likely but not discussed	**Immunological effects:** Significant decreases in serum IgG1 and IgE levels were observed in exposed workers compared to control groups. An association between IgG4 levels and urine antimony levels were found in the exposed workers; no associations were found for other IgG subgroups or for IgE. No alterations in Il-2 or interferon-gamma levels were found in the exposed workers, as compared to control workers.
Palacios et al. 2014	Linked data from the Nurses' Health Study with EPA's Air Toxic data (n=97,430 females).	**Exposure:** Median antimony concentrations for each exposure quartile were 0.000034, 0.000138, 0.000287, and 0.000682 µg/m^3. **Confounding exposure:** Co-exposure to other chemicals was likely but not discussed	**Neurological effects:** No association between antimony levels and risk of Parkinson's disease was found. Risk estimates were adjusted for age, smoking, and population density.

Table 2-1. Health Effects in Humans Exposed to Antimony Dusts

Reference	Study population	Exposure	Outcomes
Potkonjak and Pavlovich 1983	51 males employed at a smelting facility. Mean duration of employment was 17.9 years (range of 9–31 years). All workers experienced pneumoconiotic changes. No control group was used.	**Exposure:** Workers were exposed to antimony oxides; 39–89% of dust was antimony trioxide and 2.1–7.8% was antimony pentoxide. No monitoring data were provided. **Confounding exposure:** Investigators noted that the airborne dust contained silica (0.82–4.72%), ferric trioxide (0.90–3.81%), and arsenic oxide (0.21–6.48%). No information on smoking was provided.	**Respiratory effects:** Clinical signs included chronic coughing (61%) and upper airway inflammation (35%). Respiratory effects included Type 1p pneumoconiosis (67%), chronic bronchitis (37%), chronic emphysema with pulmonary function changes (34%), inactive tuberculosis (18%), and pleural adhesions (28%). No consistent pattern of lung function alterations was found. **Dermal effects:** Dermatosis (63%) was found predominantly in workers exposed to excessively high temperatures. **Ocular effects:** Conjunctivitis (28%).
Renes 1953	78 males involved in smelting or employed as maintenance workers. Workers were employed for at least 2 weeks. No control group was used.	**Exposure:** Average concentrations in the breathing zone were 10.07 mg/m^3 in the furnace area and 11.81 mg/m^3 in the cupel area. **Confounding exposure:** Arsenic was present in smelting material; average levels of arsenic in the furnace and cupel areas were 1.10 and 0.36 mg/m^3, respectively. Workers were also exposed to hydrogen sulfide and iron oxide.	**Respiratory effects:** Soreness and bleeding of the nose (>70%), laryngitis (11%), and rhinitis (20%) of workers. **Gastrointestinal effects:** 11% reported gastrointestinal symptoms (abdominal cramps, diarrhea, vomiting). **Dermal effects:** Dermatitis (20%). **Neurological effects:** Nine workers reported nerve tenderness and tingling, severe headaches, and prostration. Antimony was detected in urine samples from 7/9 of these workers.

Table 2-1. Health Effects in Humans Exposed to Antimony Dusts

Reference	Study population	Exposure	Outcomes
Schnorr et al. 1995	1,014 workers at an antimony smelter in Texas. Employed for at least 3 months; average length of employment was 6.8 years.	**Exposure:** Monitoring surveys conducted in 1975 and 1976 found geometric mean antimony levels of 0.5551 mg/m^3 using area samples and 0.747 mg/m^3 using personal samples. **Confounding exposure:** Investigators noted that the workers were also exposed to arsenic. Smoking status was not included as a potential confounding variable.	**Respiratory effects:** Increase in deaths from influenza (SMR=1.23) and pneumoconiosis/ other respiratory disease among workers with Spanish surnames. **Cardiovascular effects:** Increased deaths. from ischemic heart disease among Spanish surname workers as compared to a survey of Mexican-American population or to Spanish surnamed workers at a cadmium facility; the statistical significance of this finding was not reported. **Cancer:** Nonsignificant increase in deaths from lung cancer especially among workers with the longest period since first employed (>20 years) and the longest duration of employment (>10 years) (SMR=1.55; 90% CI 0.86–2.60). Significant positive trend in lung cancer deaths with increasing duration of employment when compared to an ethnic-specific rate.
Stevenson 1965	Case series of 23 workers at an antimony smelter exposed to antimony trioxide dust and reporting dermatitis.	**Exposure:** Antimony concentrations were not reported; investigators noted that most of the antimony trioxide dust was <1 µm in diameter. **Confounding exposure:** The antimony sulfide ore contained minute traces of lead, arsenic, and iron; the investigators also noted that sulfur dioxide was released during the smelting process.	**Dermal:** Erythematous papules were most commonly reported in the antecubital area and shins. The investigators noted that workers in these areas were most exposed to heat, which resulted in sweating. The rash typically subsided 3–14 days after the workers were transferred to cooler working environments.

Table 2-1. Health Effects in Humans Exposed to Antimony Dusts

Reference	Study population	Exposure	Outcomes
Taylor 1966	Case series of seven workers acutely exposed to high levels of antimony trichloride.	**Exposure:** It is likely that the workers were exposed to up to 73 mg Sb/m^3. **Confounding exposure:** The workers were exposed to ≤146 mg/m^3 hydrogen chloride.	**Respiratory:** 7/7 workers reported upper respiratory tract soreness; this is likely due to the hydrogen chloride exposure. **Gastrointestinal:** Abdominal pain (4/7), vomiting (3/7), and anorexia (5/7) were reported by workers.
Wu and Chen 2017	91 workers exposed to antimony trioxide or sodium antimonite and 42 control workers at glass manufacturing and plastic product engineering facilities.	**Exposure:** Average antimony levels were 2.51, 0.14, and 0.21 mg/m^3 at the antimony trioxide production, glass manufacturing, and plastic product engineering facilities. **Confounding exposure:** Co-exposure to other chemicals was not discussed.	**Immunological:** Decreases in serum IgG, IgA, and IgE levels. Inverse correlations between immunoglobins and air antimony levels and inverse correlations between blood, urine, and hair antimony levels with IgA and IgE levels.

CI = confidence interval; EKG = electrocardiogram; EPA = Environmental Protection Agency; SMR = standardized mortality ratio

Table 2-2. Health Effects in Humans Orally Exposed to Antimony

Reference	Study population	Exposure	Outcomes
Adams et al. 2006	Children 3–15 years of age living in Arizona; 51 cases with autism spectrum disorder; 40 controls.	Mean hair antimony levels were 0.19 µg/g in cases and 0.08 µg/g in controls. Maternal hair antimony levels were 0.05 µg/g in cases and 0.04 µg/g in controls.	**Neurological effects:** No significant differences in maternal or child hair antimony levels between children with autism spectrum disorder and controls.
Adams et al. 2013	Children 5–16 years of age living in Arizona; 55 cases with autism spectrum disorder, pervasive developmental disorder, or Asperger's; 44 controls.	Mean urinary antimony levels were 0.167 µg/g creatinine in cases and 0.165 µg/g creatinine in controls.	**Neurological effects:** No association between urinary antimony levels and autism severity.
Blaurock-Busch et al. 2011	Children 3–9 years of age living in Saudi Arabia; 25 cases with autism spectrum disorder; 25 controls.	Mean hair antimony levels were 0.08 µg/g in cases and 0.07 µg/g in controls. Mean urinary antimony levels were 0.48 µg/g creatinine in cases and 0.21 µg/g creatinine in controls.	**Neurological effects:** No significant differences in hair or urine antimony levels between children with autism spectrum disorder and controls.
Bloom et al. 2015	245 infants of parents participants in the Longitudinal Investigation of Fertility and the Environment study in Michigan and Texas.	Mean maternal urinary antimony level was 0.06 µg/L (range of <0.01–0.52 µg/L); mean paternal urinary antimony level was 0.10 µg/L (range of <0.01–1.06 µg/L).	**Developmental effects:** No associations between maternal or paternal urinary antimony levels and gestational age, birth weight, birth length, head circumference, ponderal index, or newborn sex.
Colak et al. 2015	Populations living in two cities in Turkey near the Black Sea; 13,012 cancer cases were registered in 2000–2007.	541 water samples were collected from the area; antimony levels were <20 µg/L in all samples.	**Cancer effects:** A positive relationship between antimony levels and cancer incidence was found. The study examined 17 metals and found that, in total, they accounted for only 8.2% of the cancer incidence of the population.
Fido and Al-Saad 2005	Boys 4–8 years of age living in Kuwait; 40 cases with autism and 25 controls.	Median hair antimony levels were 0.08 µg/g in cases and 0.06 µg/g in controls.	**Neurological effects:** No significant differences in hair antimony levels between boys with autism and controls.

Table 2-2. Health Effects in Humans Orally Exposed to Antimony

Reference	Study population	Exposure	Outcomes
Guo et al. 2016	7,781 adults (mean age of 50.3 years) participating in the 1999–2010 NHANES.	Geometric mean urinary antimony levels were 0.08 and 0.11 µg/g creatinine among alive and deceased participants, respectively.	**Death:** Association between urinary antimony levels and all-causes mortality. **Cardiovascular effects:** No association between urinary antimony and heart disease deaths. Associations for self-reported heart disease, congestive heart failure, and heart attack. No association for self-reported angina pectoris or coronary heart disease. **Cancer:** No association between urinary antimony levels and mortalities due to malignant neoplasms. No associations with self-reported cancer.
Longerich et al. 1991	Case-control study of 28 women in Newfoundland, Canada with an infant diagnosed with neural tube defect; mothers of age-matched infants living in the same geographical region served as controls.	Mean antimony levels in drinking water were 0.02 and 0.11 ppb in the control and case groups, respectively.	**Developmental effects:** No significant difference in antimony drinking water levels between the cases and controls.
Mendy et al. 2012	1,857 adults (49.6% males, 50.4% females; mean age of 50.3 years) participating in the 2007–2008 NHANES.	Geometric mean urinary antimony level was 0.06 µg/g creatinine (95% CI 0.06–0.06).	Medical conditions were self-reported. **Respiratory effects:** No association with asthma. **Cardiovascular effects:** No associations for congestive heart failure, coronary heart disease, angina pectoris, heart attack, or stroke. **Hepatic effects:** No associations with liver conditions. **Endocrine effects:** No association with thyroid conditions. **Other systemic effects:** No association with gout. **Cancer effects:** No associations with cancer.

Table 2-2. Health Effects in Humans Orally Exposed to Antimony

Reference	Study population	Exposure	Outcomes
Menke et al. 2016	9,447 adults participating in the 1999–2010 NHANES.	Not reported.	Diabetes defined as self-reported previous diagnosis or an A1C ≥6.5% (48 mmol/mol). **Other noncancer effects:** Association between urinary antimony levels and risk of diabetes. No association when evaluated in never smokers only. Association between urinary antimony and HOMA-IR among all participants and among participants without diabetes.
Navas-Acien et al. 2005	725 adults (>40 years of age) participating in the 1999–2000 NHANES.	Geometric mean urinary antimony level was 0.11 µg/L.	Peripheral arterial disease was defined as a blood pressure ankle brachial index <0.9 in at least one leg. **Cardiovascular effects:** No association between urinary antimony levels and peripheral arterial disease.
Scinicariello et al. 2017	2,654 adults aged ≥20 years participating in 2005–2008 NHANES.	Geometric mean urinary antimony level was 0.06 µg/L.	Medical conditions were self-reported. **Neurological effects:** Associations between urinary antimony levels and insufficient sleep (≤6 hours/night) and prolonged sleep-onset latency to fall asleep (more than 30 minutes per night). Obstructive sleep apnea, sleep problems, and day-time sleepiness associated with antimony levels above the reference value of 0.03 µg/L.

Table 2-2. Health Effects in Humans Orally Exposed to Antimony

Reference	Study population	Exposure	Outcomes
Shiue 2014	5,864 adults aged ≥20 years participating in 2011–2012 NHANES.	Urinary antimony level (mean levels were not reported in the study) was the biometric used for the analyses; urine samples were collected by 20–30% of the whole NHANES cohort.	High blood pressure (systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg) was found in 31.1% of the total population (this rate includes children, which were not included in the statistical analyses); blood pressure classification was based on a single blood pressure measurement. **Cardiovascular effects:** Association between urinary antimony levels and high blood pressure; OR of 1.56 (95% CI 1.29–1.89) with adjusting for urine creatinine levels, age, sex, body mass index, and ratio of family income to poverty level. In weighted model (also includes adjustment for subsample weighting), the OR was 1.39 (95% CI 1.10–1.77). The study also found associations for several other metals (cobalt, cesium, manganese, lead, tin, platinum, molybdenum, thallium, and tungsten).
Shiue 2015	5,031 adults (48.4% males, 51.6% females) aged 20-–9 years participating in 2009–2010 NHANES; the mean age was 44 years.	Urinary antimony level (mean levels were not reported in the study) was the biometric used for the analyses; urine samples were collected by 20–30% of the whole NHANES cohort.	Ankylosing spondylitis was assessed via clinical measures of occiput-to-wall distance and chest expansion; values of >2 and >2.5 cm were considered abnormal; active lumbar flexion was also used to assess ankylosing spondylitis but the criterion was not reported. **Musculoskeletal effects:** Association between urinary antimony levels and occiput-to-wall distance; OR of 1.74 (95% CI 1.15–2.62). No association with chest expansion (OR 0.90; 95% CI 1.65–1.29) or active lumbar flexion (OR -0.05; 95% CI -0.17–0.03).

Table 2-2. Health Effects in Humans Orally Exposed to Antimony

Reference	Study population	Exposure	Outcomes
Shiue and Hristova 2014	Adults aged ≥20 years participating in 2009–2012 NHANES; based on data presented in the paper, 2,391 participants were ≥18 years for age.	Urinary antimony level (mean levels were not reported in the study) was the biometric used for the analyses; urine samples were collected by 20–30% of the whole NHANES cohort.	See Shiue (2014) for blood pressure criteria. **Cardiovascular effects:** Association between urinary antimony levels and high blood pressure; OR of 1.99 (95% CI 1.30–1.95) with adjusting for urine creatinine levels, age, sex, body mass index, and ratio of family income to poverty level. In weighted model (also includes adjustment for subsample weighting), the OR was 1.44 (95% CI 1.12–1.86). The investigators estimated that antimony accounted for 6.2% of the population risk.
Vigeh et al. 2017	174 children aged 20–36 months.	Mean hair antimony levels were 0.102 and 0.188 µg/g in boys and girls, respectively.	**Body weight:** No significant differences in hair antimony levels between children weighing less than the 50th percentile at 18 months of age and those weighing more than the 50th percentile.
Wang et al. 2016	1,247 male partners from sub-fertile couples attending a reproductive clinic in China.	Median urinary antimony level was 0.17 µg/L.	**Reproductive effects:** No associations between urinary antimony levels and reproductive hormone levels (estradiol, FSH, LH, testosterone, SHBG), sperm apoptosis parameters, or sperm DNA damage
Zheng et al. 2014	1,106 women in China	Umbilical cord antimony was measured.	**Developmental effects:** Median umbilical cord antimony was significantly higher in women with adverse pregnancy outcomes (18.6 µg/L) compared to controls (0.16 µg/L); however, the risk of adverse pregnancy outcome in association with antimony was not statistically significant.

CI = confidence interval; FSH = follicle stimulating hormone; HOMA-IR = homeostatic model assessment of insulin resistance; LH = luteinizing hormone; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; SHBG = sex hormone-binding globulin

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
ACUTE EXPOSURE									
1	Rat (Sprague-Dawley) 5 M, 5 F	30 minutes	0, 122, 799, 1,395	CS, BW, GN, HP	Death			1,395	Increased mortality (7/10) at an unspecified time post-exposure
					Resp	122	1,395		Pulmonary edema and congestion
					Cardio	122			
					Hepatic	122			
					Renal	122			
					Endocr	122			
Stibine NIOSH 1979									
2	Rat (Wistar) 5 M, 5 F	16 days 6 hours/day, 5 days/week	0, 3.1, 6.3, 12, 25, 50	CS, BW, OW, GN, HP	Bd wt	50			
					Resp	12	25		Chronic inflammation in the lungs and squamous metaplasia in the epiglottis
Antimony trioxide NTP 2016									
3	Mouse (B6C3F1) 5 M, 5 F	17 days, 6 hours/day, 5 days/week	0, 3.1, 6.3, 12, 25, 50	CS, BW, OW, GN, HP	Bd wt	50			
					Resp	6.3	12[b]		Squamous metaplasia in epiglottis epithelium at 12 mg Sb/m^3; increases in relative lung weights at 3.1 mg Sb/m^3
Antimony trioxide NTP 2016									
4	Guinea pig (Hartley) 5 M,5 F	30 minutes	0, 122, 799, 1,395	CS, BW, GN, HP	Death			1,395	
					Resp	799	1,395		Pulmonary edema and congestion
					Renal	122	799		Renal tubular dilation in 3/10 animals
Stibine NIOSH 1979									

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
5	Rabbit (NS) 5 NS	5 days, 7 hours/day	0, 19.9	LE, OF, HP	Resp		19.9		Lung inflammation
					Cardio		19.9		Degenerative changes in heart; EKG alterations
					Hepatic		19.9		Degenerative liver lesions
					Renal		19.9		Degenerative kidney lesions
Antimony trisulfide Brieger et al. 1954									
INTERMEDIATE EXPOSURE									
6	Rat (NS) 10-24 F	1.5–2 months, 4 hours/day	0, 209	BW, GN, HP, MX, DX	Bd wt	209			
					Resp		209		Unspecified pathological changes in the lungs
					Hepatic		209		Unspecified pathological changes in the liver
					Renal		209		Unspecified pathological changes in the kidneys
					Endocr		209		Unspecified pathological changes in the pancreas
					Repro		209		Reduced fertility and unspecified histological alterations in reproductive organs
					Develop		209		Reduced litter size; not specified whether due to pre-implantation loss or post-implantation loss
Antimony trioxide Belyaeva 1967									
7	Rat (Wistar) 10 M	6 weeks, 7 hours/day 5 days/week	0, 2.20	LE, CS, BW, OF, GN, HP	Bd wt	2.2			
					Resp		2.2		Mild congestion and focal hemorrhages in the lungs
					Cardio		2.2		Altered EKG and microscopic changes in heart muscle consistent with degeneration of the myocardium
Antimony trisulfide Brieger et al. 1954									

