Appendix F

Potential Health Effects of Pollutants Emitted from Cruise Ship Onboard Incineration

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This section summarizes the cancer and noncancer impacts that can result from exposure to pollutants emitted from cruise ship onboard incineration.

A. Arsenic (Inorganic)

Exposure to inorganic arsenic may result in both cancer and noncancer health effects. The probable route of human exposure to arsenic is by ingestion, inhalation, and permeation of skin or mucous membranes (ARB, 1997b). Table V-1 (in Chapter V) presents the current health effects values that are used in this health risk assessment for determining the potential health impacts.

1. Cancer

Evidence for carcinogenicity in humans due to inhaled arsenic is strong. Studies of workers in smelters and in the pesticide manufacturing industry have found strong, consistent associations between respiratory cancer and arsenic exposure. The effect on respiratory cancer rates of combining smoking and arsenic exposure appears to be greater than additive and at low doses may be as high as multiplicative (ARB, 1997b). Chronic exposure to high levels of arsenic in drinking water has been identified as increasing skin cancer incidence in humans (OEHHA, 2002).

The Office of Environmental Health Hazard Assessment (OEHHA) staff has performed an extensive assessment of the potential health effects of arsenic, reviewing available carcinogenicity data. OEHHA concluded that arsenic is a potential human carcinogen with no identifiable threshold below which no carcinogenic effects are likely to occur. The Air Resources Board (ARB/Board) formally identified arsenic as a toxic air contaminant (TAC) in July 1990 (ARB, 1990). Arsenic (inorganic arsenic compounds) was listed by the State of California under Proposition 65 as a carcinogen in February 1987 (OEHHA, 2005).

In 1990, the United States (U.S.) Congress listed arsenic as a hazardous air pollutant (HAP) in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). The United States Environmental Protection Agency (U.S. EPA) has classified inorganic arsenic as Group A, human carcinogen, based on sufficient epidemiological evidence (U.S. EPA, 2005). The International Agency for Research on Cancer (IARC) has classified inorganic arsenic and arsenic compounds as Group 1: Human carcinogen based on sufficient evidence in humans (IARC, 2005).

2. Noncancer

Acute inhalation exposure may result in severe irritation of the mucous membranes of the upper and lower respiratory tract with symptoms of cough, dyspnea, and chest pain. These may be followed by garlicky breath and gastrointestinal symptoms including vomiting and diarrhea. Signs of acute poisoning are dermatitis, nasal mucosal irritation, laryngitis, mild bronchitis, and conjunctivitis. The acute toxic symptoms of trivalent arsenic poisoning are due to severe inflammation of the mucous membranes and increased permeability of the capillaries. Inorganic arsenic compounds are easily absorbed through the skin; the trivalent is more rapidly absorbed than the pentavalent. Ingestion of two grams of arsenic trioxide was fatal to an adult male (OEHHA, 1999).

Persons with skin or respiratory conditions, including allergies, may be more sensitive to the toxic effects of arsenic. Persons with higher than normal intakes of arsenic, including smokers and fish and shellfish eaters, may be more sensitive to toxic effects following arsenic exposure (OEHHA, 1999).

Chronic inhalation exposure to inorganic arsenic in humans is associated with irritation of the skin and mucous membranes, while chronic oral exposure has resulted in gastrointestinal effects, anemia, peripheral neuropathy, skin lesions, and liver or kidney damage (ARB, 1997b).

Reports of human inhalation exposure to arsenic compounds, primarily epidemiological studies of smelter workers, indicate that adverse health effects occur as a result of chronic exposure. Among the targets of arsenic toxicity are the respiratory system, the circulatory system, the skin, the nervous system, and the reproductive system. Studies in experimental animals show that inhalation exposure to arsenic compounds can produce immunological suppression, developmental defects, and histological or biochemical effects on the nervous system and lung (OEHHA, 2000a).

The oxidation state of arsenic determines the teratogenic potential of its inorganic compounds; trivalent (III) arsenic compounds possess greater teratogenic potential than pentavalent (V) compounds. Chronic exposure to arsenic has been associated with decreased birth weight and an increased rate of spontaneous abortion in female smelter workers. However, this association is confounded by the presence of other toxicants in the smelting process, including lead (OEHHA, 1999). Arsenic (inorganic oxides) was listed by the State of California under Proposition 65 as developmental toxicants in May 1997 (OEHHA, 2005).

