ATTACHMENT CI-2

Default Exposure Factors
ATTACHMENT CI-2
Default Exposure Factors

The following default exposure factors were used in the human health risk assessment for the SWMU 62, New Housing Fuel Leak site. Site-specific exposure factors are discussed in Section CI.3.3.

GENERAL EXPOSURE FACTORS

Dermal Absorption Factor. The dermal absorption factor represents the fraction of a chemical that is absorbed through the skin via contact with soil. EPA recommends evaluating the dermal pathway for those chemicals where dermal absorption data are available (USEPA 2003b). Therefore, diesel was evaluated for the dermal pathway using a dermal absorption factor of 0.1 (ADEC 1999; USEPA 2003b).

Averaging Time. For carcinogens, an averaging time of 70 years (equivalent to a lifetime), or 25,550 days, was used (USEPA 1989). For noncarcinogens, an averaging time equal to the exposure duration (1 year, or 365 days, for construction worker) was used (ADEC 1999; USEPA 1989).

CONSTRUCTION WORKER EXPOSURE FACTORS

The following default exposure factors were used in the evaluation of the construction worker scenario. The default exposure factors are the recommended values in EPA’s Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites (2002c).

Body Weight. An adult body weight of 70 kilograms (kg) was used. This is the average body weight for adult men and women combined, rounded to 70 kg (ADEC 1999; USEPA 1989).

Inhalation Rate. The recommended construction worker inhalation rate of 20 m³/day was selected for soil and groundwater exposure (USEPA 2002c). According to the Exposure Factors Handbook (USEPA 1997a), an inhalation rate for adults engaged in light activities is 1 m³/hour, 1.6 m³/hour for those engaged in moderate activities, and a rate 2.5 m³/hour for those engaged in heavy activities outdoors. In a construction scenario, this value of 20 m³/day equates to an inhalation rate of 2.5 m³/hour for 8 hours/day, which is likely an overestimate. For example, while the definitions of heavy activities are somewhat subjective, EPA (1997a) states
representative “heavy” activities include vigorous physical exercise (i.e., fast running) and climbing stairs carrying a load.

**Soil Ingestion Rate.** An RME soil ingestion rate of 330 mg/day for a construction worker was selected as recommended in the *Supplemental Soil Screening Guidance* (USEPA 2002c). This value is the upper-percentile adult ingestion rate from a soil ingestion mass-balance study conducted by Stanek et al. (1997) of adults engaged in routine day-to-day activities over a 4-week period. However, this estimate, as stated by the authors, is highly uncertain due to the small size of the study.

**Skin Surface Area.** For construction workers, an exposed skin surface area of 3,300 cm² was used as recommended in EPA’s *Supplemental Soil Screening Guidance* (USEPA 2002c); this corresponds to exposure to head, forearms, and hands.

**Adherence Factor.** A soil to skin adherence factor of 0.3 mg/cm²-event was used for the construction worker soil exposure scenario (USEPA 2003b). This value in EPA’s Soil Screening Guidance is based on studies by Kissel et al. (1996 and 1998) and Holmes et al. (1999) where data suggest that (1) soil properties influence adherence, (2) soil adherence varies considerably across different parts of the body, and (3) soil adherence varies with activity (USEPA 2002c). The adherence factor of 0.3 mg/cm² represents the 95th percentile for construction workers.

**Dermal Permeability Constant.** The dermal permeability constant reflects the movement of a specific chemical from water across the skin and into the blood stream (USEPA 1989). Dermal permeability constants were obtained from EPA’s *Dermal Risk Assessment Guidance* (USEPA 2003b). Dermal permeability constants are not available for the following COPCs: 2-methylnaphthalene, DRO, and GRO. Therefore, dermal exposures cannot be evaluated for these chemicals in groundwater. See further discussion in Section CI.7.

**RESIDENTIAL EXPOSURES**

The residential exposure factors apply to ingestion, dermal contact, and inhalation of chemicals in soil and indoor air by children and adults living in the Kuluk Bay Housing Area.