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
8	Rat (Fischer-344) 50 M, 50 F	13 weeks, 6 hours/day, 5 days/week	0, 0.21, 0.902, 4.11, 19.60	CS, BW, OP, HE, BI, HP	Bd wt	19.6			
					Resp	0.902	4.11		Increases in alveolar/ intra-alveolar macrophages, relative lung weight, and in lung clearance half-times at ≥4.11 mg Sb/m^3; chronic interstitial inflammation and fibrosis at 19.60 mg Sb/m^3 at the end of a 27-week recovery period
					Cardio	19.6			
					Hemato	19.6			
Antimony trioxide Newton et al. 1994									
9	Guinea pig (NS) 24 NR	32 weeks, 2 hours/day, 7 days/week for 2 weeks and 3 hours/day, 7 days/week for 30 weeks	0, 37.9	CS, BW, HE, OF, HP	Bd wt	37.9			
					Resp		37.9		Pneumonitis
					Hemato		37.9		Decreases in total and differential leukocyte counts
					Hepatic		37.9		Fatty degeneration in the liver
					Immuno		37.9		Hypertrophy of lymphoid follicles in the spleen
Antimony trioxide Dernehl et al. 1945									
10	Dog (NS) 2 F	7 weeks, 7 hours/day 5 days/week	0, 3.81	LE, CS, BW, HE, BI	Bd wt	3.81			
					Cardio	3.81			
					Hemato	3.81			
Antimony trisulfide Brieger et al. 1954									

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
11	Dog (NS) 2F	10 weeks, 7 hours/day, 5 days/week	0, 3.98	LE, CS, BW, HE, BI	Bd wt	3.98			
					Cardio		3.98		EKG alterations indicative of myocardial injury; occasional swelling of myocardial fibers
					Hemato	3.98			
Antimony trisulfide Brieger et al. 1954									
12	Rabbit (NS) 6M	6 weeks, 7 hours/day, 5 days/week	0, 4.02	LE, HE, BI, OF, GN, HP	Cardio		4.02 M		Altered EKG, heart enlargement, swelling of myocardial fibers; only qualitative data were presented
					Hemato	4.02			
					Hepatic	4.02			
					Renal	4.02			
Antimony trisulfide Brieger et al. 1954									
CHRONIC EXPOSURE									
13	Rat (Sprague-Dawley) 50 M	14.5 months, 25 hours/week	0.2, 84–105	GN, HP	Resp		84 M		Gross and microscopic alterations in the lungs consistent with lipoid pneumonia
Antimony trisulfide Gross et al. 1952									
14	Rat (Wistar) 90 M, 90 F	52 weeks, 7 hours/day, 5 days/week	0, 36	LE, CS, BW, GN, HP	Bd wt	36			
					Resp		36		Interstitial fibrosis and alveolar-wall cell hypertrophy and hyperplasia persisting months after exposure ceased.
					Cardio	36			
					Hepatic	36			
					Renal	36			
					Dermal	36			
					Endocr	36			
					Immuno	36			
					Neuro	36			

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
					Repro	36			
					Other noncancer	36			
					Cancer			36 F	Lung neoplasms
Antimony trioxide Groth et al. 1986									
15	Rat (Wistar) 90 M, 90 F	52 weeks, 7 hours/day, 5 days/week	0, 17.5	LE, CS, BW, GN, HP	Bd wt	17.5			
					Resp		17.5		Interstitial fibrosis and alveolar-wall cell hypertrophy and hyperplasia persisting months after exposure ceased
					Cardio	17.5			
					Gastro	17.5			
					Hepatic	17.5			
					Renal	17.5			
					Dermal	17.5			
					Ocular	17.5			
					Endocr	17.5			
					Immuno		17.5		Mononuclear cell granulomas in tracheobronchial lymph nodes
					Repro	17.5			
					Other noncancer	17.5			
					Cancer			17.5 F	Lung neoplasms
Antimony Groth et al. 1986									

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
16	Rat (Fischer-344) 65 M, 65 F	12 months, 6 hours/day, 5 days/week	0, 0.05, 0.43, 3.8	CS, BW, OP, HE, BC, HP	Bd wt	3.8			
					Resp	0.05	0.43[c]		Increase in alveolar/intra-alveolar macrophages at ≥0.05 mg Sb/m^3 at the end of the exposure period and 12-month recovery period; increase in chronic interstitial inflammation ≥0.43 mg Sb/m^3 in rats killed during the recovery period; decreases in lung clearance (40 and 80%) at 0.43 and 3.8 mg Sb/m^3
					Hemato	3.8			
					Ocular	0.05	0.43		Moderate or severe lenticular degeneration
					Immuno	0.43	3.8		Reticuloendothelial cell hyperplasia in peribronchiolar lymph nodes
Antimony trioxide Newton et al. 1994									
17	Rat (Wistar) 50 M, 50 F	2 years, 6 hours/day, 5 days/week	0, 2.5, 8.3, 25	CS, LE, BW, GN, HP	Death			8.3	Decreased survival in females and decreased survival trend in males
					Bd wt	2.5 F	8.3 F		Decreases in body weight gain in females at 2.5 (10%), 8.3 (20%), and 25 (28%) mg Sb/m^3 and in males at 25 mg Sb/m^3 (20%)
					Resp		2.5		Inflammation, proteinosis, hyperplasia, and fibrosis at ≥2.5 mg Sb/m^3; hyperplasia of nasal respiratory epithelium at 2.5 mg Sb/m^3 (males only) and 25 mg Sb/m^3 (males and females) and squamous metaplasia of nasal epithelium in males at 25 mg Sb/m^3
					Cardio	2.5 F	8.3 F		Chronic inflammation of muscular arteries at 8.3 (females only) and 25 mg Sb/m^3
					Gastro	8.3			
					Musc/skel	8.3	25		Bone marrow hyperplasia
					Hepatic	25			

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
					Renal	2.5 F	8.3 F		Hyaline droplet accumulation at 8.3 (females only) and 25 mg Sb/m^3 and nephropathy in females at 25 mg Sb/m^3
					Ocular		2.5 F		Ciliary body inflammation at 25 mg Sb/m^3 and retinal atrophy in females at ≥2.5 mg Sb/m^3
					Endocr	25			
					Immuno		2.5		Lymphoid hyperplasia in bronchial and mediastinal lymph nodes
					Neuro	25			
					Repro		2.5 M		Epithelial hyperplasia of the prostate gland at 2.5 and 8.3 mg Sb/m^3; increases in severity were observed in all antimony exposed groups
					Other noncancer	25			
					Cancer			8.3 F	Alveolar/bronchiolar adenomas in females at ≥8.3 mg Sb/m^3, benign pheochromocytoma in adrenal medulla at 25 mg Sb/m^3 and combined incidence of benign and malignant pheochromocytomas in females at 25 mg Sb/m^3
Antimony trioxide NTP 2016									
18	Rat (Fischer-344) 49–50 F	55 weeks, 6 hours/day, 5 days/week	0, 1.6, 4.2	CS, LE, BW, OW, HE, BI, GN, HP	Resp		1.6		Focal fibrosis, adenomatous hyperplasia, multinucleated giant cells, cholesterol clefts, pneumocyte hyperplasia, and pigmented macrophages in the lungs
					Cardio	4.2			
					Gastro	4.2			
					Hemato	4.2			

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
					Musc/skel	4.2			
					Hepatic	4.2			
					Renal	4.2			
					Endocr	4.2			
					Immuno	4.2			
					Neuro	4.2			
					Repro	4.2			
					Other noncancer	4.2			
					Cancer			4.2	Lung neoplasms
Antimony trioxide Watt 1983									
19	Mouse (B6C3F1) 50 M, 50 F	2 years, 6 hours/day, 5 days/week	0, 2.5, 8.3, 25	CS, LE, BW, GN, HP	Death			8.3	Decreased survival
					Bd wt	2.5 M	8.3 M		Decreases in body weight gain in males at 8.3 and 25 mg Sb/m^3 (11 and 25%) and in females at 25 mg Sb/m^3 (21%).
					Resp		2.5		Chronic, inflammation, fibrosis (alveolus and pleural), and alveolar and bronchiolar epithelial hyperplasia at ≥2.5 mg Sb/m^3; laryngeal respiratory epithelial hyperplasia was observed at ≥8.3 mg Sb/m^3; squamous metaplasia of nasal respiratory epithelium in females at 25 mg Sb/m^3; and epithelial hyperplasia in the trachea of males exposed to 25 mg Sb/m^3
					Cardio	2.5	8.3		Chronic inflammation of epicardium
					Gastro	8.3 M	25 M		Chronic active inflammation in the forestomach of males
					Hemato	8.3 F	25 F		Hematopoietic cell proliferation in the spleen in females
					Musc/skel		2.5		Bone marrow hyperplasia

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
					Hepatic	25			
					Renal	25			
					Endocr	25			
					Immuno		2.5		Lymphoid hyperplasia in the bronchial and mediastinal (males only) lymph nodes and thymic cellular depletion
					Neuro	25			
					Repro	25			
					Other noncancer	25			
					Cancer			2.5	Increased incidences of alveolar/ bronchiolar adenomas, carcinomas, or combined at ≥2.5 mg Sb/m^3; other neoplastic lesions included malignant lymphoma in females at ≥2.5 mg Sb/m^3 and fibrous histiocytoma in the skin in males at 25 mg Sb/m^3
Antimony trioxide									
NTP 2016									
20	Pig (Sinclair S-1 miniature) 2-3 F	55 weeks, 6 hours/day, 5 days/week	0, 1.6, 4.2	CS, LE, BW, OW, HE, BI, GN, HP	Bd wt	4.2			
					Resp	4.2			
					Cardio	4.2			
					Gastro	4.2			
					Hemato	4.2			
					Hepatic	4.2			
					Renal	4.2			
					Endocr	4.2			
					Immuno	4.2			

Table 2-3. Levels of Significant Exposure to Antimony – Inhalation

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/m^3)	Parameters monitored	Endpoint	NOAEL (mg Sb/m^3)	Less serious LOAEL (mg Sb/m^3)	Serious LOAEL (mg Sb/m^3)	Effects
					Neuro	4.2			
					Repro	4.2			
					Other noncancer	4.2			
Antimony trioxide									
Watt 1983									

[a]The number corresponds to entries in Figure 2-2; differences in levels of health effects and cancer effects between male and females are not indicated in Figure 2-2. Where such differences exist, only the levels of effect for the most sensitive gender are presented.
[b]Used to derive an acute-duration inhalation minimal risk level (MRL) for antimony; based on a $BMCL_{HEC}$ of 0.035 mg Sb/m^3 and an uncertainty factor of 30 (3 for extrapolation from animals to humans with dosimetric adjustments and 10 for human variability); see Appendix A for more detailed information regarding the MRL.
[c]Used to derive a chronic-duration inhalation MRL for antimony; based on a $BMCL_{HEC}$ of 0.008 mg Sb/m^3 and an uncertainty factor of 30 (3 for extrapolation from animals to humans with dosimetric adjustments and 10 for human variability); see Appendix A for more detailed information regarding the MRL.

BC = serum (blood) chemistry; Bd wt or BW = body weight; BI = biochemical changes; BMDL = 95% lower confidence limit on the benchmark dose; Cardio = cardiovascular; CS = clinical signs; Develop = developmental; DX = developmental toxicity; Endocr = endocrine; EKG = electrocardiogram; F = female(s); Gastro = gastrointestinal; GN = gross necropsy; HE = hematology; HEC = human equivalent concentration; Hemato = hematological; HP = histopathology; Immuno = immunological; LE = lethality; LOAEL = lowest-observed-adverse-effect level; M = male(s); Musc/skel = musculoskeletal; MX = maternal toxicity; Neuro = neurological; NOAEL = no-observed-adverse-effect level; NS = not specified; OF = organ function; OP = ophthalmology; OW = organ weight Repro = reproductive; Resp = respiratory; Sb = antimony

Figure 2-2. Levels of Significant Exposure to Antimony – Inhalation

Acute (≤14 days)

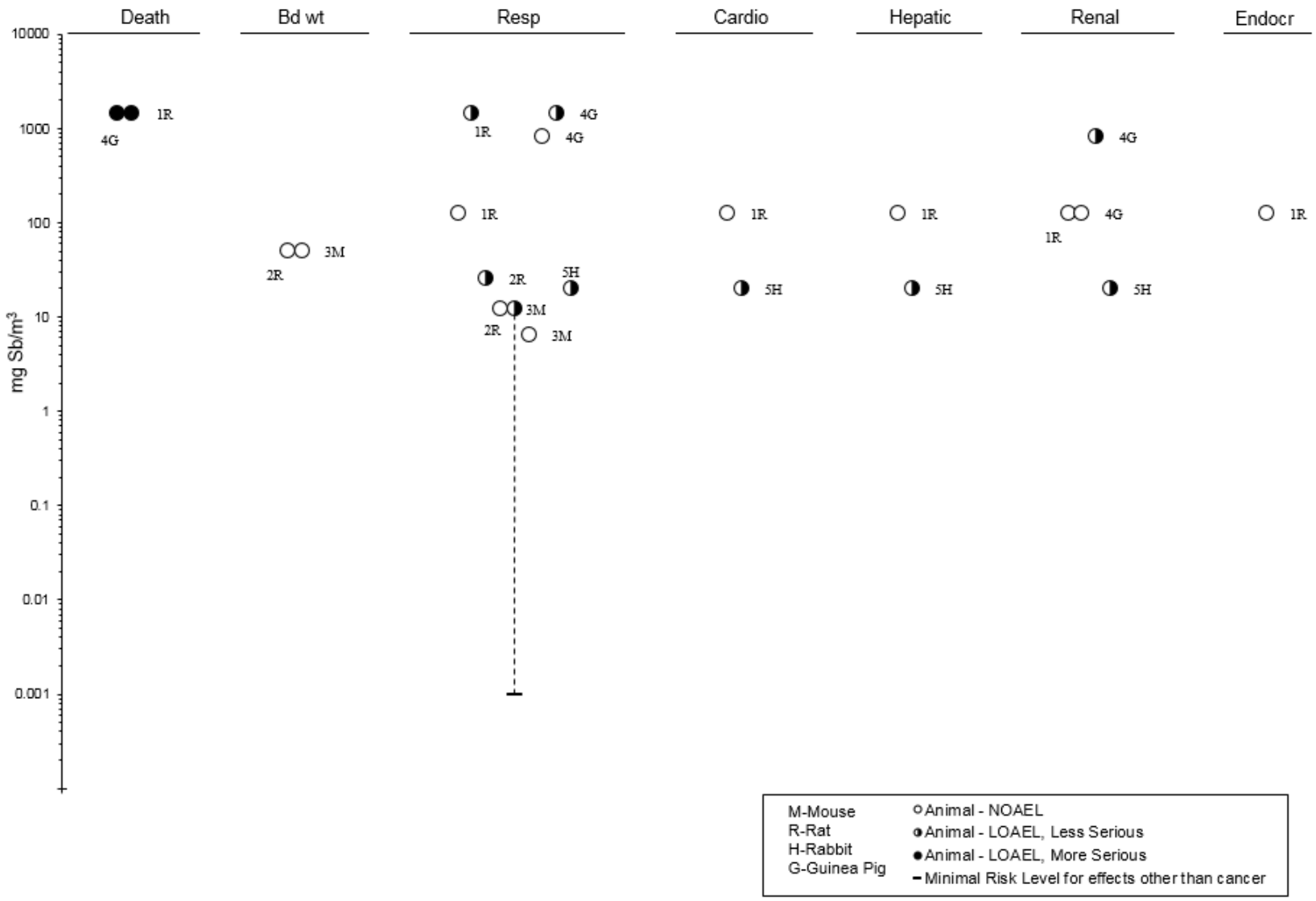


Figure 2-2. Levels of Significant Exposure to Antimony – Inhalation

Intermediate (15-364 days)

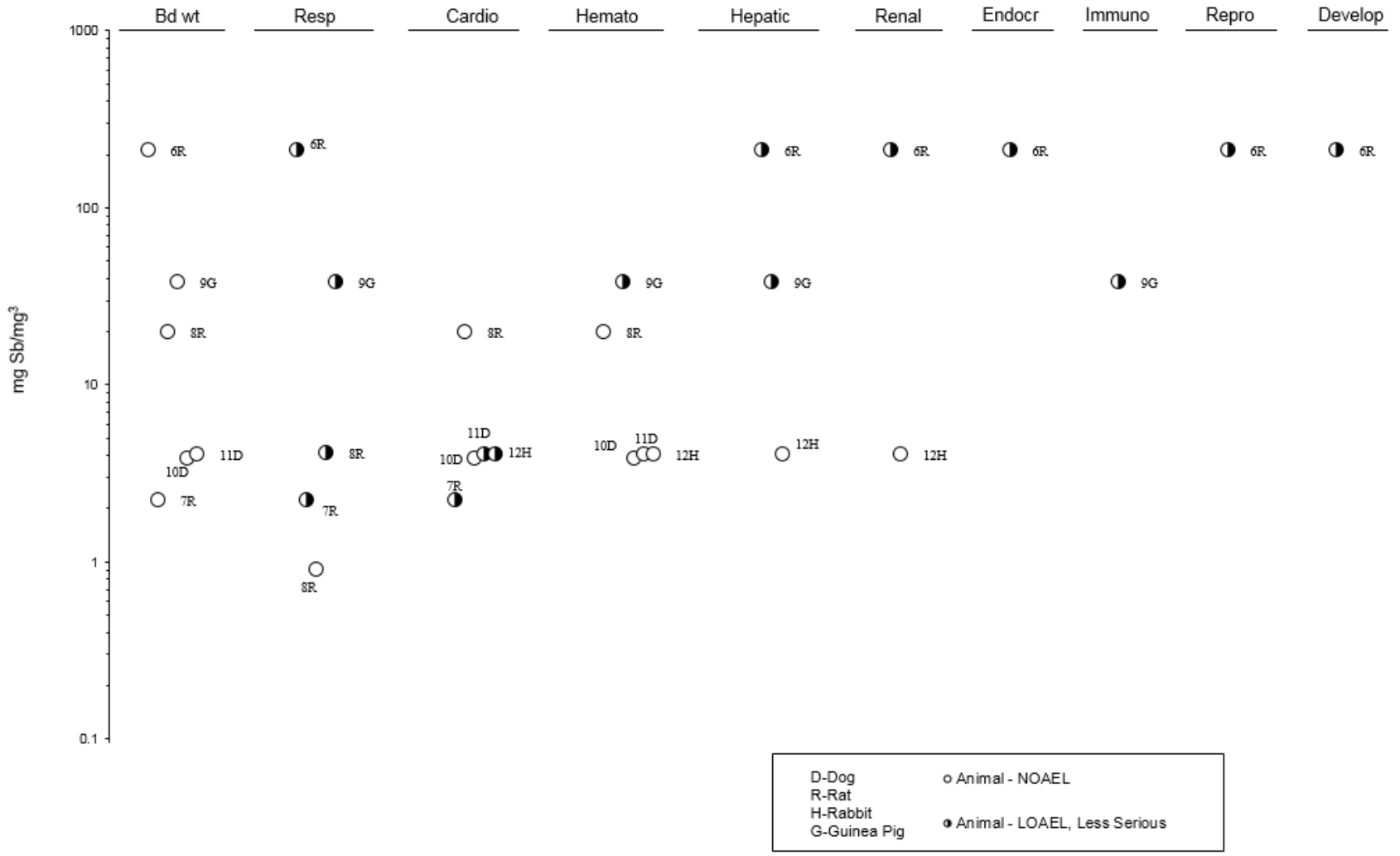


Figure 2-2. Levels of Significant Exposure to Antimony – Inhalation

Chronic (≥365 days)