B. Beryllium

Exposure to beryllium may result in both cancer and noncancer health effects. The probable routes of human exposure to beryllium are inhalation ingestion, and dermal contact (ARB, 1997b). Table V-1 presents the current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

Several studies found increased incidences of lung cancer in beryllium processing workers (OEHHA, 2002). Beryllium is a federal HAP and was identified as a toxic air contaminant by the Board in April 1993 under AB 2728 (ARB, 1993). The OEHHA staff has performed an extensive assessment of the potential health effects of beryllium, reviewing available carcinogenicity data. OEHHA concluded that beryllium is a potential human carcinogen with no identifiable threshold below which no carcinogenic effects are likely to occur. Beryllium and beryllium compounds were listed by the State of California under Proposition 65 as carcinogens in October 1987 (OEHHA, 2005).

In 1990, the U.S. Congress listed beryllium compounds as HAPs in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). The U.S. EPA has classified beryllium as Group B1; probable human carcinogen (U.S. EPA, 2005). The International Agency for Research on Cancer has classified beryllium and beryllium compounds as Group 1: Human carcinogen (IARC, 2005).

2. Noncancer

Acute inhalation of high levels of beryllium can cause inflammation of the lungs in humans; these symptoms may be reversible after exposure ends (ARB, 1997b). The respiratory tract is the major target organ system in humans following the inhalation of beryllium. The common symptoms of chronic beryllium disease (CBD) include shortness of breath upon exertion, weight loss, cough, fatigue, chest pain, anorexia, and overall weakness. Most studies reporting adverse respiratory effects in humans involve occupational exposure to beryllium. Exposure to soluble beryllium compounds is associated with acute beryllium pneumonitis. Exposure to either soluble or insoluble beryllium compounds may result in obstructive and restrictive diseases of the lung, called chronic beryllium disease (berylliosis). The total number of beryllium-related disease cases has declined since the adoption of industrial standards (OEHHA, 2000a).

C. Cadmium

Exposure to cadmium may result in both cancer and noncancer health effects. The probable routes of human exposure to cadmium are inhalation and ingestion (ARB, 1997b). Table V-1 presents the current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

Epidemiological evidence strongly supports an association between cadmium exposure and neoplasia, including respiratory and renal cancers. Cancer resulting from inhalation exposure to several forms of cadmium has been reported in animal studies (ARB, 1997b).

OEHHA staff has performed an extensive assessment of the potential health effects of cadmium and compounds, reviewing available carcinogenicity data. OEHHA concluded that cadmium and compounds are potential human carcinogens with no identifiable threshold below which no carcinogenic effects are likely to occur. The Board formally identified cadmium and cadmium compounds as a TAC in January 1987 (ARB, 1986b). Cadmium and cadmium compounds were listed by the State of California under Proposition 65 as carcinogens in October 1987 (OEHHA, 2005).

In 1990, the U.S. Congress listed cadmium compounds as HAPs in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). The U.S. EPA classified cadmium in Group B1: Probable human carcinogen, based on human and animal studies showing an increase of lung cancer (U.S. EPA, 2005). The International Agency for Research on Cancer classified cadmium and cadmium compounds in Group 1: Human carcinogen based on epidemiological evidence of carcinogenicity in humans and carcinogenic effects observed in animals (IARC, 2005). There is limited evidence in experimental animals for the carcinogenicity of cadmium metal (ARB, 1997b).

2. Noncancer

Although ingestion is the major source of exposure, only one to ten percent of ingested cadmium appears to be absorbed systemically. Pulmonary absorption of inhaled cadmium is estimated to range from 10 to 50 percent of deposited cadmium. The biological half-life of cadmium in humans has been estimated to range from 10 to 30 years. Cadmium has moderate acute toxicity, producing gastrointestinal or pulmonary irritation effects from ingestion or inhalation, respectively. Subchronic and chronic exposures to cadmium have been associated with renal, cardiovascular, endocrine, hepatic, bone, hematological, and immunological effects. Respiratory conditions include bronchiolitis and emphysema. The U.S. EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, considers cadmium oxide to be a “high concern” pollutant based on severe acute toxicity (ARB, 1997b).

Human developmental studies are limited, although there is some evidence to suggest that maternal cadmium exposure may result in decreased birth weights. Cadmium oral exposure induces testicular necrosis in experimental animals, ovarian damage, infertility, placental toxicity and embryo and fetotoxicity and teratogenicity. Developmental effects such as decreased weight gain and neurobehavioral deficits have been reported in animal studies (ARB, 1997b). Cadmium was listed by the State of California under Proposition 65 as a male reproductive and developmental toxicant in May 1997 (OEHHA, 2005).