**Body Weight.** An adult body weight of 70 kilograms (kg) was assumed. This is the average body weight for adult men and women combined, rounded to 70 kg (USEPA 1991a, 1991b). For children aged 0 to 6 years, an average body weight of 15 kg was assumed (USEPA 1991a, 1991b).
Exposure Duration. For evaluation of the residential exposures to groundwater through the vapor intrusion pathway, an exposure duration of 30 years was assumed. This represents the 90th percentile for time spent at one residence (USEPA 1991a). Of the 30 years total exposure duration, ages 0 to 6 accounts for the period of lowest body weight. A 24-year duration was assessed for older children and adults (USEPA 1991a).

Exposure Frequency. The EPA default residential exposure frequency of 350 days/year was used (USEPA 1991a). This value assumes that two weeks of vacation per year will be spent out of the residence.

Inhalation Rate. The default inhalation rates of 20 cubic meters per day (m³/day) and 10 m³/day were used for adults and children, respectively (USEPA 1998b).

Soil Ingestion Rate. An RME soil ingestion rate of 200 mg/day for children and 100 mg/day for adults were selected as recommended in the Supplemental Soil Screening Guidance (USEPA 2002c).

Skin Surface Area. For residents, an exposed skin surface area of 2,800 cm² for children and 5,700 cm² for adults were used as recommended by the EPA (2002c).

Adherence Factor. A soil to skin adherence factor of 0.2 mg/cm²-event for children and 0.07 mg/cm²-event for adults were used for the residential soil exposure scenario (USEPA 2002c).

BUILDING WORKER

The following exposure factors apply specifically to the building workers.

Exposure Duration. For the RME, a building worker was conservatively assumed to work for 25 years in the same area; this represents the 95th percentile for length of time that employees work in the same location, according to the Bureau of Labor Statistics (as cited in USEPA 1991a). For CT, 6 years was used because this value is the average time a worker is assumed to work at one job (USEPA 1997).

Exposure Frequency. The default RME occupational exposure frequency of 250 days per year was used (USEPA 1991a) for building workers. This is based on a 5-day workweek with 2 weeks of vacation a year.
Inhalation Rate. An inhalation rate of 1.3 m$^3$/hour was conservatively assumed for both the RME and CT scenarios for a building worker. This value is the hourly average inhalation rate for an outdoor worker as reported in the Exposures Factors Handbook (USEPA 1997a). This value was conservatively assumed because workers at the Elmendorf Facility spend a significant portion of their time sedentary while indoors, thus reducing their inhalation rate.

TRESPASSER EXPOSURE FACTORS

The following default exposure factors were used in the evaluation of the construction worker scenario. Site-specific exposure factors are discussed in Section CI.3.3.

Body Weight. For children ages 6 to 12 years, a value of 33 kg was used; this is the 50th percentile body weight for boys and girls combined (USEPA 1997). Average body weight was used, because when combined with the other variables in the intake equation, it is believed to result in the most reasonable estimate of intake (USEPA 1989). For example, it would not be reasonable to assume that the smallest person would have the highest intake.

Sediment Ingestion Rate. The RME sediment ingestion rate selected for the 6 to 12 year old trespasser were the 90th percentile (300 mg/day) soil intake estimated from a soil and feces tracer study (van Winjen et al. 1990). This study measured ingestion rates for 78 children at campgrounds. The “campground” intake rate is now considered by EPA Region 10 to be the appropriate ingestion rate for intermittent recreational exposures (USEPA 1999c).

Adherence Factor. A soil adherence factor of 0.2 was assumed for trespassing children engaged in recreational activities. This is EPA’s default adherence factor for residential children (USEPA 2003b). This value is based on data reported by Kissel et al. (1996a, 1996b, 1998) and Holmes et al. (1999) as cited in USEPA (2002c).