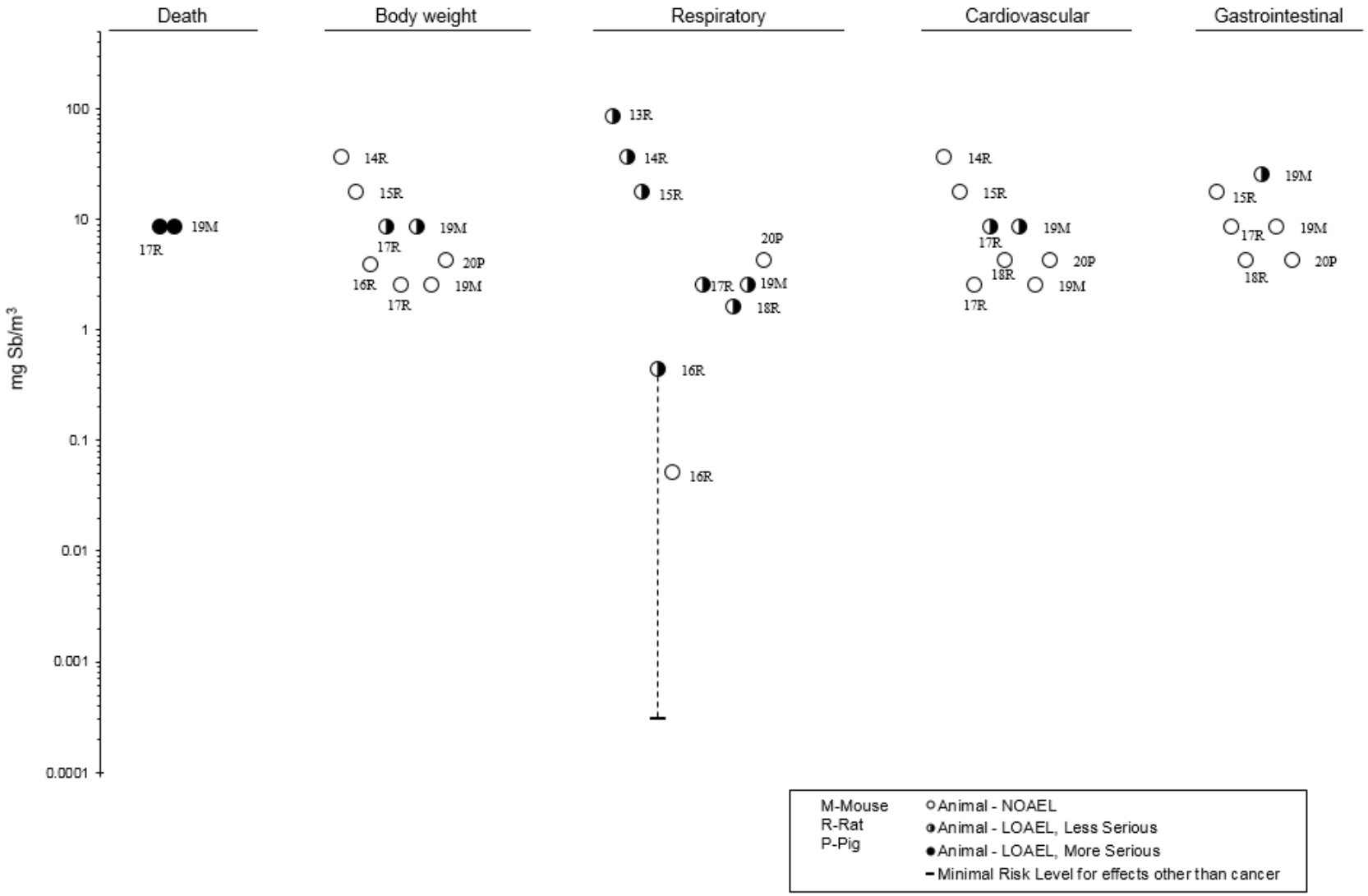


Figure 2-2. Levels of Significant Exposure to Antimony – Inhalation

Chronic (≥365 days)

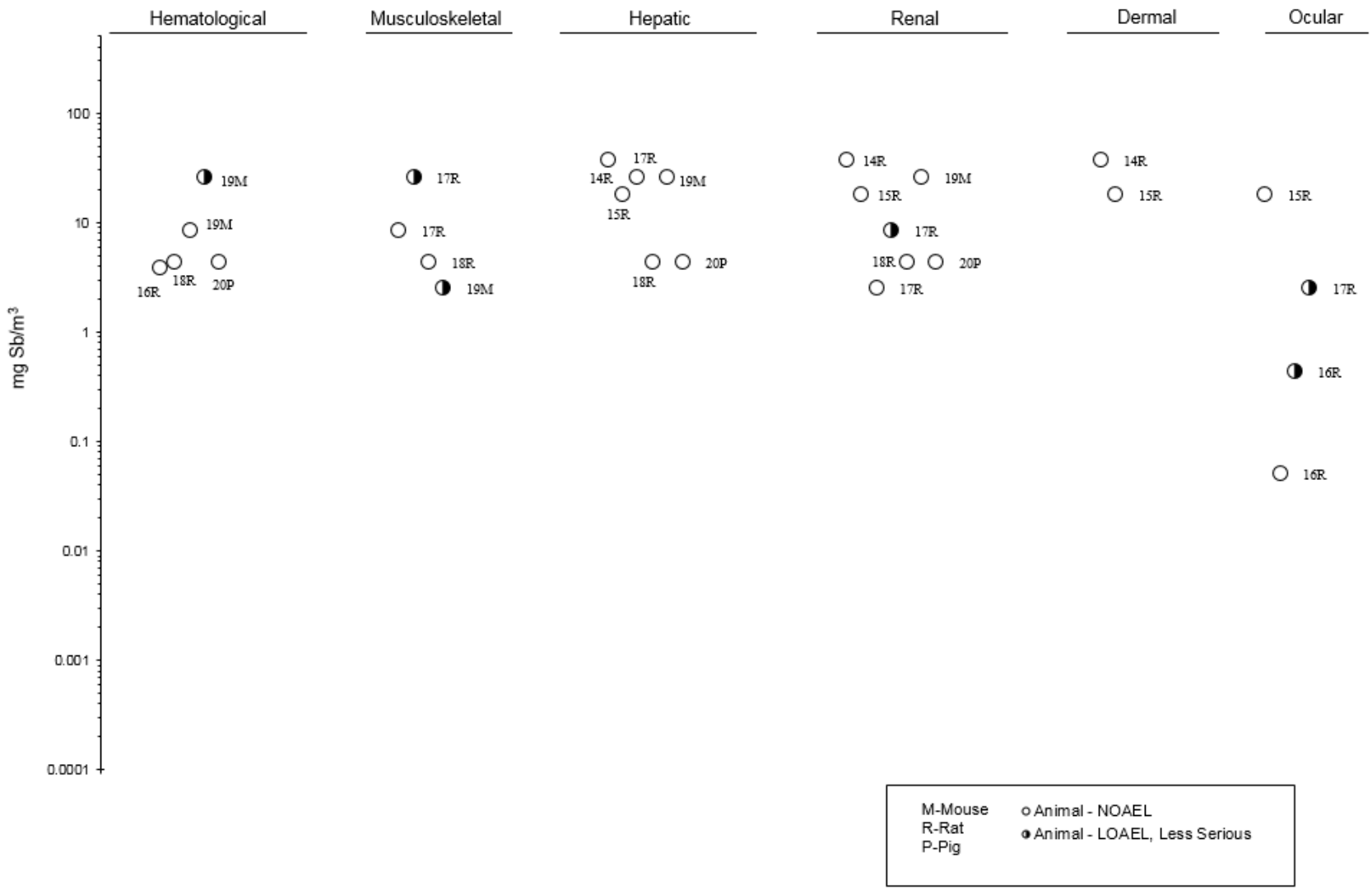


Figure 2-2. Levels of Significant Exposure to Antimony – Inhalation

Chronic (≥365 days)

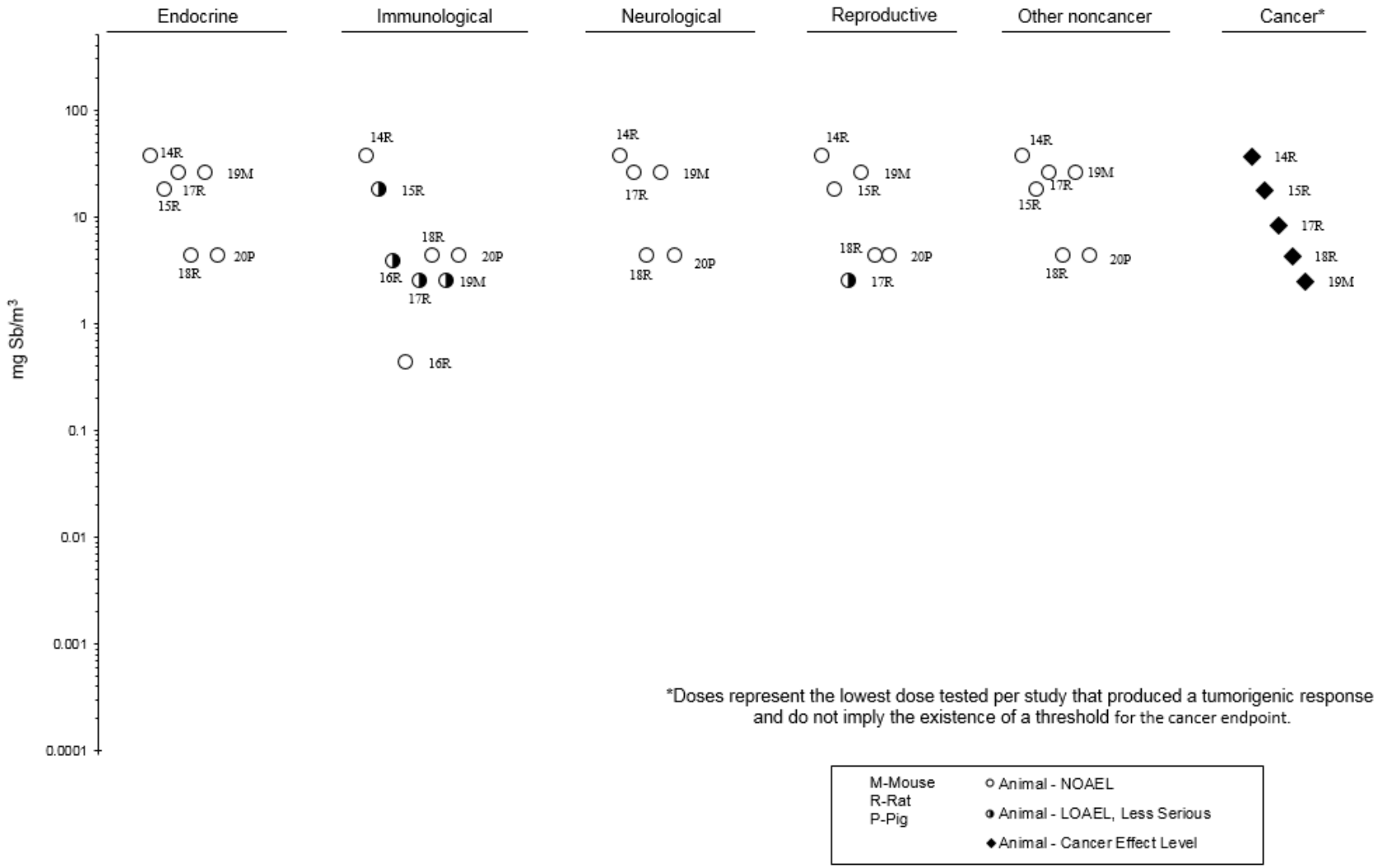


Table 2-4. Levels of Significant Exposure to Antimony – Oral

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/kg/day)	Parameters monitored	Endpoint	NOAEL (mg Sb/kg/day)	Less serious LOAEL (mg Sb/kg/day)	Serious LOAEL (mg Sb/kg/day)	Effects
ACUTE EXPOSURE									
1	Rat (Fischer-344) 10 M, 10 F	14 days (W)	0, 5.8, 10, 21, 34, 61	BW, WI, CS, OW, HP	Bd wt	61			
					Resp	61			
					Cardio	61			
					Gastro	61			
					Musc/skel	61			
					Hepatic	61			
					Renal	61			
					Endocr	61			
Antimony potassium tartrate NTP 1992									
2	Mouse (B6C3F1) 10 M, 10 F	14 days (W)	0, 21, 36, 63, 99, 150	BW, WI, CS, OW, HP	Bd wt	63	99		Decreased body weight gain was observed at ≥99 mg Sb/kg/day midway through the study; terminal body weights were within 93% of controls
					Resp	150			
					Cardio	150			
					Gastro	99	150		Focal ulceration in the forestomach
					Hepatic	99[b]	150		Minimal-to-moderate hepatocellular cytoplasmic vacuolization
					Endocr	150			
Antimony potassium tartrate NTP 1992									

Table 2-4. Levels of Significant Exposure to Antimony – Oral

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/kg/day)	Parameters monitored	Endpoint	NOAEL (mg Sb/kg/day)	Less serious LOAEL (mg Sb/kg/day)	Serious LOAEL (mg Sb/kg/day)	Effects
3	Dog (Beagle) 13 M, F	Once (W)	4.8	CS	Gastro		4.8		Vomiting
Antimony potassium tartrate Houpt et al. 1984									
INTERMEDIATE EXPOSURE									
4	Rat (NS) 30 F	22 days (W)	0, 0.07, 0.8	BW, OF	Bd wt	0.8			
					Cardio	0.8			
Antimony trichloride Angrisani 1988; Marmo et al. 1987									
5	Rat (NS) 10 M, F	38 days (W)	0, 0.1, 1	BW, OF	Bd wt	1			
					Cardio		0.1		Altered vasomotor response to 1-noreadrenaline and 1-isoprenaline in pups
Antimony trichloride Angrisani 1988; Marmo et al. 1987									
6	Rat (Wistar) 12 M, 1 2F	90 days (F)	M: 0, 70, 353, 1,408; F: 0, 81, 413, 1,570	CS, OP, BW, FI, UR, HE, BC, OW, HP	Bd wt	1,408			
					Resp	1,408			
					Cardio	1,408			
					Gastro	1,408			
					Hemato	1,408			
					Musc/skel	1,408			
					Hepatic	1,408			
					Renal	1,408			
					Ocular	1,408			
					Endocr	1,408			
Antimony trioxide Hext et al. 1999									

Table 2-4. Levels of Significant Exposure to Antimony – Oral

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/kg/day)	Parameters monitored	Endpoint	NOAEL (mg Sb/kg/day)	Less serious LOAEL (mg Sb/kg/day)	Serious LOAEL (mg Sb/kg/day)	Effects
7	Rat (Wistar) 12 M	12 weeks (F)	0, 700	CS, BW, OW, HE, BC	Bd wt	700			
					Hemato	700			
Antimony trioxide Hiraoka 1986									
8	Rat (Wistar) 12 M	12 weeks (F)	0, 85, 850	CS, BW, OW, HE, BC	Bd wt		85		Decrease in body weight gain (10% at 85 mg Sb/kg/day and 18% at 850 mg Sb/kg/day)
					Hemato	850			
Antimony Hiraoka 1986									
9	Rat (NS) 30 F	44 days (W)	0, 0.07, 0.7	BW, OF	Bd wt	0.07	0.7		11% decrease in body weight gain
					Cardio	0.7			
Antimony trichloride Marmo et al. 1987; Rossi et al. 1987									
10	Rat (Wistar) 7–8 M	4 weeks, 3 days/week (G)	0, 10, 1,000	OW, HP	Repro	1,000			
Antimony trioxide Omura et al. 2002									
11	Rat (Wistar) 8 M	4 weeks, 3 days/week (G)	0, 10	OW, HP	Repro	10			
Antimony potassium tartrate Omura et al. 2002									