D. Chromium

Exposure to chromium and chromium compounds may result in both cancer and noncancer health effects. The probable routes of human exposure to chromium compounds are inhalation, ingestion, and dermal contact (OEHHA, 2000). Table V-1

presents the current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

There are a number of human occupational studies that have demonstrated that inhalation exposure to chromium results in an increased risk of lung cancer mortality in humans. An oral chromium carcinogenicity bioassay study also shows that there is a significantly increased incidence of stomach carcinomas in female mice and benign tumors (papillomas and hyperkeratomas) in both male and female mice (OEHHA, 2002).

The OEHHA staff has performed an extensive assessment of the potential health effects of chromium (hexavalent), reviewing available carcinogenicity data. OEHHA concluded that chromium and chromium compounds are potential human carcinogens with no identifiable threshold below which no carcinogenic effects are likely to occur. The Board formally identified hexavalent chromium as a TAC in January 1986 (ARB, 1985). Chromium (hexavalent compounds) was listed by the State of California under Proposition 65 as carcinogens in February 1987 (OEHHA, 2005).

In 1990, the U.S. Congress listed chromium compounds as HAPs in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). The U.S. EPA has classified chromium (VI) in Group A: Human carcinogen and chromium (III) in Group D: Not classifiable as to carcinogenicity in humans (U.S. EPA, 2005). The International Agency for Research on Cancer has classified chromium (VI) compounds in Group 1: Human carcinogen, and metallic chromium and chromium (III) in Group 3: Not classifiable (IARC, 2005).

2. Noncancer

The principal chronic effect of chromium (VI) exposure is that Cr(VI) forms oxyanions at physiological pH ($CrO4^{2}$), which are quite similar to sulfate ($SO4^{-2}$) and phosphate ($HPO4^{-3}$) anions. Therefore, it is able to penetrate virtually every cell in the body because all cells transport sulfate and phosphate. Harmful effects are speculated to be related to the reduction of Cr(VI) to Cr(III) intracellularly when it crosses the cell membrane and forms complexes with intracellular macromolecules. Thus, Cr(VI) compounds have the potential to injure numerous organ systems. Toxicity following chronic Cr(VI) exposure has been reported in the respiratory tract, gastrointestinal system, eyes and conjunctiva, kidney, and hematopoietic system. Cr(VI) is corrosive and exposure to chromic acid mists may cause chronic skin ulcerations and upper respiratory lesions. In addition, allergic skin and respiratory reactions can occur with no relation to dose (OEHHA, 2000a).

Nasal tissue damage has been frequently observed in chromium plating workers exposed chronically to chromic acid mists. However, workers in the chromate extraction and ferrochromium industry, exposed to particulates containing soluble Cr(VI)

compounds, have also reported nasal lesions. Nasal lesions include perforated septum, ulcerated septum, nasal atrophy, nosebleed, and inflamed mucosa (OEHHA, 2000a).

E. Hydrochloric Acid

Exposure to hydrochloric acid (HCl) may result noncancer health effects. The probable routes of human exposure to hydrochloric acid are inhalation and dermal contact (ARB, 1997b). Table V-1 presents the current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

Hydrochloric acid is a federal HAP and was identified as a TAC in April 1993 under AB 2728. No information is available on the carcinogenic effects of hydrochloric acid in humans. In one study, no carcinogenic response was observed in rats exposed by inhalation. The U.S. EPA has not classified hydrochloric acid as to its human carcinogenicity (U.S. EPA, 2005). The International Agency for Research on Cancer has classified hydrochloric acid in Group 3: Not classifiable as to its potential human carcinogenicity (IARC, 2005).

2. Noncancer

Inhalation exposure to high concentrations of HCl fumes may result in coughing, a choking sensation, burning of the respiratory tract, and pulmonary edema. Dental erosion has been reported in workers chronically exposed to low levels of gaseous hydrogen chloride. Reactive Airway Dysfunction Syndrome (RADS; acute, irritant-induced asthma) was reported in three male police officers (36 to 45 years old) who responded to a roadside chemical spill. Other reports of RADS include individual occupational cases (OEHHA, 1999).

Persons with preexisting skin, eye, gastrointestinal tract (including ulcers) or respiratory conditions or underlying cardiopulmonary disease may be more sensitive to the effects of HCl exposure. Persons also exposed to formaldehyde might be at increased risk for developing cancer (OEHHA, 1999).