Table 2-4. Levels of Significant Exposure to Antimony – Oral

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/kg/day)	Parameters monitored	Endpoint	NOAEL (mg Sb/kg/day)	Less serious LOAEL (mg Sb/kg/day)	Serious LOAEL (mg Sb/kg/day)	Effects
12	Rat (Sprague-Dawley) 15 M, 15 F	13 weeks (W)	M: 0, 0.06, 0.56, 5.58, 42.17; F: 0, 0.06, 0.64, 6.13, 45.69	BW, FI, WI, HE, BI, OW, HP	Bd wt	42.17			
					Resp	42.17			
					Cardio	42.17			
					Gastro	42.17			
					Hemato	5.58 M	42.17 M		5% decrease in red blood cell levels and 12% decrease in platelet counts
					Hepatic	42.17			
					Renal	42.17			
					Dermal	42.17			
					Endocr	42.17			
					Immuno	0.06 M	0.56 M		Increase in medullary volume in thymus gland in males at ≥0.56 mg Sb/kg/day and females at ≥6.13 mg Sb/kg/day
					Other noncancer	0.56	5.58		Mild sinus congestion in spleen at ≥0.56 mg Sb/kg/day (males); hyperplasia at ≥0.64 mg Sb/kg/day (females) and at 42.17 mg Sb/kg/day (males)
					Other noncancer	0.06 F[c]	0.64 F		Decreases in serum glucose levels (15–17%)
Antimony potassium tartrate Poon et al. 1998									

Table 2-4. Levels of Significant Exposure to Antimony – Oral

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/kg/day)	Parameters monitored	Endpoint	NOAEL (mg Sb/kg/day)	Less serious LOAEL (mg Sb/kg/day)	Serious LOAEL (mg Sb/kg/day)	Effects
13	Rat (NS) 10 M, F	38 days (W)	0, 0.1, 1	BW, OF	Develop		0.1		Significant alterations in vasomotor response to 1-noradrenaline and 1 isoprenaline at ≥0.1 mg Sb/kg/day at 60 days of age and to acetylcholine at 1 mg Sb/kg/day at 60 days of age
Antimony trichloride Rossi et al. 1987; Marmo et al. 1987									
14	Rat (NS) 30 F	44 days (W)	0, 0.07, 0.7	BW, CS, MX, DX	Develop	0.07	0.7		Decreased pup growth on PNDs10–60; pups weighed 26 and 47% less than controls on PNDs 10 and 22, respectively
Antimony trichloride Rossi et al. 1987									
15	Rat (NS) 10 M	30 days (F)	0, 50, 230, 890	BW, OW, HE	Hemato	230	890		Significantly increased (21%) red blood cell count.
					Renal	890			
Antimony trioxide Smyth and Thompson 1945									
16	Rat (Wistar) 5 M	24 weeks (F)	0, 620, 1,200	CS, BW, FI, WI, OW, HE, BI, HP	Bd wt	1,200			
					Hemato		620		Reduced red blood cell count
					Hepatic		620		Cloudy swelling in hepatic cords at 620 (3/5) and 1,200 (2/5) mg Sb/kg/day
Antimony trioxide Sunagawa 1981									

Table 2-4. Levels of Significant Exposure to Antimony – Oral

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/kg/day)	Parameters monitored	Endpoint	NOAEL (mg Sb/kg/day)	Less serious LOAEL (mg Sb/kg/day)	Serious LOAEL (mg Sb/kg/day)	Effects
17	Rat (Wistar) 5 M	24 weeks (F)	0, 370, 740, 1,500	CS, BW, FI, WI, OW, HE, BI, HP	Bd wt	740	1,500		Decreased terminal body weight
					Hemato	740	1,500		Decreased hematocrit and hemoglobin
					Hepatic	370	740		Increased incidence of disorder of the hepatic cords
Antimony Sunagawa 1981									
18	Mouse (CD) 9–10 M	4 weeks, 5 days/week (G)	0, 10, 1,000	OW, HP	Repro	1,000			
Antimony trioxide Omura et al. 2002									
19	Mouse (CD) 10 M	4 weeks, 5 days/week (G)	0, 10	OW, HP	Repro	10			
Antimony potassium tartrate Omura et al. 2002									
CHRONIC EXPOSURE									
20	Rat (Long-Evans) 50–60 M, 50–60 F	Lifetime (W)	0, 0.63	LE, BW, OW, UR, GN	Death			0.63	Reduced survival rate in male and female rats; at the median life spans, males survived 106 days and females 107 days less than controls
					Bd wt	0.63			
					Cardio	0.63			
					Other noncancer		0.63		Decreased (28–30%) non-fasting serum glucose
Antimony potassium tartrate Schroeder et al. 1970									

Table 2-4. Levels of Significant Exposure to Antimony – Oral

Figure key[a]	Species (strain) No./group	Exposure parameters	Doses (mg Sb/kg/day)	Parameters monitored	Endpoint	NOAEL (mg Sb/kg/day)	Less serious LOAEL (mg Sb/kg/day)	Serious LOAEL (mg Sb/kg/day)	Effects
21	Mouse (CD-1) 54 M, 54 F	Lifetime (W)	0, 0.35	LE, BW, HP	Death			0.35 F	Decreased survival
					Bd wt	0.35			
					Hepatic	0.35			
Antimony potassium tartrate Kanisawa and Schroeder 1969									

[a]The number corresponds to entries in Figure 2-3; differences in levels of health effects and cancer effects between male and females are not indicated in Figure 2-3. Where such differences exist, only the levels of effect for the most sensitive gender are presented.
[b]Used to derive an acute-duration oral minimal risk level (MRL) for antimony; based on a NOAEL of 99 mg Sb/kg/day and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability); see Appendix A for more detailed information regarding the MRL.
[c]Used to derive an intermediate-duration oral MRL for antimony; based on a NOAEL of 0.06 mg Sb/kg/day and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability); see Appendix A for more detailed information regarding the MRL.

BC = serum (blood) chemistry; Bd wt or BW = body weight; BI = biochemical changes; Cardio = cardiovascular; CS = clinical signs; Develop = developmental; DX = developmental toxicity; Endocr = endocrine; (F) = feed; F = female(s); FI = food intake; (G) = gavage-not specified; (GO) = gavage-oil; Gastro = gastrointestinal; GN = gross necropsy; HE = hematology; Hemato = hematological; HP = histopathology; Immuno = immunological; LOAEL = lowest-observed-adverse-effect level; M = male(s); Musc/skel = musculoskeletal; MX = maternal toxicity; NOAEL = no-observed-adverse-effect level; NS = not specified; OF = organ function; OP = ophthalmology; OW = organ weight; PND = postnatal day; Repro = reproductive; Resp = respiratory; Sb = antimony; UR= urinalysis; (W) = drinking water; WI = water intake

Figure 2-3. Levels of Significant Exposure to Antimony – Oral

Acute (≤14 days)

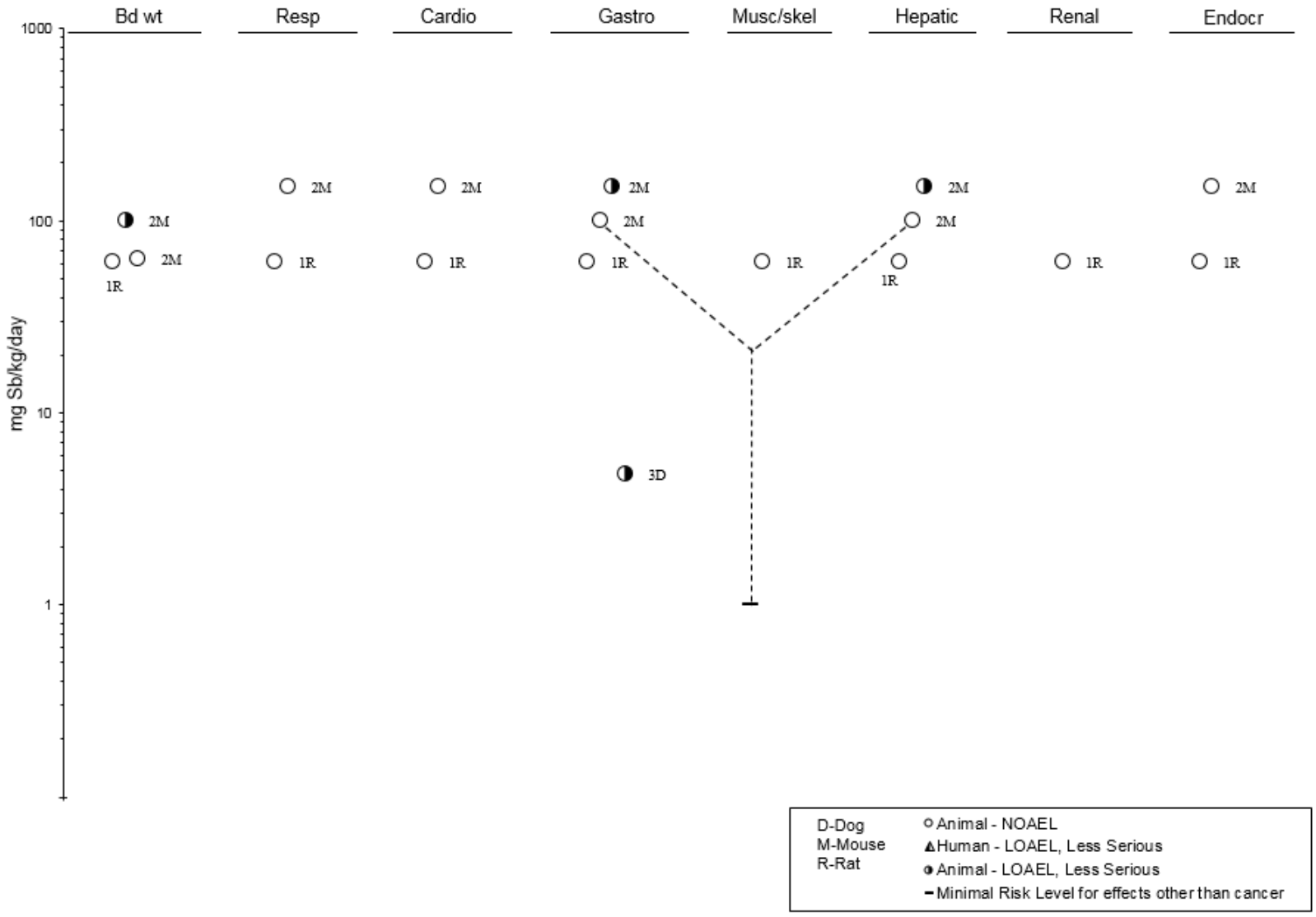


Figure 2-3. Levels of Significant Exposure to Antimony – Oral

Intermediate (15-364 days)

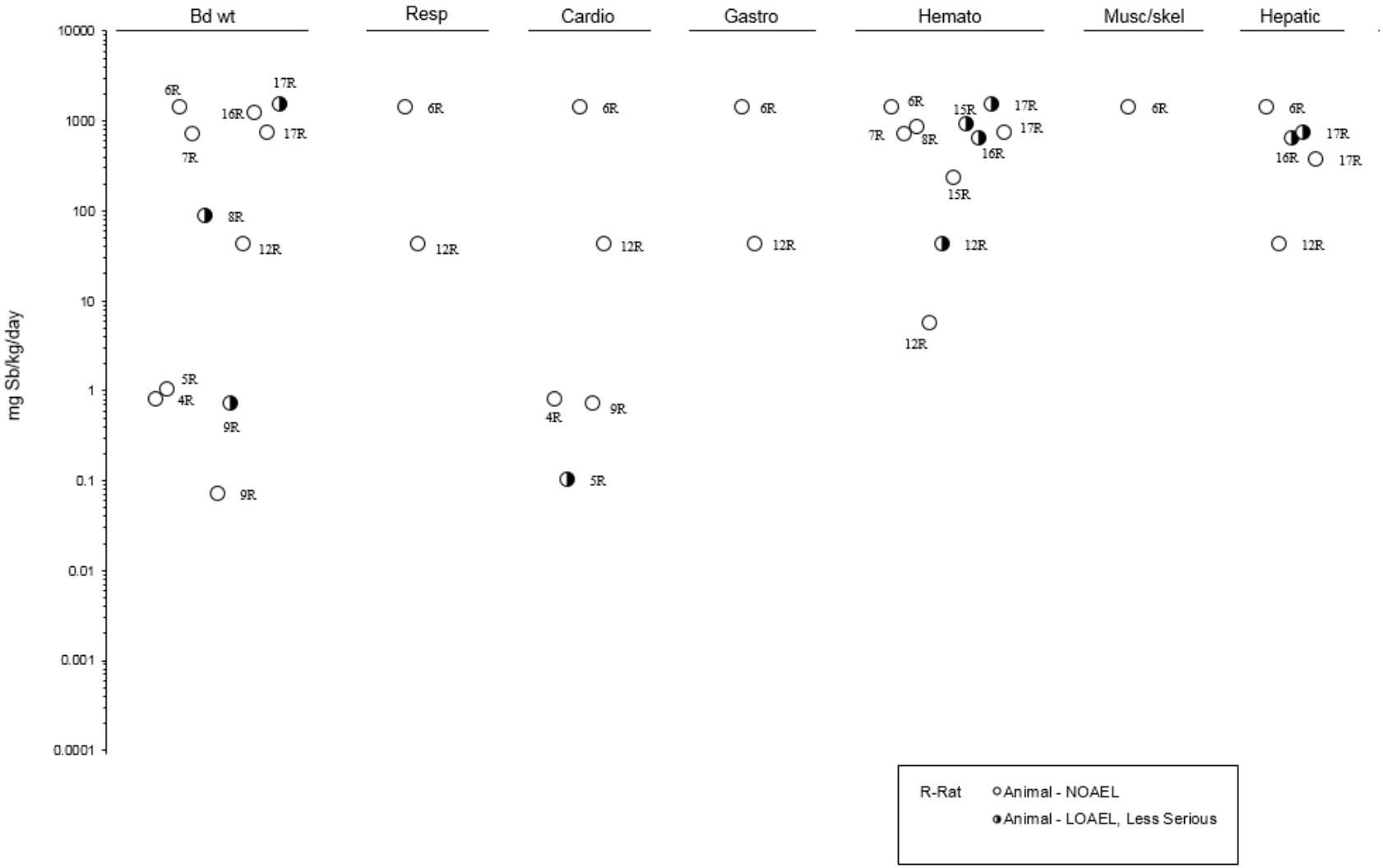


Figure 2-3. Levels of Significant Exposure to Antimony – Oral

Intermediate (15-364 days)

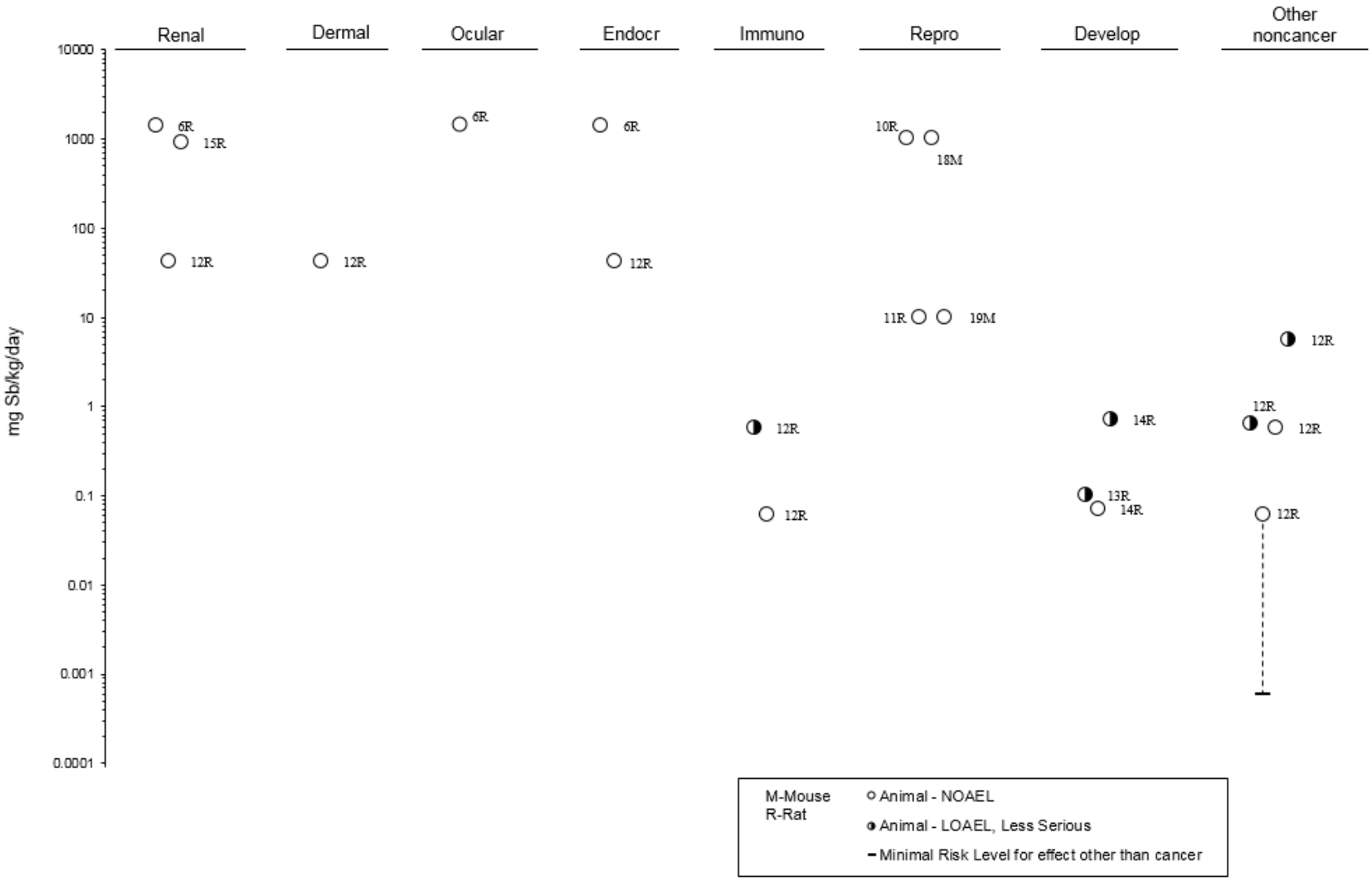


Figure 2-3. Levels of Significant Exposure to Antimony – Oral

Chronic (≥365 days)

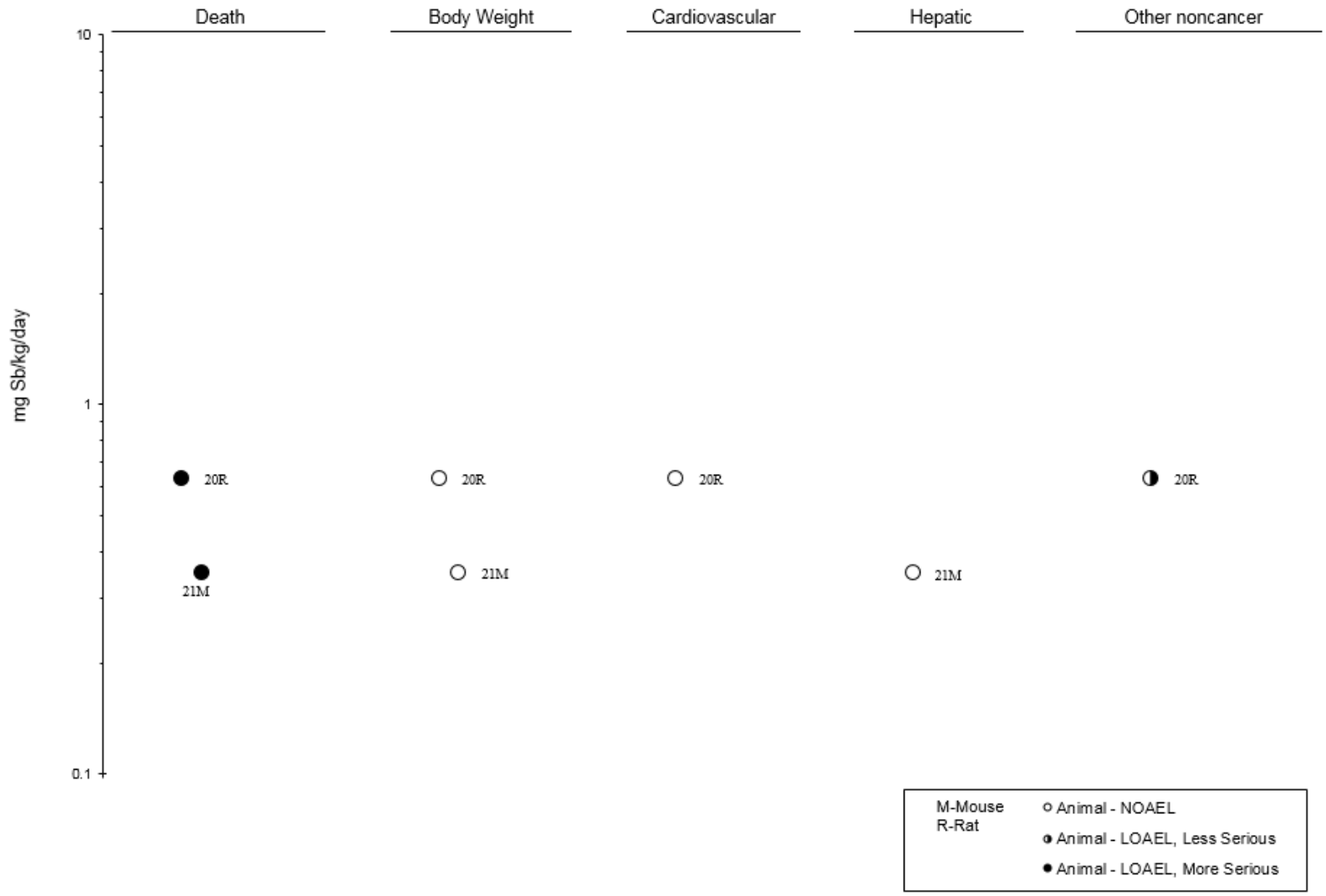


Table 2-5. Levels of Significant Exposure to Antimony – Dermal

Species (strain) No./group	Exposure parameters	Doses	Parameters monitored	Endpoint	NOAEL	Less serious LOAEL	Serious LOAEL	Effects
ACUTE EXPOSURE								
Rat (Sprague-Dawley) 5 M, 5 F **Stibine** **NIOSH 1979**	30 minutes	0, 122, 799, 1,395 mg/m^3	CS, BW, GN	Ocular	122	799		Eye irritation and closure
Guinea pig (Hartley) 10 F **Antimony sulfide** **Horton et al. 1986**	4 times	0, 3.3, 6.6 mg	CS	Immuno	6.6			
Guinea pig (Hartley) 5 M, 5 F **Stibine** **NIOSH 1979**	30 minutes	0, 122, 799, 1,395 mg/m^3	CS, BW, GN, HP	Ocular	1,395			
Rabbit (NS) 10 M **Antimony trioxide** **Gross et al. 1955**	Once	84 mg	CS	Ocular	84			
Rabbit (NS) 8 NS **Antimony trioxide** **Gross et al. 1955**	Once	20,900 mg	CS	Dermal	20,900			
Rabbit (New Zealand) 12 NS **Antimony sulfide** **Horton et al. 1986**	Once	66 mg	CS	Ocular		66		Eye irritation
INTERMEDIATE EXPOSURE								
Rat (Fischer-344) 50 M, 50 F **Antimony trioxide** **Newton et al. 1994**	13 weeks, 6 hours/day, 5 days/week	0, 0.21, 0.902, 4.92, 19.60 mg/m^3	OP	Ocular		0.21		Corneal irregularities were observed (approximately 30% in each group)

Table 2-5. Levels of Significant Exposure to Antimony – Dermal

Species (strain) No./group	Exposure parameters	Doses	Parameters monitored	Endpoint	NOAEL	Less serious LOAEL	Serious LOAEL	Effects
Rabbit (New Zealand) 10 M,10 F	13 weeks, 5 days/week	0, 6.5, 65 mg	CS, BW, HE, BC, OF, HP	Bd wt	65			
				Cardio	65			
				Hemato	65			
				Hepatic	65			
				Renal	65			
				Dermal	65			
				Endocr	65			
				Repro	65			
Antimony sulfide **Horton et al. 1986**								
CHRONIC EXPOSURE								
Rat (Wistar) 90 M, 90 F	52 weeks, 7 hours/day, 5 days/week	0, 36	CS	Dermal	36			
				Ocular	36			
Antimony trioxide **Groth et al. 1986**								
Rat (Wistar) 90 M, 90 F	52 weeks, 7 hours/day, 5 days/week	0, 17.5	CS	Dermal	17.5			
				Ocular	17.5			
ANTIMONY **Groth et al. 1986**								
Rat (Wistar) 50 M, 50 F	2 years, 6 hours/day, 5 days/week	0, 2.5, 8.3, 25	CS	Dermal	8.3 F	25 F		Chronic inflammation and ulcers of the skin
Antimony trioxide **NTP 2016**								

Table 2-5. Levels of Significant Exposure to Antimony – Dermal

Species (strain) No./group	Exposure parameters	Doses	Parameters monitored	Endpoint	NOAEL	Less serious LOAEL	Serious LOAEL	Effects
Mouse (B6C3F1) 50 M, 50 F	2 years, 6 hours/day, 5 days/week	0, 2.5, 8.3, 25	CS	Dermal	25			
				Ocular	25			
Antimony trioxide NTP 2016								

BC = serum (blood) chemistry; Bd wt or BW = body weight; Cardio = cardiovascular; CS = clinical signs; Endocr = endocrine; F = female(s); GN = gross necropsy; HE = hematology; Hemato = hematological; HP = histopathology; Immuno = immunological; LOAEL = lowest-observed-adverse-effect level; M = male(s); NOAEL = no-observed-adverse-effect level; NS = not specified; OF = organ function; Repro = reproductive

2.2 DEATH

A study of NHANES participants reported an association between urinary antimony levels and increased risk of deaths from all causes (Guo et al. 2016); the results of this study are not adequate to establish a relationship between antimony and death.

Deaths occurred in guinea pigs exposed to approximately 37.9 mg Sb/m^3 as antimony trioxide dust for approximately 60–178 days (Dernehl et al. 1945) and in guinea pigs and rats exposed to 1,395 mg Sb/m^3 as stibine gas for 30 minutes (NIOSH 1979). Pulmonary edema was a contributing factor to the death of rats and guinea pigs exposed to stibine (NIOSH 1979). None of the rats or guinea pigs exposed to ≤799 mg Sb/m^3 for 30 minutes died (NIOSH 1979). Lower concentrations of antimony trisulfide (84–105 mg Sb/m^3), antimony trioxide (≥36 mg Sb/m^3), or antimony ore (17.5 mg Sb/m^3) did not affect the survival of rats exposed for approximately 1 year (Gross et al. 1952; Groth et al. 1986; Newton et al. 1994; Watt 1983). However, a 2-year exposure to ≥8.3 mg Sb/m^3 as antimony trioxide resulted in decreased survival in female rats and male and female mice (NTP 2016). The decreased survival was attributed to lung inflammation and/or lung carcinomas (mice only).

Mortality was not observed in rats following a single exposure to ≤188–17,000 mg Sb/kg as antimony trioxide (Fleming 1938; Myers et al. 1978; Smyth and Carpenter 1948; Smyth and Thompson 1945) or to a 7,000 mg Sb/kg dose of metallic antimony (Bradley and Frederick 1941). However, a lower single dose of organic antimony (300 mg Sb/kg dose as antimony potassium tartrate) resulted in death in rats (Bradley and Frederick 1941). Death was attributed to myocardial failure. Significant increases in deaths were not observed in rats or mice exposed to 61 or 150 mg Sb/kg/day as antimony potassium tartrate in drinking water for 14 days (NTP 1992). These data for death in animals suggest that organic antimony is more lethal than the inorganic compounds, probably due to increased absorption of the antimony potassium tartrate, likely due to its increased solubility.

Intermediate-duration exposure to inorganic antimony compounds or metallic antimony did not result in increases in deaths in rats exposed to ≤1,570 mg Sb/kg/day as antimony trioxide in the diet (Hext et al. 1999; Hiraoka 1986) or ≤850 mg Sb/kg/day as metallic antimony (Hiraoka 1986). Chronic administration of a low dose of antimony potassium tartrate (0.63 mg Sb/kg/day) resulted in decreased lifespan in rats (Schroeder et al. 1970). A decrease in survival was also noted in female mice exposed to 0.35 mg Sb/kg/day as antimony potassium tartrate (Kanisawa and Schroeder 1969); however, there was no statistical analysis of the data.

In a repeated dermal exposure study, three of eight rabbits died due to exposure to antimony trioxide in an artificial sweat paste for 5–8 treatments; the remaining animals received 21 treatments and survived (Fleming 1938). Since the application area was not occluded, it is likely that the animals ingested the paste; the results of this study was therefore not included in the LSE table. Damage to the cardiac portion of the stomach was noted in two of the three rabbits that died. No antimony-related deaths were reported in rabbits exposed to 65 mg antimony as antimony sulfide in calcium cup grease for 13 weeks (Horton et al. 1986).

2.3 BODY WEIGHT

Data on possible associations between antimony and body weight in humans is limited to a study in children that examined body weight at 18 months of age and hair antimony levels at 20–36 months of age (Vigeh et al. 2017). No significant differences in hair antimony levels were found in children with body weights below the 50th percentile compared to those with body weights above the 50th percentile.

No alterations in body weight gain have been observed in inhalation studies in rats and mice exposed to antimony trioxide for acute (NTP 2016), intermediate (Belyaeva 1967; Newton et al. 1994), or chronic (Groth et al. 1986; Newton et al. 1994; NTP 2016; Watt 1983) durations at concentrations as high as 50, 209, or 36 mg Sb/m^3, respectively. No body weight alterations were observed in rats exposed to 17.5 mg Sb/m^3 as antimony ore for approximately 1 year (Groth et al. 1986).

Similarly, most oral exposure studies have not reported decreases in body weight gain in laboratory animals exposed to metallic antimony, antimony trioxide, or antimony potassium tartrate (Angrisani et al. 1988; Fleming 1938; Hext et al. 1999; Hiraoka 1986; Kanisawa and Schroeder 1969; NTP 1992; Poon et al. 1998; Schroeder et al. 1970; Sunagawa 1981). Four studies did report decreases in body weight and/or weight loss. NTP (1992) reported significant decreases in body weight gain in mice exposed to 99 mg Sb/kg/day (males) or 150 mg Sb/kg/day (males and females). Although these decreases in body weight gain were observed midway through the 2-week study, the body weights of all groups of mice were within 93% of the controls at termination. Decreases in body weight gain (body weights were 11–18% lower than controls) were observed in rats exposed to ≥85 mg Sb/kg/day as metallic antimony for 12 weeks; the lower body weights in the 850 mg Sb/kg/day group were still lower than controls after a 12-week recovery period (Hiraoka 1986). Smyth and Thompson (1945) reported a decrease in body weight gain in rats exposed to 890 mg Sb/kg/day as antimony trioxide in the diet for 30 days; however, a

decrease in food intake was also observed at that dose level. A fourth study reported an 11% decrease in maternal weight gain in rats exposed to 0.7 mg Sb/kg/day as antimony trichloride in drinking water during gestation and lactation (Rossi et al. 1987).

No dermal exposure studies examining body weight were identified.

2.4 RESPIRATORY

Studies of workers exposed to antimony compounds (primarily antimony trioxide) have reported upper and lower respiratory effects. Upper respiratory effects included soreness and bleeding of the nose, rhinitis, and laryngitis in workers at an antimony smelter (Renes 1953). One of the more commonly reported lower respiratory effects is pneumoconiosis in workers involved in extraction of antimony trioxide from antimony ores and workers at antimony smelters (Cooper et al. 1968; Potkonjak and Pavlovich 1983; Schnorr et al. 1995). Other lower respiratory effects include chronic coughing, upper airway inflammation, and chronic bronchitis (Potkonjak and Pavlovich 1983). In the two studies that conducted lung function tests, no consistent pattern of alterations was found (Cooper et al. 1968; Potkonjak and Pavlovich 1983). Three studies provided some monitoring data. In the study reporting upper respiratory effects, the average antimony concentrations were 10.07–11.81 mg/m^3 (Renes 1953). In the two studies reporting pneumoconiosis, antimony levels were 0.081–138 mg/m^3 in one study (Cooper et al. 1968) and 0.747 mg/m^3 (geometric mean concentration) in the second study (Schnorr et al. 1995). Several studies reported that the workers were also exposed to arsenic, which was present in the antimony ores (Jones 1994; Potkonjak and Pavlovich 1983; Renes 1953; Schnorr et al. 1995); the workers were also exposed to other compounds including iron oxide and hydrogen sulfide (Potkonjak and Pavlovich 1983; Renes 1953). In contrast to these studies of workers exposed to antimony ores and/or antimony oxides, respiratory irritation was not noted in workers exposed to ≤3.9 mg Sb/m^3 as antimony trisulfide for 8 months to 2 years (Brieger et al. 1954).

Studies in laboratory animals, particularly rats, support the findings of the epidemiology studies and suggest that the respiratory tract is one of the most sensitive targets of inhaled antimony toxicity. The lungs appear to be the most sensitive portion of the respiratory tract, and the severity of the respiratory effects appear to be concentration- and duration-related. Although most of the studies were conducted using antimony trioxide, studies with stibine (NIOSH 1979), antimony trisulfide (Brieger et al. 1954), and antimony ore (Groth et al. 1986) have also reported lung effects.

Exposure to antimony aerosols results in deposition of the particles in the lungs, which leads to increases in the number of alveolar macrophages, inflammation, and fibrosis. The earliest and most sensitive effect of inhaled antimony is increased alveolar and/or intra-alveolar macrophages. Intermediate- and chronic-duration studies found increases in alveolar and/or intra-alveolar macrophages in rats exposed to concentrations as low as 4.11 mg Sb/m^3 as antimony trioxide following a 13-week exposure (Newton et al. 1994) and 0.05 mg Sb/m^3 as antimony trioxide following a 1-year exposure (Newton et al. 1994). The increases in macrophages persisted for at least 27 weeks or 1 year, respectively, after exposure termination. The proliferation of macrophages is a normal physiological response to the deposition of insoluble particulates in the lung and increases in the number of alveolar macrophages in the absence of evidence of lung damage were not considered adverse. The increases in antimony lung deposition also resulted in increases in lung clearance half-times. Following a 13-week exposure (Newton et al. 1994), the lung clearance half-times were 5.5 and 5.25 months in male and female rats, respectively, exposed to 4.11 mg Sb/m^3 and 10 and 8.25 months in male and female rats, respectively, exposed to 19.60 mg Sb/m^3; by comparison, the half-times were 3.75 months in both male and female rats exposed to 0.902 mg Sb/m^3. Similarly, in the 1-year exposure study (Newton et al. 1994; data reported in Bio/Dynamics 1990), the antimony lung clearance half-times in male and female rats were 3.0 and 4.2 months, respectively, at 0.43 mg Sb/m^3 and 8.7 and 10.2 months, respectively, at 3.8 mg Sb/m^3, as compared to 2.5 and 2.2 months, respectively, in the 0.05 mg Sb/m^3 group. The investigators noted that the decrease in lung clearance was higher than anticipated if it was solely due to volumetric overloading, suggesting that clearance was also affected by the intrinsic toxicity of antimony trioxide. In a 2-year study using smaller particles (mass median aerodynamic diameter [MMAD] of 1.0–1.4 μm compared to 3.05 μm in the Newton et al. [1994] study), estimated clearance half-times were 136, 206, and 262 days (approximately 4.5, 6.8, and 8.6 months) for exposures to 2.5, 8.3, and 25 mg Sb/m^3, respectively, as antimony trioxide (NTP 2016).