The reproductive hazard of hydrogen chloride to humans is unknown. Few studies on the reproductive effects of HCl exposure were found in the literature. Maternal exposure to a high concentration of a strong acid could result in metabolic acidosis and subsequent fetal acidemia which has been linked with low Apgar scores, neonatal death, and seizures. However, there is no evidence linking HCl exposure to fetal academia (OEHHA, 1999).

F. Lead (Inorganic)

Exposure to lead may result in cancer health effects. The probable routes of human exposure to lead are inhalation and ingestion (ARB, 1997b). Table V-1 presents

the current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

There are several inconclusive epidemiological studies of exposed workers which provided limited evidence of cancers of the kidney, stomach, and respiratory tract. Rodent studies have found increased kidney cancers following the oral administration of lead (ARB, 1997b).

OEHHA staff has performed an extensive assessment of the potential health effects of lead and lead compounds, reviewing available carcinogenicity data. OEHHA concluded that lead and lead compounds (inorganic) are a potential human carcinogen with no identifiable threshold below which no carcinogenic effects are likely to occur. The Board formally identified inorganic lead as a TAC in April 1997 (ARB, 1997a). Lead and lead compounds, lead acetate, lead phosphate, and lead subacetate were listed by the State of California under Proposition 65 as carcinogens in October 1992, January 1988, April 1988, and October 1989, respectively (OEHHA, 2005).

In 1990, the U.S. Congress listed lead compounds (including inorganic lead) as HAPs in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). U.S. EPA has classified lead in Group B2: Probable human carcinogen (U.S. EPA, 2005). The International Agency for Research on Cancer has classified lead and inorganic lead compounds in Group 2B: Possibly carcinogenic to humans, and organic lead in Group 3: Not classifiable (IARC, 2005).

2. Noncancer

Lead salts (e.g., lead acetate, lead subacetate) are considered to be forms of inorganic lead. Most significant non-workplace, outdoor air exposure to lead in California is expected to be to inorganic lead particulate. Although different lead species (e.g., lead oxide, lead sulfide, etc.) are absorbed to varying degrees following inhalation, all are capable of causing adverse health effects once they reach sensitive tissues (ARB, 1997b).

Lead is slowly excreted by the body. Exposures to small amounts of lead over a long time can slowly accumulate to reach harmful levels. Harmful effects may therefore develop gradually without warning. Short-term exposure to high levels of lead may also cause harm. Lead can adversely affect the nervous, reproductive, digestive, cardiovascular blood-forming systems, and the kidney. Symptoms of nervous system effects include fatigue and headaches. More serious symptoms include feeling anxious or irritable and difficulty sleeping or concentrating. Severe symptoms include loss of short-term memory, depression, and confusion. More severe exposures can prove fatal. Lead can also injure the peripheral nerves to cause weakness in the extremities. Children are a sensitive population as they absorb lead more readily and the developing nervous system puts them at increased risk for lead-related harm, including learning

disabilities. Effects on the gastrointestinal tract include nausea, constipation, and loss of appetite. Recovery from severe effects on the nervous system or kidneys is not always complete. Other ill effects include hypertension and anemia. The toxicological endpoints considered for chronic toxicity are the kidney, cardiovascular or blood system, immune, reproductive, and central or peripheral nervous systems (ARB, 1997b).

In men, adverse reproductive effects include reduced sperm count and abnormal sperm. In women, adverse reproductive effects include reduced fertility. Still-birth, miscarriage, low birth weight, and neurobehavioral deficits may be more likely (ARB, 1997b). Lead was listed by the State of California under Proposition 65 as developmental toxicant and a male and female reproductive toxicant in February 1987 (OEHHA, 2005).

G. Manganese

Exposure to manganese and compounds may result in noncancer health effects. The probable route of human exposure to manganese and compounds is by ingestion and inhalation (ARB, 1997b). Table V-1 presents the current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

No studies are available regarding the carcinogenic effects of manganese and manganese compounds in humans or animals (ARB, 1997b).

In 1990, the U.S. Congress listed manganese compounds as HAPs in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). Manganese compounds were identified as TACs by the Board in April 1993 under AB 2728 (ARB, 1993). The U.S. EPA has classified manganese in Group D: Not classifiable as to human carcinogenicity (U.S. EPA, 2005). The International Agency for Research on Cancer has not classified manganese as to its carcinogenicity (IARC, 2005).

2. Noncancer

Short-term exposure to manganese may cause irritation to the eyes, nose, throat, and respiratory tract. Long-term exposure to manganese may affect the central nervous system, causing a psychosis which may include symptoms similar to Parkinson's disease. Respiratory effects may also be seen (ARB, 1997b).