The lowest antimony trioxide concentrations resulting in histological alterations (lung inflammation) in rats are 19.60 and 0.43 mg Sb/m^3 in intermediate- and chronic-duration studies (Newton et al. 1994), respectively. In both studies, the increases in the incidence of lung inflammation were observed at the end of a 27-week or 1-year recovery period; these effects were not observed at the end of the exposure period (highest concentrations tested were 19.60 and 3.8 mg Sb/m^3 in the intermediate and chronic studies, respectively). In contrast, NTP (2016) found significant increases in the incidence in chronic inflammation and other lung lesions in rats exposed to ≥2.5 mg Sb/m^3 for 1 year; the smaller particle size in the NTP (2016) study may explain the difference between the studies. The lowest concentrations in mice resulting in lung inflammation are 25 mg Sb/m^3 following a 16-day exposure and 0.25 mg Sb/m^3

following a 2-year exposure (NTP 2016). Inflammation was also observed in rabbits exposed to 19.9 mg Sb/m^3 as antimony trisulfide for 5 days (Brieger et al. 1954) and in guinea pigs after intermediate-duration exposure to 37.9 mg Sb/m^3 as antimony trioxide (Dernehl et al. 1945). Chronic exposure to higher concentrations (≥1.6 mg Sb/m^3 as antimony trioxide or 17.5 mg Sb/m^3 as antimony ore) resulted in lung fibrosis in rats (Groth et al. 1986; Newton et al. 1994; NTP 2016; Watt 1983). Other lesions observed in the lungs include proteinosis and alveolar/bronchiolar epithelial hyperplasia in rats and mice exposed to 2.5 mg Sb/m^3 as antimony trioxide for 1 or 2 years (NTP 2016), pulmonary edema and congestion in rats and guinea pigs exposed to a lethal stibine concentration of 1,395 mg Sb/m^3 for 30 minutes (NIOSH 1979), alveolar hypertrophy and hyperplasia and cholesterol clefts in rats exposed to 36 mg Sb/m^3 as antimony trioxide or 17.5 mg Sb/m^3 as antimony ore for 52 weeks (Groth et al. 1986) or rats exposed to 4.2 mg Sb/m^3 for 55 weeks (Watt 1983), lipoid pneumonia in rats exposed to 84–105 mg Sb/m^3 as antimony trioxide for 14.5 months (Gross et al. 1952), and focal hemorrhages in the lungs of rats exposed to 2.20 mg Sb/m^3 as antimony trisulfide for 6 weeks (Brieger et al. 1954).

The NTP (2016) 2-year antimony trioxide study also reported hyperplasia of the nasal respiratory epithelium in rats exposed to ≥2.5 mg Sb/m^3, squamous metaplasia of the respiratory epithelium in rats and mice exposed to 25 mg Sb/m^3, laryngeal epithelial hyperplasia in mice exposed to ≥8.3 mg Sb/m^3, and hyperplasia of tracheal epithelium in mice exposed to 25 mg Sb/m^3.

Oral exposure studies have not reported respiratory tract lesions in humans or laboratory animals. In the only human study examining respiratory endpoints, no significant association between urinary antimony levels and the prevalence of asthma was found among participants in the 2007–2008 NHANES (Mendy et al. 2012).

No histological alterations were observed in the respiratory tract in several oral exposure studies at the highest doses tested; the highest NOAEL values were 61 or 150 mg Sb/kg/day in rats or mice, respectively, exposed to antimony potassium tartrate in drinking water for 14 days (NTP 1992), 1,408 mg Sb/kg/day in rats exposed to antimony trioxide in the diet for 90 days (Hext et al. 1999), and 42.17 mg Sb/kg/day in rats exposed to antimony potassium tartrate in drinking water for 13 weeks (Poon et al. 1998).

No studies were located regarding respiratory effects in humans following dermal exposure to antimony. Hyperemia in the lungs was observed in a rabbit that died after six or eight applications of an antimony trioxide paste to shaven and abraded skin. The antimony trioxide (concentration not reported) was

combined with a mixture resembling acidic sweat (Fleming 1938). The application area was not occluded; thus, the ingestion of the paste likely occurred and the results of this study was not included in the LSE table.

2.5 CARDIOVASCULAR

Altered EKG readings were observed in workers exposed to 0.42–3.9 mg Sb/m^3 as antimony trisulfide for 8 months to 2 years (Brieger et al. 1954). Of the 75 workers examined, 37 showed changes in the EKG, mostly of the T-waves; these workers had also been exposed to phenol formaldehyde resin (Brieger et al. 1954). In a cohort mortality study, an increase in death from ischemic heart disease was observed among antimony smelter workers with Spanish surnames (Schnorr et al. 1995); the statistical significance of this finding was not reported. Guo et al. (2016) did not find an association between urinary antimony levels in NHANES participants and deaths from heart disease. However, the study did find association for the risks of self-reported heart disease, congestive heart failure, and heart attack; no associations were found for self-reported angina pectoris or coronary heart disease. Another study of NHANES participants did not find an association between urinary antimony levels and peripheral arterial disease (Navas-Acien et al. 2005).

These limited data on cardiovascular effects in humans are supported by the finding of cardiac effects following parenteral administration of antimony to humans. Alterations in EKGs, particularly prolongation of QT interval, have been reported following injection of sodium antimony tartrate (Honey 1960), sodium antimony gluconate (Dancaster et al. 1966; Lawn et al. 2006; Sundar et al. 1998; Thakur 1998), sodium stibogluconate (Pandey et al. 1988), and meglumine antimoniate (Neves et al. 2009). Whereas a very high incidence was reported in patients treated with sodium antimony tartrate (98%, with 30% categorized as severe EKG changes) (Honey 1960), a much lower incidence (8–25%) was found in patients treated with pentavalent antimony (Dancaster et al. 1966; Neves et al. 2009). The cardiotoxicity of antimony (Alvarez et al. 2005; Bromberger-Barnea and Stephens 1965; Cotten and Logan 1966) and the differences in the cardiotoxicity of trivalent and pentavalent antimony (Alvarez et al. 2005) are supported by animal studies. Whereas intramuscular injections of 16 mg Sb/kg/day as meglumine antimoniate for 26 days resulted in a slight prolongation of the QT duration in guinea pigs, intramuscular administration of 10 mg Sb/kg/day as antimony potassium tartrate for 8–12 days resulted in bradycardia and a more marked elongation of the QT interval (Alvarez et al. 2005).

Inhalation exposure to antimony trisulfide dust (dust sample taken from an antimony production facility) resulted in degenerative changes in the myocardium and related EKG abnormalities (elevation of the RS-T segments and flattening of T-waves) in a variety of animal species (Brieger et al. 1954). Five days of exposure to 19.9 mg Sb/m^3 as antimony trisulfide resulted in EKG alterations in rabbits. In intermediate-duration studies, EKG alterations were observed in rats, rabbits, and dogs exposed to 2–4 mg Sb/m^3 as antimony trisulfide for 6–10 weeks (Brieger et al. 1954). It should be noted that elevated levels of arsenic were also present in the facilities' dust samples. This study also reported degenerative changes of the myocardium in rats, rabbits, and dogs exposed to antimony trisulfide, which consisted of hyperemia and swelling of myocardial fibers (Brieger et al. 1954). Most studies with antimony trioxide exposure did not find cardiovascular effects. No EKG alterations were observed in pigs exposed to 4.2 mg Sb/m^3 as antimony trioxide for 1 year (Watt 1983) or guinea pigs exposed to 37.9 mg Sb/m^3 for an intermediate-duration (Dernehl et al. 1945), and myocardial damage was not observed in rats exposed to concentrations as high as 19.60 mg Sb/m^3 for 13 weeks (Newton et al. 1994) or 36 mg Sb/m^3 for approximately 1 year (Groth et al. 1986; Newton et al. 1994; Watt 1980) or guinea pigs exposed to 37.9 mg Sb/m^3 for 2–30 weeks (Dernehl et al. 1945). NTP (2016) found chronic inflammation of the epicardium of mice exposed to ≥8.3 mg Sb/m^3 for 2 years and chronic inflammation of muscular arteries in rats exposed to ≥8.3 mg Sb/m^3.

Several investigators have utilized the NHANES dataset to examine the possible association between antimony and cardiovascular toxicity. No significant associations were found between urinary antimony levels and the prevalence of congestive heart failure, coronary heart disease, angina pectoris, heart attack, or stroke (Mendy et al. 2012). In two studies, significant associations between urinary antimony levels and the prevalence of high blood pressure were found in adults (Shiue and Hristova 2014; Shiue 2014); antimony accounted for 6.2% of the population risk (Shiue and Hristova 2014).

No histopathological alterations were observed in the heart following acute-duration oral exposure of rats and mice to 61 or 150 mg Sb/kg/day as antimony potassium tartrate (NTP 1992) or following intermediate-duration exposure to 1,408 mg Sb/kg/day as antimony trioxide (Hext et al. 1999) or 42.17 mg Sb/kg/day as antimony potassium tartrate (Poon et al. 1998). In studies evaluating cardiovascular function, no significant alterations in blood pressure were observed in rats exposed to 0.7 mg Sb/kg/day as antimony trichloride during pregnancy and/or lactation (Angrisani et al. 1988; Marmo et al. 1987; Rossi et al. 1987) or rats chronically exposed to 0.63 mg Sb/kg/day as antimony potassium tartrate (Schroeder et al. 1970). Alterations in vasomotor responses were observed in pups exposed to antimony chloride; these effects are discussed under Developmental Effects.

No studies were located regarding cardiovascular effects in humans following dermal exposure to antimony. Application of 65 mg antimony as antimony sulfide in calcium cup grease did not result in alterations in EKG readings or heart pathology in rabbits (Horton et al. 1986).

Several *in vitro* studies have investigated the cardiotoxicity of antimony, particularly damage to the myocytes, which results in cell death and alterations and could lead to abnormalities in EKGs and arrhythmias. Tirmenstein (1995, 1997) found that exposure to antimony potassium tartrate resulted in several biochemical alterations in cardiac myocytes including the disruption of cellular thiol homeostasis, particularly the depletion of glutathione, induction of lipid peroxidation, and binding to vicinal thiols such as pyruvate dehydrogenase. The inhibition of pyruvate dehydrogenase subsequently leads to a decrease in cellular ATP levels. These biochemical alterations all contribute to cell death. Additionally, exposure to antimony potassium tartrate disrupts calcium homeostasis in myocytes. Wey et al. (1997) found a progressive elevation of resting (or diastolic) transient calcium levels in myocytes and an eventual cessation of beating activity that preceded cell death. Further investigations by this group found that antimony potassium tartrate reduced calcium availability during excitation-contraction and that there was a decreased flux of calcium through voltage-dependent L-type calcium channels in the myocyte (Toraason et al. 1997). The decreased influx of calcium was likely due to enhanced removal of calcium (Toraason et al. 1997). The investigators noted that the reduced influx and enhanced efflux of calcium could account for the reduced cardiac output observed in *in vivo* studies. Another study found that trivalent antimony increased cardiac calcium currents, resulting in a prolonged action potential (Kuryshev et al. 2006). The prolonged action potential results in a delay in cardiac repolarization, which could explain the QT prolongation observed in EKGs and arrhythmias in humans administered antimony for the treatment of leishmaniasis (Kuryshev et al. 2006). Similar findings were observed in myocytes exposed to pentavalent antimony, although the investigators concluded that this was likely due to the conversion of pentavalent antimony to trivalent antimony. Pentavalent antimony also increased sodium current amplitude, which was not observed in trivalent antimony exposed myocytes. However, the change in sodium current amplitude was not likely to contribute to arrhythmia since it was not accompanied by any obvious changes in channel gating (Kuryshev et al. 2006).

2.6 GASTROINTESTINAL

A variety of gastrointestinal symptoms have been reported in workers with acute exposure to antimony trichloride (Taylor 1966) and chronic exposure to antimony trisulfide (Brieger et al. 1954) or antimony

oxide (Renes 1953). The symptoms include abdominal pain, diarrhea, vomiting, and ulcers. A causal relationship to antimony exposure has not been definitely established because workers were exposed to a variety of other agents, in addition to antimony, that might cause or contribute to gastrointestinal effects (e.g., hydrogen chloride, sodium hydroxide), and the studies did not examine unexposed workers. Furthermore, in all likelihood, both inhalation and oral exposure to antimony occur at the workplace. Assuming that gastrointestinal effects are related to antimony exposure, site monitoring data indicate that effective exposure levels may range from approximately 2 to 70 mg Sb/m^3.

Symptoms of gastrointestinal disturbances were not reported in animals exposed to airborne antimony compounds, and no histopathological alterations were observed in rats exposed to ≤36 mg Sb/m^3as antimony trioxide or 17.5 mg Sb/m^3 as antimony ore for 1 year (Groth et al. 1986; Watt 1980) or pigs exposed to 4.2 mg Sb/m^3 as antimony trioxide for 55 weeks (Watt 1983). However, chronic active inflammation was observed in the forestomach of mice exposed to 25 mg Sb/m^3 as antimony trioxide for 2 years (NTP 2016).

Shortly after drinking lemonade contaminated with antimony potassium tartrate, workers began to vomit (Dunn 1928). Vomiting was observed in dogs following a single exposure to antimony potassium tartrate (Houpt et al. 1984). Other studies have not reported overt signs of gastrointestinal effects in rats or mice following acute- or intermediate-duration exposures to antimony trioxide or antimony potassium tartrate (Fleming 1938; Hext et al. 1999; NTP 1992; Poon et al. 1998). Focal ulceration was observed in the forestomach of mice exposed to 150 mg Sb/kg/day as antimony potassium tartrate for 2 weeks (NTP 1992). Histological alterations were not observed in rats (Hext et al. 1999; NTP 1992; Poon et al. 1998).

No studies were located regarding gastrointestinal effects in humans following dermal exposure to antimony. Hemorrhages in the cardiac portion of the stomach were observed in a rabbit that died after six or eight applications of an antimony trioxide-acidic sweat paste (Fleming 1938). Because the application area was not occluded, ingestion of the paste is possible; the results of this study was therefore not included in the LSE table.

2.7 HEMATOLOGICAL

Information on the hematological toxicity of inhaled antimony is limited to a case report of three workers exposed to stibine, arsine, and hydrogen sulfide (Dernehl et al. 1944). Two of the three workers reported hematuria with weakness, headache, and abdominal and lumbar pain. It is not known if stibine was the

causative agent of these effects. No studies were located regarding hematological effects in humans after inhalation exposure to other antimony compounds.

Toxicologically significant hematological effects have not been observed in rats and pigs following intermediate- or chronic-duration inhalation exposure to antimony aerosols ranging from approximately 4 to 20 mg Sb/m^3 as antimony trioxide (Newton et al. 1994; Watt 1983). One study reported decreases in total leukocyte counts and in polymorphonuclear leukocyte and eosinophil counts in guinea pigs exposed to 36.9 mg Sb/m^3 as antimony trioxide for 2–30 weeks (Dernehl et al. 1945) and another study reported hematopoietic cell proliferation in the spleen of female mice exposed to 25 mg Sb/m^3 for 2 years (NTP 2016).

No studies were located regarding hematological effects in humans after oral exposure to antimony. Animal studies have examined potential hematological effects of three antimony compounds (metallic antimony, antimony trioxide, and antimony potassium tartrate) following intermediate-duration exposure. No alterations in hemoglobin levels or hematocrit were observed in rats exposed to 850 mg Sb/kg/day as metallic antimony; however, a decrease in hematocrit level was observed 4 weeks postexposure (Hiraoka 1986). In a second study, no consistent dose-related alterations in red blood cell counts were observed in rats exposed to 370–1,500 mg Sb/kg/day; however, significant decreases in hemoglobin and hematocrit were observed at 1,500 mg Sb/kg/day (Sunagawa 1981). Mixed results were found for antimony trioxide. Smyth and Thompson (1945) reported an increase in red blood cell count in rats at 894 mg Sb/kg/day and Sunagawa (1981) reported a decrease in red blood cell counts at 620 mg Sb/kg/day; neither study found alterations in hemoglobin levels. In contrast, no alterations in hematological parameters (including red blood cell counts) were found in rats exposed to 700 mg Sb/kg/day (Hiraoka 1986) or 1,408 mg Sb/kg/day (Hext et al. 1999). Decreases in red blood cell and platelet counts were observed in male rats exposed to 42.17 mg Sb/kg/day as antimony potassium tartrate; no effects were found in female rats (Poon et al. 1998). The inconsistent findings across studies and compounds preclude determining whether antimony adversely affects the hematological system.

No studies were located regarding hematological effects in humans following dermal exposure to antimony. No alterations in hematological indices were observed in rabbits exposed to 65 mg antimony as antimony sulfide for 13 weeks (Horton et al. 1986).

2.8 MUSCULOSKELETAL

No studies were located regarding musculoskeletal effects in humans after inhalation exposure to antimony. No histopathological alterations were noted in the musculoskeletal system in rats exposed to 4.2 mg Sb/m^3 as antimony trioxide for 1 year (Watt 1980). Bone marrow hyperplasia was observed in rats exposed to 25 mg Sb/m^3 and mice exposed to ≥2.5 mg Sb/m^3 for 2 years (NTP 2016); the investigators noted that the hyperplasia in the mice was predominantly of myeloid cell type, which may have been secondary to the lung inflammation.

Shiue (2015) found a significant association between urinary antimony levels and one of the three clinical measures of ankylosing spondylitis among adults participating in the NHANES; however, no associations were found for the other two measures of ankylosing spondylitis. No histological alterations in musculoskeletal tissue were observed in rats or mice acutely exposed to 61 or 150 mg Sb/kg/day as antimony potassium tartrate (NTP 1992) or in rats exposed to 1,408 mg Sb/kg/day as antimony trioxide for 90 days (Hext et al. 1999).

2.9 HEPATIC

No studies were located regarding hepatic effects in humans after inhalation exposure to antimony. Parenchymatous or fatty degeneration was observed in rabbits exposed to 19.9 mg Sb/m^3 as antimony trisulfide for 5 days (Brieger et al. 1954) and in guinea pigs exposed to 37.9 mg Sb/m^3 as antimony trioxide for 2–30 weeks (Dernehl et al. 1945). No hepatic effects were observed in rats exposed to ≤36 mg Sb/m^3 as antimony trioxide for 1 year (Groth et al. 1986; Watt 1983) or 17.5 mg Sb/m^3 as antimony ore (Groth et al. 1986), or in rats or mice exposed to 25 mg Sb/m^3 as antimony trioxide for 2 years (NTP 2016).

Mendy et al. (2012) did not find a significant association between urinary antimony levels and liver conditions among NHANES participants. Minimal to mild hepatocellular cytoplasmic vacuolization, primarily in the centrilobular region, was observed in mice exposed to 150 mg Sb/kg/day as antimony potassium tartrate for 2 weeks (NTP 1992). Minimal cloudy swelling of the hepatic cords has been observed in rats exposed to 620 mg Sb/kg/day as antimony trioxide or 740 mg Sb/kg/day as metallic antimony for 24 weeks (Sunagawa 1981). Increases in the incidence of nuclear anisokaryosis and hepatocellular portal density were observed in all groups of rats exposed to antimony potassium tartrate in the drinking water for 13 weeks (Poon et al. 1998); the severity of either alteration was considered mild in

males at ≥5.58 mg Sb/kg/day and in females at ≥0.64 mg Sb/kg/day. However, these alterations are adaptative changes and were not considered to be biologically adverse. Other studies have not found hepatic effects at doses as high as 61 mg Sb/kg/day as antimony potassium tartrate in rats for 14 days (NTP 1992), 1,408 mg Sb/kg/day as antimony trioxide in rats for 90 days (Hext et al. 1999), or 0.35 mg Sb/kg/day as antimony potassium tartrate in mice for lifetime exposure (Kanisawa and Schroeder 1969).

Two studies reported alterations in serum cholesterol levels in rats exposed to antimony potassium tartrate; however, one study reported a decrease in female rats exposed to 45.69 mg Sb/kg/day (Poon et al. 1998), and the other reported an increase in rats exposed to 0.63 mg Sg/kg/day (Schroeder et al. 1970).

No studies were located regarding hepatic effects in humans following dermal exposure to antimony. No alterations in serum clinical chemistry parameters or histopathology of the liver were observed in rabbits exposed to 65 mg antimony as antimony sulfide for 13 weeks (Horton et al. 1986).

2.10 RENAL

No studies were located regarding renal effects in humans after inhalation, oral, or dermal exposure to antimony. A small number of laboratory animal studies have reported renal effects following inhalation or dermal exposure to antimony. In acute-duration inhalation studies, tubular dilation was observed in guinea pigs exposed to 799 mg Sb/m^3 as stibine gas for 30 minutes (NIOSH 1979) and parenchymatous degeneration was observed in rabbits exposed to 19.9 mg Sb/m^3 as antimony trisulfide for 5 days (Brieger et al. 1954). A 2-year inhalation exposure antimony trioxide study reported an increase in hyaline droplet accumulation at ≥8.3 mg Sb/m^3 in female rats and 25 mg Sb/m^3 in males and nephropathy at 25 mg Sb/m^3 in female rats (NTP 2016). Increases in blood urea nitrogen and creatinine levels were observed in male rabbits dermally exposed to 65 mg antimony as antimony sulfide; however, the levels were within the normal species variation and no histological alterations were observed in the kidneys (Horton et al. 1986). Other chronic inhalation studies and oral studies have not reported renal effects. No renal histological alterations were noted in rats exposed via inhalation to 17.5 mg Sb/m^3 as antimony ore or up to 36 mg Sb/m^3 as antimony trioxide for 1 year (Groth et al. 1986; Watt 1983) or in mice exposed to 25 mg Sb/m^3 as antimony trioxide for 2 years (NTP 2016). Similarly, no histological alterations were observed in the kidneys of rats and mice acutely exposed to 61 or 150 mg Sb/kg/day as antimony potassium tartrate (NTP 1992), rats exposed to ≤1,408 mg Sb/kg/day as antimony trioxide for an intermediate duration (Hext et al. 1999; Smyth and Thompson 1945), or rats exposed to 42.17 mg Sb/kg/day as antimony potassium tartrate for an intermediate duration (Poon et al. 1998).

2.11 DERMAL

Dermal effects have been reported in workers exposed to antimony oxides. These effects are likely due to direct skin contact with the antimony. Several studies have reported dermatitis in workers exposed to airborne antimony dust (Potkonjak and Pavlovich 1983). The dermatitis associated with exposure to airborne antimony is characterized as epidermal cellular necrosis with associated acute inflammatory cellular reactions (Stevenson 1965). The dermatitis is seen more often during the summer months and in workers exposed to high temperatures (Potkonjak and Pavlovich 1983; Stevenson 1965). Stevenson (1965) concluded that the dermatitis resulted from the action of antimony trioxide on the dermis after dissolving in sweat and penetrating the sweat glands. Transferring the worker to a cooler environment often resulted in the rash clearing up within 3–14 days. Antimony trioxide is not a skin sensitizer in humans following topical application (see Section 2.14).

In general, animal studies involving exposure to airborne antimony have not reported dermal effects (Groth et al. 1986; Newton et al. 1994). In a 13-week rat study (Newton et al. 1994 as reported in Bio/Dynamics 1985), alopecia was observed in females exposed to 0.902 or 4.11 mg Sb/m^3, but not females exposed to 19.60 mg Sb/m^3 or in males. Additionally, alopecia was not observed in a 1-year study conducted by this group (Newton et al. 1994). No dermal effects were observed in rats exposed to antimony trioxide in drinking water for 13 weeks at doses as high as 42.17 mg Sb/kg/day (Poon et al. 1998).

No evidence of skin irritation were observed in rabbits dermally exposed to 20,900 mg antimony as antimony trioxide (Gross et al. 1955). An intermediate-duration dermal exposure study did not report antimony-related skin irritation in rabbits exposed to 65 mg antimony as antimony sulfide (Horton et al. 1986); hyperkeratosis was observed in the vehicle control and antimony groups at similar incidences.

2.12 OCULAR

Eye irritation and damage has been observed in humans and animals exposed to airborne antimony or following instillation into the eye. Eye irritation was reported in 27.5% of workers at an antimony smelter; it is unclear if this was due to antimony oxides or other constituents in the smelter dust (Potkonjak and Pavlovich 1983). Eye irritation and closure were observed in rats exposed to ≥799 mg Sb/m^3 as stibine gas (NIOSH 1979); eye irritation was not noted in similarly exposed guinea pigs (NIOSH

1979). Exposure to airborne antimony trioxide resulted in corneal opacities in rats exposed to ≥0.21 mg Sb/m^3 for 13 weeks (Newton et al. 1994), and cataracts (focal posterior cataracts, posterior subcapsular cataracts, and complete cataracts) were observed in rats exposed to ≥0.43 mg Sb/m^3 for 1 year followed by a 1-year recovery period (Newton et al. 1994). An increase in the incidence of chromodacryorrhea was also observed in the chronic study; the investigators suggested that this may have been secondary to dental abnormality, infectious disease, or xerosis. NTP (2016) reported an increased incidence of ciliary body inflammation in rats exposed to 25 mg Sb/m^3 for 2 years. A non-concentration-related increase in retinal atrophy was also observed in female rats exposed to ≥2.5 mg Sb/m^3 (NTP 2016); the severity of the atrophy was similar to that observed in the concurrent controls. It is not known if these effects are due to direct contact or are systemic effects. Instillation of 66 mg antimony as antimony sulfide into the eyes of rabbits resulted in eye irritation (Horton et al. 1986).

No histological alterations were observed in the eyes of rats exposed to 1,408 mg Sb/kg/day as antimony trioxide for 90 days (Hext et al. 1999).

No evidence of eye irritation was observed in rabbits following instillation of 84 mg antimony as antimony trioxide (Gross et al. 1955). In contrast, conjunctival erythema, chemosis, and ocular discharge were observed 24 hours after instillation of 66 mg antimony as antimony sulfide (Horton et al. 1986). Seven day post-exposure, superficial corneal injury was observed in a third of the rabbits.

2.13 ENDOCRINE

Histological alterations have not been observed in the thyroid glands of laboratory animals following chronic exposure to concentrations as high as 36 mg Sb/m^3 as antimony trioxide (Groth et al. 1986; NTP 2016; Watt 1983) or 17.5 mg Sb/m^3 as antimony ore (Groth et al. 1986).

No significant association between urinary antimony levels and self-reported thyroid conditions were found in NHANES participants (Mendy et al. 2012). In general, oral studies examining endocrine organs have not reported adverse effects at 61 or 150 mg Sb/kg/day as antimony potassium tartrate in rats and mice exposed for 14 days (NTP 1992) or in rats exposed to 1,408 mg Sb/kg/day as antimony trioxide for 90 days (Hext et al. 1999). Poon et al. (1998) reported minimal to mild epithelial changes in the thyroid of rats exposed to ≥0.06 mg Sb/kg/day; however, the alterations were not dose-related and did not appear to affect thyroid function, and the investigators did not consider them adverse.

2.14 IMMUNOLOGICAL

Two studies examined the possible immunotoxicity of antimony in workers. Both studies evaluated serum immunoglobin levels. Kim et al. (1999) reported decreases in IgG2 and IgE levels in antimony trioxide workers. Wu and Chen (2017) also reported decreases in serum IgG, IgA, and IgE levels among antimony trioxide and sodium antimonite workers. This study also found significant inverse correlations between air antimony levels and IgG, IgA, and IgE levels and between blood, urine, and hair antimony levels and IgA and IgE levels.

No animal studies evaluated immune function following inhalation exposure to antimony. In chronic-exposure studies, hyperplasia of the reticuloendothelial cells in the peribronchiolar lymph nodes was observed in female rats exposed to 3.8 mg Sb/m^3 as antimony trioxide for 1 year with a 1-year recovery period (Newton et al. 1994), and lymphoid hyperplasia was observed in the bronchial and mediastinal lymph nodes of rats and mice exposed to ≥2.5 mg Sb/m^3 as antimony trioxide for 2 years (NTP 2016). Another study reported the presence of mononuclear cell granulomas in rats exposed to17.5 mg Sb/m^3 as antimony ore for 1 year (Groth et al. 1986); this effect was not found in rats similarly exposed to 36 mg Sb/m^3 as antimony trioxide (Groth et al. 1986). The investigators noted that the granulomas were similar to those found in the early stages of silicosis and sarcoidosis.

No studies were located regarding immunological effects in humans after oral exposure to antimony. Limited information on the immunotoxicity of antimony is available in animals. In the thymus of rats exposed to antimony potassium tartrate for 13 weeks, increases in medullary volume were observed in males exposed to ≥0.56 mg Sb/kg/day and in females exposed to ≥6.13 mg Sb/kg/day; a decrease in cortical volume was also observed in females exposed to ≥6.13 mg Sb/kg/day (Poon et al. 1998). The biological significance of these findings is not known.

No studies were located regarding immunological effects in humans following dermal exposure to antimony. In a skin sensitization assay, 6.6 mg antimony as antimony sulfide in liquid petrolatum did not result in sensitization in guinea pigs (Horton et al. 1986). When the antimony sulfide was administered in calcium cup grease, a positive result for sensitization was found; however, this was likely due to the vehicle, since no reaction was found when antimony sulfide in petrolatum was used as the challenge agent (Horton et al. 1986).

2.15 NEUROLOGICAL

A causal relationship between exposure to airborne antimony and neurological effects in humans has not been established. Nerve tenderness and a tingling sensation, headaches, and prostration were reported in workers exposed to antimony oxide at a concentration of 10.07 mg Sb/m^3 (Renes 1953). However, the factory workers were also exposed to arsenic, lead, copper, and possibly hydrogen sulfide and sodium hydroxide. Thus, it is difficult to determine if this effect was the result of antimony exposure. Another study attempted to link air monitoring levels of antimony with the risk of Parkinson's disease in nurses and did not find a significant association (Palacios et al. 2014); it should be noted that the air concentrations were very low (the median level in the highest quartile was 0.000682 μg/m^3). In a study utilizing the NHANES database, Scinicariello et al. (2017) found associations between urinary antimony levels and several self-reported sleep-related disorders including insufficient sleep duration (≤6 hours/night), prolonged sleep-onset latency (>30 minutes per night), obstructive sleep apnea, sleep problems, and day-time sleepiness.

Several studies have evaluated the possible relationship between urinary or hair antimony and autism or autism spectrum disorder. Studies of children have not found significant differences between hair antimony or urine antimony levels in children with autism or autism spectrum disorder compared to controls (Adams et al. 2006; Blaurock-Busch et al. 2011; Fido and Al-Saad 2005). A fourth study found no association between urinary antimony levels and autism severity (Adams et al. 2013). A meta-analysis of four studies (Adams et al. 2006; Blaurock-Busch et al. 2011; Fido and Al-Saad 2005; Saghazadeh and Rezaei 2017) found slightly higher hair antimony levels among children with autistic spectrum disorder than in controls (standardized mean difference 0.24, 95% confidence interval [CI] 0.03–0.45) (Saghazadeh and Rezaei 2017). It is noted that the observational studies and the meta-analysis did not account for potential confounding factors and was based a small number of subjects (181 cases and 185 controls in the meta-analysis).

None of the available laboratory animal studies adequately examined the potential neurotoxicity of antimony following inhalation, oral, or dermal exposure. No histological alterations were observed in the brains following acute- and intermediate-duration oral exposure (Hext et al. 1999; NTP 1992; Poon et al. 1998) or chronic-duration inhalation exposure to antimony trioxide (Groth et al. 1986; NTP 2016; Watt 1983).

2.16 REPRODUCTIVE

Disturbances in the menstrual cycle were reported in 61.2% of women exposed to airborne metallic antimony, antimony pentasulfide, and antimony trioxide in a metallurgical plant compared to the 35.7% occurrence in controls (Belyaeva 1967); no other details were provided. No information (such as age and whether they had similar jobs as the workers) was provided that could be used to evaluate the appropriateness of the control group. The investigators noted that 77.5% of the workers and 56% of the controls had reproductive disturbances. The study also found an increase in the rate of spontaneous abortions (particularly late term abortions) in the workers (12.5%) as compared to the rate in controls (4.1%). In a study of men of subfertile couples, no associations between urinary antimony levels and reproductive hormone levels (estradiol, follicle stimulating hormone, testosterone, or sex hormone-binding hormone) were reported (Wang et al. 2016).

Data on the reproductive toxicity of inhaled antimony are limited to an intermediate-duration study conducted by Belyaeva (1967), which found a reduction in fertility (67% conceived compared to 100% in controls) in rats exposed to 209 mg Sb/m^3 as antimony trioxide. No histological alterations were observed in the reproductive tissues of rats exposed to antimony trioxide or antimony ore for 1 year (Groth et al. 1986; Watt 1983) or mice exposed to antimony trioxide for 2 years (NTP 2016). Increases in the incidence of epithelial hyperplasia were observed in the prostate of rats exposed to 2.5 or 8.3 mg Sb/m^3 for 2 years (NTP 2016).

No studies were located regarding reproductive effects in humans after oral exposure to antimony. Information on the reproductive toxicity of antimony in laboratory animals is limited to a series of experiments conducted by Omura et al. (2002). No significant alterations in sperm count, motility, or morphology or histological alterations of the testes were observed in rats and mice exposed to 1,000 mg Sb/kg/day as antimony trioxide or 10 mg Sb/kg/day as antimony potassium tartrate.

2.17 DEVELOPMENTAL

The study of women working at a metallurgical facility (Belyaeva 1967) also reported decreases in infant body weight gain beginning at 6 months of age; at 12 months of age, they weighed 11% less than infants from the control group. Interpretation of the results of this study is limited by the lack of information on the control group, type of work the women performed, when the workers returned to work after giving birth, and information on confounding exposure to other compounds. A second epidemiological study

evaluated possible associations between urinary antimony levels and birth outcomes in participants of the Longitudinal Investigation of Fertility and the Environment study (Bloom et al. 2015). No associations between maternal or paternal urinary antimony levels and gestational age, birth weight, birth length, head circumference, ponderal index, or newborn sex were found.

A decreased number of offspring was observed in rats exposed to 209 mg Sb/m^3 as antimony trioxide prior to conception and throughout gestation. No difference in fetal body weights was observed (Belyaeva 1967).

A case-control study examined the possible relationship between levels of metals in drinking water and neural tube defects and did not find a significant association for antimony (Longerich et al. 1991). Zheng et al. (2014) found significantly higher median umbilical cord antimony levels in women with adverse pregnancy outcomes, but did not find a statistically significant association between antimony and adverse pregnancy outcomes. See Table 2-1 for more information on these studies.

Decreases in growth on postnatal days (PNDs) 10–22 were observed in the pups of rats exposed to 0.7 mg Sb/kg/day during gestation and lactation (Rossi et al. 1987); a decrease in maternal body weight gain was also observed at these doses. No differences in the number of newborn pups per litter or macroscopic teratogenic effects were observed in the offspring of rats treated during gestation with 0.7 mg Sb/kg/day as antimony trichloride (Rossi et al. 1987).

Studies by Angrisani et al. (1988) and Rossi et al. (1987) (data from both studies were also reported in Marmo et al. 1987) suggest that antimony may interfere with the normal development of the cardiovascular system. Alterations in vasomotor reactivity were observed in 30- and 60-day-old pups exposed during gestation and/or lactation and from weaning to PND 60; the estimated dose during the postnatal period was 0.1 mg Sb/kg/day. However, no alterations in arterial blood pressure were observed. Although the investigators describe this as altered development, comparisons were not made between the vasomotor responses in mature rats and in pups.

Three parenteral studies have evaluated the developmental toxicity of pentavalent antimony. Subcutaneous administration of 300 mg Sb/kg as meglumine antimoniate or intramuscular administration of 100 or 300 mg Sb/kg/day as sodium stibogluconate or meglumine antimoniate to rats during gestation or during gestation and lactation resulted in decreases in birth weight and number of viable offspring (Alkhawajah et al. 1996; Coelho et al. 2014a; Miranda et al. 2006). Intramuscular administration of

100 mg Sb/kg/day as antimony trichloride also resulted in decreases in viable fetuses and fetal body weight (Alkhawajah et al. 1996). Increases in resorptions were also observed in rats administered ≥100 mg Sb/kg/day as sodium stibogluconate, meglumine antimoniate, or antimony trichloride (Alkhawajah et al. 1996). Miranda et al. (2006) also found a significant increase in dilated ureters following gestation exposure; no other external or visceral abnormalities were found. No alterations in neurological development or sperm counts were observed in offspring exposed during gestation and lactation (Coelho et al. 2014a).