I. Mercury (Inorganic)

Exposure to mercury and mercury compounds may result in noncancer health effects. The probable routes of human exposure to mercury and mercury compounds are inhalation, ingestion, and dermal contact (ARB, 1997b). Table V-1 presents the

current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

The human studies available regarding elemental mercury and cancer are inconclusive due to lack of valid exposure data and confounding factors. No studies are available on the carcinogenic effects of methyl mercury in humans. One available animal study reported renal tumors in mice. A chronic study on mercuric chloride in rats and mice reported an increased incidence of forestomach and thyroid tumors in rats, and an increased incidence of renal tumors in mice (ARB, 1997b).

In 1990, the U.S. Congress listed mercury compounds as HAPs in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). The Board formally identified mercury as a TAC in April 1993 under AB 2728 (ARB, 1993). Methyl mercury compounds were listed by the State of California under Proposition 65 as carcinogens in May 1996 (OEHHA, 2005). The U.S. EPA has classified inorganic and methyl mercury in Group C: Possible human carcinogen; and elemental mercury in Group D: Not classifiable as a carcinogen (U.S. EPA, 2005). The International Agency for Research on Cancer has classified methyl mercury compounds in Group 2B: Possible human carcinogen, and metallic mercury and inorganic mercury compounds in Group 3: Not classifiable (IARC, 2005).

2. Noncancer

The respiratory tract is the first organ system affected in the case of acute inhalation poisonings. Acute exposure to mercury can lead to shortness of breath within 24 hours and a rapidly deteriorating course leading to death due to respiratory failure (OEHHA, 1999).

Central nervous system (CNS) effects such as tremors or increased excitability are sometimes seen in cases of acute accidental exposures. Long-term effects from a single exposure to mercury have been reported in six male workers exposed to an estimated concentration of 44 mg Hg/m^3 for a period of several hours. Long-term CNS effects included nervousness, irritability, lack of ambition, and loss of sexual drive for several years. Shortness of breath also persisted for years in all cases. Similar cases of CNS disturbances, including irritability, insomnia, malaise, anorexia, fatigue, ataxia, and headache have been reported in children exposed to vapor from spilled elemental mercury in their home (OEHHA, 1999).

Persons with preexisting allergies, skin conditions, chronic respiratory disease, nervous system disorders, or kidney diseases might have increased toxicity. Persons exposed to other neurotoxicants might have increased sensitivity. People who consume significant amounts of fish from areas with advisories for daily fish intake due to mercury contamination may be more susceptible to the acute toxicity of airborne mercury (OEHHA, 1999).

The primary effects of chronic exposure to mercury vapor are on the central nervous system. Chronic duration exposures to elemental mercury have resulted in tremors (mild or severe), unsteady walking, irritability, poor concentration, short-term memory deficits, tremulous speech, blurred vision, performance decrements, paresthesia, and decreased nerve conduction. Motor system disturbance can be reversible upon cessation of exposure; however, memory deficits may be permanent. Studies have shown effects such as tremor and decreased cognitive skills in workers exposed to approximately 25 $\mu g/m^3$ mercury vapor (OEHHA, 2000a).

The kidney is also a sensitive target organ of mercury toxicity. Effects such as proteinuria, proximal tubular and glomular changes, albuminuria, glomerulosclerosis, and increased urinary N-acetyl-β-glucosaminidase have been seen in workers exposed to approximately 25 to 60 $\mu g/m^3$ mercury vapor. Chronic exposure to mercury vapors has also resulted in cardiovascular effects such as increased heart and blood pressure and in leukocytosis and neutrophilia (OEHHA, 2000a).

In rats, elemental mercury readily crosses the placental barrier and accumulates in the placenta following inhalation. One study reported decreased crown-rump length and increased incidence of edema in hamster fetuses following single subcutaneous administration of 4 mg/kg Hg as mercuric acetate on day 8 of gestation. Exposure to 2.5 mg/kg Hg resulted in no significant developmental defects in these hamsters. This study later showed that the most common manifestations of mercury-induced embryotoxicity in hamsters were resorption, edema, and cardiac abnormalities. Pregnant rats exposed by inhalation to 1.8 mg/m^3 of metallic mercury for 1 hour or 3 hours/day during gestation (days 11 through 14 plus days 17 through 20) bore pups that displayed significant dose-dependent deficits in behavioral measurements three to seven months after birth compared to unexposed controls. Behaviors measured included spontaneous motor activity, performance of a spatial learning task, and habituation to the automated test chamber. The pups also showed dose-dependent, increased mercury levels in their brains, livers, and kidneys two to three days after birth (OEHHA, 1999). Mercury and mercury compounds were listed by the State of California under Proposition 65 as developmental toxicants in July 1987 (OEHHA, 2005).