2.18 OTHER NONCANCER

Epidemiological and laboratory animal studies have evaluated several other noncancer effects: diabetes and alterations in blood glucose levels, gout, and spleen damage. Menke et al. (2016) reported an association between urinary antimony levels and the risk of diabetes among NHANES participants. The association was found among all participants and among participants who were current smokers or former smokers, but was not found among never smokers. An association was also found between urinary antimony and homeostatic model assessment of insulin resistance (HOMA-IR); this association was found among all participants and among participants without diabetes (Menke et al. 2016). Two oral exposure studies in rats have reported significant decreases in serum glucose levels following exposure to antimony potassium tartrate. In an intermediate-duration study, dose-related decreases in serum glucose levels were observed in female rats at ≥0.64 mg Sb/kg/day (Poon et al. 1998); the investigators did not report whether blood samples were from fasting or nonfasting rats. ATSDR notes that the serum glucose levels in all groups (including controls) were higher than the normal range reported by the animal supplier (Charles River Laboratories 2006). Decreases in nonfasting glucose were observed in male and female rats exposed for a lifetime to 0.63 mg Sb/kg/day as antimony potassium tartrate (Schroeder et al. 1970); no significant alterations in fasting glucose levels were found. Alterations in blood glucose levels have also been observed in parenteral studies. Significant decreases in blood glucose levels were observed in rats exposed to 900 mg Sb/kg/day as stibogluconate or 300 or 900 mg Sb/kg/day meglumine antimoniate administered via intramuscular injections for 30 days (Alkhawajah et al. 1992); the investigator did not note whether the animals were fasted prior to measurement of blood glucose levels.

Mendy et al. (2012) did not find a significant association between urinary antimony levels and the incidence of self-reported gout among NHANES participants.

Splenic sinus congestion in males at ≥0.56 mg Sb/kg/day, sinus hyperplasia in females at ≥0.64 Sb/kg/day and males at 42.17 Sb/kg/day, and arterial cuff atrophy in males at 42.17 mg Sb/kg/day were observed in rats exposed to antimony potassium tartrate (Poon et al. 1998).

2.19 CANCER

Several studies of antimony oxide workers have examined the carcinogenic potential of antimony. A positive trend in lung cancer deaths with increasing duration of employment was observed in workers at an antimony smelter facility (Schnorr et al. 1995). Similarly, another study of workers exposed to metallic antimony, antimony alloys, and antimony trioxide found increases in lung cancer deaths in workers hired prior to 1940 or between 1946 and 1950 (Jones 1994). In both studies, the workers were also exposed to arsenic and neither study included smoking status as a confounding variable

Four studies have evaluated the carcinogenicity of inhaled antimony trioxide in rats. Increases in lung neoplasms (squamous cell carcinomas, bronchioalveolar adenomas and carcinomas, and scirrhous carcinoma) were observed in female rats exposed to 4.2 mg Sb/m^3 for 55 weeks with a 1-year recovery period (Watt 1983) or 36 mg Sb/m^3 for 52 weeks with a 20-week recovery period (Groth et al. 1986). However, a third study (Newton et al. 1994) did not find any neoplasms in male or female rats exposed to 3.8 mg Sb/m^3 for 1 year with a 1-year recovery period. Newton et al. (1994) stated that a pathologist who examined the slides from the Groth et al. (1986), Watt (1983), and Newton et al. (1994) studies noted more extensive lung damage and a considerable higher amount of antimony trioxide in the lungs of rats tested in the Watt (1983) study as compared to those tested in the Newton et al. (1994) study even though the concentrations were similar, suggesting that the actual concentrations tested by Watt (1983) may have been higher than reported. A fourth study found significant increases in the incidence of alveolar/bronchiolar adenomas at 8.3 mg Sb/m^3 and benign pheochromocytomas in the adrenal gland of rats exposed to 25 mg Sb/m^3 for 2 years (NTP 2016). Increases in lung neoplasms were also observed in rats exposed to 17.5 mg Sb/m^3 as antimony ore for 52 weeks followed by a 1-year recovery period (Groth et al. 1986). In mice, a 2-year exposure to antimony trioxide resulted in significant increases in alveolar/bronchiolar adenomas, carcinomas, or combined incidences at ≥2.5 mg Sb/m^3, malignant lymphomas in females exposed to ≥2.5 mg Sb/m^3, and fibrous histiocytomas in the skin of males exposed to 25 mg Sb/m^3 (NTP 2016). No increases in lung tumors were observed in pigs exposed to 4.2 mg Sb/m^3 as antimony trioxide (Watt 1983).

Three epidemiology studies evaluated the possible association between antimony and cancer incidence associated with environmental exposure (see Table 2-1). Colak et al. (2015) found an association between antimony levels in drinking water samples and cancer incidence among populations of three Turkish cities; the antimony levels in the water were <20 μg/L. Guo et al. (2016) and Mendy et al. (2012) did not find associations between urinary antimony levels and self-reported cancer among adult NHANES participants; Guo et al. (2016) also did not find an association with cancer deaths.

No alterations in neoplastic lesion incidence were observed in rats (Schroeder et al. 1970) or mice (Kanisawa and Schroeder 1969) orally exposed 0.63 or 0.35 mg Sb/kg/day, respectively, as antimony potassium tartrate in drinking water for a lifetime. The use of these studies to assess carcinogenicity is limited because only one exposure level was used, which was below the maximum tolerated dose.

HHS (NTP 2018) categorized antimony trioxide as reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity from experimental animal studies and supporting mechanistic data. IARC (2015) has determined that antimony trioxide is possibly carcinogenic to humans (Group 2B) and antimony trisulfide is not classifiable as to carcinogenicity in humans (Group 3). The EPA has not evaluated the carcinogenicity of antimony.

2.20 GENOTOXICITY

The genotoxicity of trivalent and pentavalent antimony has been evaluated in *in vivo* studies in humans, rats, and mice and in *in vitro* studies in bacterial and mammalian systems. No alterations in micronuclei formation in reticulocytes or DNA damage in leukocytes or lung tissue (see Table 2-6) were observed in rats chronically exposed via inhalation to antimony trioxide (NTP 2016). In contrast, a similar exposure in mice resulted in increases in micronuclei formation in micronucleated mature erythrocytes (no alterations were found in reticulocytes) and increases in DNA damage in lung tissue (no alterations in leukocytes) (NTP 2016). As summarized in Table 2-6, most studies of antimony trioxide did not find clastogenic alterations in orally exposed (gavage administration) rats or mice (Elliott et al. 1998; Gurnani et al. 1992a, 1992b; Kirkland et al. 2007). One study (Gurnani et al. 1992a, 1993) found significant increases in chromosomal aberrations in mice bone marrow cells following repeated exposure to antimony trioxide; no significant alterations were found following a single exposure. However, other studies testing similar doses did not find increases in chromosomal aberrations (Kirkland et al. 2007) or micronuclei formation (Elliott et al. 1998; Kirkland et al. 2007) following repeated exposure. One occupational exposure study of workers exposed to a flame retardant containing antimony trioxide did not

find increases in the occurrence of micronuclei or sister chromatid exchange (Cavallo et al. 2002). Two studies of pentavalent organic antimony found positive results for micronuclei formation (Hantson et al. 1996; Lima et al. 2010) or DNA damage (Lima et al. 2010). A study of NHANES participants found an inverse association between telomer length and urinary antimony levels (Scinicariello and Buser 2016); when the participants were categorized by age, the associations were found in participants 40–85 years of age.

Table 2-6. Genotoxicity of Antimony *In Vivo*

Species (test system)	Endpoint	Results	Reference	Compound
Mouse bone marrow; single exposure (gavage)	Chromosomal aberrations	–	Gurnani et al. 1992a, 1992b	Antimony trioxide
Mouse bone marrow; 7–21 exposures (gavage)	Chromosomal aberrations	+	Gurnani et al. 1992a, 1993	Antimony trioxide
Rat bone marrow; single exposure (gavage)	Chromosomal aberrations	–	Kirkland et al. 2007	Antimony trioxide
Rat bone marrow; 7–21 exposures (gavage)	Chromosomal aberrations	–	Kirkland et al. 2007	Antimony trioxide
Human peripheral lymphocytes (intramuscular)	Chromosomal aberrations	–	Hantson et al. 1996	Meglumine antimonate
Human peripheral lymphocytes (inhalation)	Micronuclei formation	–	Cavallo et al. 2002	Antimony trioxide
Human peripheral lymphocytes (intramuscular)	Micronuclei formation	+	Hantson et al. 1996	Meglumine antimonate
Rat reticulocytes 12-month exposure (inhalation)	Micronuclei formation	–	NTP 2016	Antimony trioxide
Mouse reticulocytes 12-month exposure (inhalation)	Micronuclei formation	–	NTP 2016	Antimony trioxide
Mouse micronucleated mature erythrocytes 12-month exposure (inhalation)	Micronuclei formation	+	NTP 2016	Antimony trioxide
Mouse bone marrow (gavage)	Micronuclei formation	+	Lima et al. 2010	N-Methyl-glucamine antimonate
Mouse bone marrow; single exposure (gavage)	Micronuclei formation	–	Elliott et al. 1998	Antimony trioxide
Mouse bone marrow; 7–21 exposures (gavage)	Micronuclei formation	–	Elliott et al. 1998	Antimony trioxide
Rat bone marrow; single exposure (gavage)	Micronuclei formation	–	Kirkland et al. 2007	Antimony trioxide
Rat bone marrow; 7–21 exposures (gavage)	Micronuclei formation	–	Kirkland et al. 2007	Antimony trioxide
Human peripheral lymphocytes (inhalation)	Sister chromatid exchange	–	Cavallo et al. 2002	Antimony trioxide

Table 2-6. Genotoxicity of Antimony *In Vivo*

Species (test system)	Endpoint	Results	Reference	Compound
Human peripheral lymphocytes (intramuscular)	Sister chromatid exchange	–	Hantson et al. 1996	Meglumine antimonate
Rat leukocytes 12-month exposure (inhalation)	DNA damage (comet assay)	–	NTP 2016	Antimony trioxide
Rat lung tissue samples 12-month exposure (inhalation)	DNA damage (comet assay)	–	NTP 2016	Antimony trioxide
Mouse leukocytes 12-month exposure (inhalation)	DNA damage (comet assay)	–	NTP 2016	Antimony trioxide
Mouse lung tissue samples 12-month exposure (inhalation)	DNA damage (comet assay)	+	NTP 2016	Antimony trioxide
Mouse peritoneal macrophages (gavage)	DNA damage	+	Lima et al. 2010	N-Methyl-glucamine antimonate
Rat liver (gavage)	DNA repair	–	Elliott et al. 1998	Antimony trioxide
Mouse sperm (gavage)	Sperm head abnormalities	–	Gurnani et al. 1992a, 1993	Antimony trioxide

– = negative result; + = positive result; DNA = deoxyribonucleic acid

The results of *in vitro* genotoxicity studies are presented in Table 2-7. In general, no alterations in the occurrence of gene mutations were found in bacterial assays testing metallic antimony (Asakura et al. 2009), antimony trioxide (Elliott et al. 1998; Kuroda et al. 1991), antimony trichloride (Kubo et al. 2002; Kuroda et al. 1991), antimony pentachloride (Kuroda et al. 1991), or antimony pentoxide (Kuroda et al. 1991) or in mammalian assays with antimony thioantimonate (Tu and Sivak 1984) or antimony trioxide (Elliott et al. 1998). Evidence of DNA damage was observed for antimony trioxide, antimony trichloride, and antimony pentachloride in rec assays with *Bacillus subtilis* (Kanematsu et al. 1980; Kuroda et al. 1991). Unlike the *in vivo* data, most studies found increases in the occurrence of chromosomal aberrations (Asakura et al. 2009; Elliott et al. 1998; Paton and Allison 1972; Tu and Sivak 1984), micronuclei formation (Gebel et al. 1998a; Huang et al. 1998; Migliore et al. 1999; Schaumlöffel and Gebel 1998), and sister chromatid exchange (Kuroda et al. 1991) in mammalian cells exposed to trivalent antimony compounds or metallic antimony. Pentavalent antimony compounds were negative in sister chromatid exchange assays (Kuroda et al. 1991). Similarly, DNA damage was observed in mammalian cells exposed to antimony trichloride (Gebel et al. 1998a; Kopp et al. 2018; Schaumlöffel and Gebel 1998), but negative for pentavalent organic antimony (Lima et al. 2010); evidence of impaired repair of DNA double strand breaks was also observed for antimony trichloride (Koch et al. 2017).

Table 2-7. Genotoxicity of Antimony *In Vitro*

Species (test system)	Endpoint	Results		Reference	Compound
		With activation	Without activation		
Prokaryotic organisms					
Salmonella typhimurium TA100, TA1535, TA98, TA1537	Gene mutation (reverse mutation)	–	+[a]	Asakura et al. 2009	Metallic antimony
S. typhimurium TA100, TA1535, TA1537, TA98	Gene mutation (plate incorporation)	–	–	Elliott et al. 1998	Antimony trioxide
S. typhimurium TA100, TA98	Gene mutation (plate incorporation)	–	–	Kuroda et al. 1991	Antimony trioxide
S. typhimurium TA100, TA98	Gene mutation (Ames test)	–	–	Kubo et al. 2002	Antimony trichloride
S. typhimurium TA100, TA98	Gene mutation (plate incorporation)	–	–	Kuroda et al. 1991	Antimony trichloride
S. typhimurium TA100, TA1535, TA97, TA98	Gene mutation	–	–	Zeiger et al. 1992; NTP 1992	Antimony potassium tartrate
S. typhimurium TA100, TA98	Gene mutation (plate incorporation)	–	–	Kuroda et al. 1991	Antimony pentachloride
S. typhimurium TA100, TA98	Gene mutation (plate incorporation)	–	–	Kuroda et al. 1991	Antimony pentoxide
Escherichia coli WP2uvrA/pKM101	Gene mutation (reverse mutation)	–	–	Asakura et al. 2009	Metallic antimony
E. coli WP2P, WP2PuvrA	Gene mutation (plate incorporation)	–	–	Elliott et al. 1998	Antimony trioxide
E. coli PQ37	Gene mutation (SOS chemotest)	No data	–	Lantzsch and Gebel 1997	Antimony trichloride
Bacillus subtilis	DNA damage (rec assay)	No data	+	Kuroda et al. 1991	Antimony trioxide
B. subtilis	DNA damage (rec assay)	No data	+	Kanematsu et al. 1980	Antimony trioxide
B. subtilis	DNA damage (rec assay)	No data	+	Kanematsu et al. 1980	Antimony trichloride
B. subtilis	DNA damage (rec assay)	No data	+	Kuroda et al. 1991	Antimony trichloride
B. subtilis	DNA damage (rec assay)	No data	+	Kuroda et al. 1991 (	Antimony pentachloride
B. subtilis	DNA damage (rec assay)	No data	+	Kanematsu et al. 1980	Antimony pentachloride
B. subtilis	DNA damage (rec assay)	No data	–	Kuroda et al. 1991	Antimony pentoxide

Table 2-7. Genotoxicity of Antimony *In Vitro*

Species (test system)	Endpoint	Results		Reference	Compound
		With activation	Without activation		
Mammalian cells					
Chinese hamster ovary cells (HGPRT locus)	Gene mutation	–	–	Tu and Sivak 1984	Antimony thioantimonate
L5178Y mouse lymphoma	Gene mutation	–	–	Elliott et al. 1998	Antimony trioxide
Human leukocytes	Chromosomal aberrations	No data	+	Paton and Allison 1972	Antimony sodium tartrate
Human leukocytes	Chromosomal aberrations	+	+	Elliott et al. 1998	Antimony trioxide
Chinese hamster ovary cells	Chromosomal aberrations	+	+	Asakura et al. 2009	Metallic antimony
Chinese hamster ovary cells	Chromosomal aberrations	+	+	Tu and Sivak 1984	Antimony thioantimonate
Human bronchial epithelial cells (BES-6)	Micronuclei formation	No data	+	Huang et al. 1998	Antimony trichloride
Human fibroblasts	Micronuclei formation	No data	+	Huang et al. 1998	Antimony trichloride
Human lymphocytes	Micronuclei formation	No data	+	Schaumlöffel and Gebel 1998	Antimony trichloride
Human lymphocytes	Micronuclei formation	No data	+	Migliore et al. 1999	Potassium antimonate
V79 Chinese hamster cells	Micronuclei formation	No data	+	Gebel et al. 1998a	Antimony trichloride
Chinese hamster ovary cells	Micronuclei formation	No data	+	Huang et al. 1998	Antimony trichloride
V79 Chinese hamster ovary cells	Sister chromatid exchange	No data	+	Kuroda et al. 1991	Antimony trichloride
V79 Chinese hamster ovary cells	Sister chromatid exchange	No data	+	Kuroda et al. 1991	Antimony trioxide
V79 Chinese hamster ovary cells	Sister chromatid exchange	No data	–	Kuroda et al. 1991	Antimony pentachloride
V79 Chinese hamster ovary cells	Sister chromatid exchange	No data	–	Kuroda et al. 1991	Antimony pentoxide
Human lymphocytes	DNA damage (comet assay)	No data	+	Schaumlöffel and Gebel 1998	Antimony trichloride
Human lymphocytes	DNA damage (comet assay)	No data	–	Lima et al. 2010	N-Methyl-glucamine antimonate
HepG2 cells (human cell line)	DNA damage (γH2AX ICW assay)	No data	+	Kopp et al. 2018	Antimony trichloride

Table 2-7. Genotoxicity of Antimony *In Vitro*

Species (test system)	Endpoint	Results		Reference	Compound
		With activation	Without activation		
LS-174T cells (human cell line)	DNA damage (γH2AX ICW assay)	No data	+	Kopp et al. 2018	Antimony trichloride
V79 Chinese hamster cells	DNA damage (comet assay)	No data	+	Gebel et al. 1998a	Antimony trichloride
HeLa S3 cells	DNA repair (double strand break)	No data	+	Koch et al. 2017	Antimony trichloride

[a]Only positive for TA1537 strain.

– = negative result; + = positive result