J. Nickel

Exposure to nickel and nickel compounds may result in both cancer and noncancer health effects. The probable route of human exposure to nickel is by ingestion, inhalation, and dermal (ARB, 1997b). Table V-1 presents the current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

Inhalation exposure to nickel refinery dust and nickel subsulfide has been shown to cause nasal and lung cancer in refinery workers. Nickel carbonyl has been reported to cause lung tumors in animal studies. OEHHA staff concluded that based on available

genotoxicity and carcinogenicity data and physiochemical properties of nickel compounds, all nickel compounds should be considered potentially carcinogenic to humans by inhalation, and total nickel should be considered when evaluating the risk by inhalation (ARB, 1997b).

OEHHA staff has performed an extensive assessment of the potential health effects of nickel, reviewing available carcinogenicity data. OEHHA concluded that nickel and compounds are potential human carcinogen with no identifiable threshold below which no carcinogenic effects are likely to occur. The Board formally identified nickel and nickel compounds as TACs in August 1991 (ARB, 1991). Nickel and certain nickel compounds (nickel acetate, nickel carbonate, nickel carbonyl, nickel refinery dust from the pyrometallurgical process, nickel subsulfide) were listed by the State of California under Proposition 65 as carcinogens in October 1987, October 1989, and May 2004 (OEHHA, 2005).

In 1990, the U.S. Congress listed nickel compounds as HAPs in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). The U.S. EPA has classified nickel refinery dusts and nickel subsulfide in Group A: Human carcinogen and nickel carbonyl in Group B2: Probable human carcinogen (U.S. EPA, 2005).

The International Agency for Research on Cancer (IARC) reviewed nickel and nickel compounds in 1990 and concluded that there is sufficient evidence in humans for the carcinogenicity of nickel sulfate, and of the combinations of nickel sulfides and oxides encountered in the nickel refining industry; there is inadequate evidence in humans for the carcinogenicity of metallic nickel and nickel alloys; there is sufficient evidence in experimental animals for the carcinogenicity of metallic nickel, nickel monoxides, nickel hydroxides and crystalline nickel sulfides; there is limited evidence in experimental animals for the carcinogenicity of nickel alloys, nickelocene, nickel carbonyl, nickel salts, nickel arsenides, nickel antimonide, nickel selenides, and nickel telluride; and there is inadequate evidence in experimental animals for the carcinogenicity of nickel trioxide, amorphous nickel sulfide and nickel titanate. IARC concluded that nickel compounds are carcinogenic to humans, classifying them in Group 1: Human carcinogen; and classified metallic nickel in Group 2B: Possible human carcinogen (ARB, 1997b).

The International Committee on Nickel Carcinogenesis in Man indicated that the epidemiological evidence points to insoluble and soluble nickel compounds as contributing to the cancers seen in occupationally exposed persons. Both insoluble and soluble nickel compounds have produced tumors in animals by a variety of routes, primarily by injection. Both soluble and insoluble nickel compounds are genotoxic in a wide variety of assays. Evidence is available indicating that the Ni^{2+} ion is probably the carcinogenic agent (ARB, 1997b). IARC has classified inorganic arsenic and arsenic compounds as Group 1: Human carcinogen based on sufficient evidence in humans (IARC, 2005).

2. Noncancer

Soluble nickel compounds appear to be the greatest concern for acute health effects. The soluble forms of nickel are absorbed as Ni^{2+}. Divalent nickel competes with copper for binding to serum albumin and is systemically transported in this way. The kidneys, lungs, and placenta are the principal organs for systemic accumulation of nickel. In contrast to the long half-life of the insoluble forms of nickel in the nasal mucosa, the elimination half-life of Ni^{2+} in the plasma is one to two days in mice (OEHHA, 1999).

The effects from long-term exposure to nickel include respiratory tract irritation and immune alterations such as dermatitis ("nickel itch") and asthma. Acute exposure to nickel and nickel compound fumes may cause irritation of the respiratory tract, skin, and eyes. A daily requirement of 50 micrograms of nickel has been estimated to be an essential element in human nutrition. Nickel carbonyl is the most acutely toxic form of nickel. Exposure to nickel carbonyl can cause irritation of the lower respiratory tract and delayed pulmonary edema. It may also injure the liver and central nervous system (ARB, 1997b).

Although there are insufficient data to assess nickel's effect on reproductive functions in humans, all forms of nickel examined to date in laboratory animals have exhibited adverse effects on male reproductive function. Animal studies also demonstrate that nickel adversely affects spermatogenesis, litter size and pup body weight; however, no teratogenic effects have been clearly demonstrated for compounds other than nickel carbonyl (ARB, 1997b). Nickel carbonyl was listed by the State of California under Proposition 65 as developmental toxicants in September 1996 (OEHHA, 2005).

K. Polychlorinated Dibenzodioxins and Polychlorinated Dibenzofurans

There are 210 polychlorinated dibenzodioxin (PCDD) and dibenzofuran (PCDF) isomers. The various isomers are not equally toxic nor are they considered equally potent as carcinogens or non-carcinogens. For the purpose of assessing cancer and noncancer risk associated with these chemicals, OEHHA has adopted the World Health Organization 1997 ($WHO\text{-}_{97}$) Toxicity Equivalency Factor scheme for evaluating the cancer and noncancer risk due to exposure to samples containing mixtures of PCDD and PCDF (OEHHA, 2003). In cases where speciation of PCDDs and PCDFs has not been performed, then 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) serves as the surrogate for PCDD and PCDF emissions (OEHHA, 2003).

Exposure to PCDDs and PCDFs may result in both cancer and noncancer health effects. The probable route of human exposure to TCDD is by ingestion, inhalation, and dermal exposure through contact with contaminated soils (ARB, 1997b). Table V-1 presents the current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

Mother's milk may expose a nursing baby to 4 to 12 percent of the estimated lifetime dose. Once dioxin enters the human body, a small amount is metabolized and eliminated, while the rest bioaccumulates in body fat. As fat is metabolized, stored dioxin is released and excreted primarily in feces. The body's concentration is dependent on the rates of ingestion, elimination, and storage capacity of dioxin. The approximate half-life of dioxin in humans was estimated to range from six to ten years (ARB, 1997b).

Human studies which have reported cancer increases are inconclusive because of inadequate data. There is adequate evidence to support a conclusion that TCDD is carcinogenic in rodents and should be considered a potential carcinogen to humans. Ingestion studies in rodents have shown increases in tumors of the liver, lung, squamous cell, nasal turbinates, and hard palate (ARB, 1986a).

OEHHA staff has performed an extensive assessment of the potential health effects of PCDDs and PCDFs, reviewing available carcinogenicity data. OEHHA concluded that PCDDs and PCDFs are potential human carcinogens with no identifiable threshold below which no carcinogenic effects are likely to occur. The Board formally identified PCDDs and PCDFs as TACs in July 1986 (ARB, 1986a). PCDDs and PCDFs were listed by the State of California under Proposition 65 as carcinogens in October 1992 (OEHHA, 2005).

In 1990, the U.S. Congress listed TCDD as a HAP in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). U.S. EPA has classified hexachlorodibenzo-*p*-dioxin (HxCDD), mixture of 1,2,3,6,7,8-HxCDD and 1,2,3,7,8,9-HxCDD as B2; probable human carcinogen (U.S. EPA, 2005). The International Agency for Research on Cancer has classified TCDD as Group 1: Human carcinogen, based on sufficient evidence in humans (IARC, 2005).

2. Noncancer

Acute exposure of humans to dioxins has caused chloracne, liver toxicity, skin rashes, nausea, vomiting, and muscular aches and pains. A severe weight loss in animals has been observed following acute exposure to dioxin as have hyperkeratosis, facial alopecia, inflammation of the eyelids, and loss of fingernails and eyelashes. The immune system appears to be very sensitive to dioxin toxicity. Thymic atrophy is a prominent finding in exposed animals and has been observed in all laboratory species examined. Other lymphoid tissues such as the spleen, lymph nodes, and bone marrow are also affected. Symptoms of chronic exposure to dioxins include splenic and testicular atrophy, elevated gamma-glutamyl transpeptidase levels, elevated cholesterol levels, and abnormal neurological findings. Other effects may include risk of enzyme induction, diabetes, and endocrine changes (ARB, 1997b).

Potential effects of a toxicant on normal fetal development include fetal death, growth retardation, structural malformations and organ system dysfunction. Evidence for all four of these responses has been seen in human populations exposed to dioxin-like compounds. In these poisoning episodes populations were exposed to a complex mixture of halogenated aromatic hydrocarbons contained within PCBs, PCDFs and PCDDs mixtures thus limiting the conclusions that could be drawn from the data (OEHHA, 2000a). Animal studies have shown TCDD to be both teratogenic and fetotoxic. Reproductive and teratogenic effects observed in animals are cleft palate, kidney abnormalities, decreased fetal weight and survival, hydrocephalus, open eye, edema, resorptions, petechiae, and infertility (ARB, 1997b). TCDD was listed by the State of California under Proposition 65 as developmental toxicants in January 1988 (OEHHA, 2005).

L. Polycyclic Aromatic Hydrocarbons (PAHs)

Polycyclic organic matter (POM) consists of over 100 compounds and is defined by the Federal Clean Air Act as organic compounds with more than one benzene ring that have a boiling point greater than or equal to 100^{o}C. POM can be divided into the subgroups of polycyclic aromatic hydrocarbons (PAHs) and PAH-derivatives. PAHs are organic compounds which include only carbon and hydrogen with a fused ring structure containing at least two benzene (six-sided) rings. PAHs may also contain additional fused rings that are not six-sided. PAH-derivatives also have at least two benzene rings and may contain additional fused rings that are not six-sided rings. However, PAH-derivatives contain other elements in addition to carbon and hydrogen (ARB, 1997b).

Health values and potency equivalency factors (PEFs) have been developed for approximately 26 PAHs. When speciation of PAHs has been performed on facility emissions, these health values and PEFs should be used. In those cases where speciation of PAHs has not been performed, then benzo(a)pyrene [B(a)P] serves as the surrogate carcinogen for all PAH emissions (OEHHA, 2003).

Exposure to PAHs may result in both cancer and noncancer health effects. The probable route of human exposure to PAHs is by ingestion, inhalation, and dermal contact (ARB, 1997b). Table V-1 presents the current health effects values that are used in this HRA for determining the potential health impacts.

1. Cancer

Available epidemiological information is from persons exposed to mixtures such as tobacco smoke, diesel exhaust, air pollutants, synthetic fuels, or other similar materials. Several IARC publications have been dedicated to the analysis of cancer in processes which involve exposure to polynuclear aromatic compounds (PAHs). The types of cancer reported are often consistent with the exposure pathway: scrotal cancer and lung cancer in chimney sweeps exposed to soot; skin cancer (including scrotal cancer) where shale oils are used; and lung cancer where airborne exposure of PAHs

occurs, such as in iron and steel foundries. In animal studies, B(a)P is carcinogenic by intratracheal, inhalation, dermal exposure, intraperitoneal injection, and when given in the diet (OEHHA, 2002).

OEHHA staff has performed an extensive assessment of the potential health effects of PAHs, reviewing available carcinogenicity data. OEHHA concluded that PAHs are potential human carcinogens with no identifiable threshold below which no carcinogenic effects are likely to occur. POM is a federal HAP and was identified as a TAC in April 1993 under AB 2728. The Board formally identified B(a)P as a TAC in April 1994 (ARB, 1994). Several POM compounds (including benzo(a)pyrene) were listed by the State of California under Proposition 65 as carcinogens in July 1987 (OEHHA, 2005).

In 1990, the U.S. Congress listed POM as a HAP in subsection (b) of Section 112 of the Federal Clean Air Act (42 U.S.C. 7412). U.S. EPA has classified benzo[a]pyrene in Group B2: Probable human carcinogen, based on sufficient evidence of carcinogenicity in animals (U.S. EPA, 2005). The International Agency for Research on Cancer has classified benzo[a]pyrene in Group 2A: Probable human carcinogen based on sufficient evidence in animals and limited evidence in humans (IARC, 2005).

2. Noncancer

No information is available on the acute effects of POM in humans. Enzyme alterations in the mucosa of the gastrointestinal tract and increased liver weights have been reported in animals exposed orally to several PAHs. Chronic exposure to benzo(a)pyrene in humans has resulted in dermatitis, photosensitization in sunlight, eye irritation and cataracts. Animal studies have reported effects on the blood and liver from oral exposure to benzo(a)pyrene and effects on the immune system from dermal exposure to benzo(a)pyrene (ARB, 1997b).

No information is available on adverse reproductive or developmental effects of POM in humans. Oral exposure to benzo(a)pyrene in animals has been reported to result in adverse reproductive effects, including reduced incidence of pregnancy and decreased fertility; and developmental effects such as reduced viability of litters and reduced mean pup weight, and decreased fertility in offspring. Benzo(a)pyrene has been demonstrated to cause transplacental carcinogenesis in animals (ARB, 1997b).

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