Skin Surface Area. A skin surface area of 2,314 cm$^2$ was assumed for the 6- to 12-year-old trespasser contact with surface materials. This value was derived from the average amount of skin a child might have exposed throughout the period of exposure. It was assumed that a child would be wearing short sleeves and shorts in the summer and spring months (16 weeks), and short sleeves and long pants in the fall months (5 weeks) (USEPA 1997a).
ATTACHMENT CI-3

Chemical Toxicity Profiles for Human Health
ATTACHMENT CI-3
Chemical Toxicity Profiles

Toxic effects of the chemicals of potential concern are presented in this Appendix. In general, the information has been summarized from the latest available Agency for Toxic Substances and Disease Registry (ATSDR), U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), and Oak Ridge National Laboratory Toxicity Values online databases.
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TABLE

1 Fractions, Surrogates and Toxicity Reference Doses for Total Petroleum
Hydrocarbon Compounds (ADEC 2000) ......................................................... 6
1.0 PETROLEUM HYDROCARBONS

Petroleum products are complex mixtures of hundreds of different hydrocarbon compounds. These mixtures can roughly be divided into four categories based on the boiling point (i.e., the distillation fraction) of the individual hydrocarbons and the length of the carbon chains. These four categories are (1) gasoline, where the majority of the hydrocarbons have carbon chain lengths ranging from 5 carbons to 10 carbons (C5 to C10), (2) the middle distillates (e.g., kerosene, diesel, jet fuels, and lighter fuel oils [C8 to C18]), (3) heavy fuel oils and lubricating oils (C19 to C45), and (4) asphalts (C30+) (API 1989; Sullivan and Johnson 1993).

Total petroleum hydrocarbons (TPH) are defined by the analytical method used to evaluate them, i.e., concentrations of TPH will differ depending on the type of analysis. The current recommended approach for assessing petroleum toxicity is to identify the original source and analyze the environmental samples by methods that test for specific carbon fraction ranges as well as aliphatic and aromatic fractions (TPHCWG 1999a, b). These divisions were selected based on both the similarity of behavior in the environment (i.e., fate and transport characteristics) and toxicity. If these data are available, then surrogate compounds for which toxicity information is available can be selected for each fraction and the mixture can be evaluated. The surrogate approach involves the separation of the petroleum mixtures into aliphatic and aromatic equivalent carbon-range fractions (i.e., EC5 to EC8) and the use of surrogate compounds or derived values to represent the toxicity of those fractions (ADEC 2000). Alaska DEC recommends the toxicity criteria selected by the Total Petroleum Hydrocarbon Criteria Working Group (TPHCWG) for sites in Alaska (ADEC 2000). The State’s carbon chain lengths for their recommended divisions of petroleum compounds, i.e., gasoline-range organics (GRO), diesel-range organics (DRO), and residual-range organics (RRO), are not identical to the fractions proposed by the TPHCWG on which TPHCWG based their toxicity studies. It is not known if the relatively slight differences in carbon chain length fractions would have an impact on toxicity. The surrogate compounds and toxicity criteria for the various aliphatic and aromatic carbon-range fractions developed by the TPHCWG and recommended by the ADEC guidance are summarized on Table 1. Only noncancer toxicity criteria are available for the petroleum groups. Carcinogenic effects are not evaluated for the petroleum ranges. Rather, the individual carcinogenic compounds present in petroleum (i.e., benzene) are evaluated separately.

A discussion of the surrogate compounds and toxicity criteria used to evaluate petroleum compounds at this site (GRO and DRO) is provided below. The criteria used are based on two of the State’s three categories of petroleum fuels, GRO, DRO, and RRO.
1.1 GRO (ALASKA DEC CARBON CHAIN LENGTH C6–C10)

Gasoline (unweathered) is a complex mixture of over 200 petroleum-derived chemicals consisting primarily of aliphatic hydrocarbons (up to 62 percent; MDEP 1994), and to a lesser extent of aromatic hydrocarbons, and polycyclic aromatic hydrocarbons (PAHs). Additives or octane enhancers are frequently added to gasoline. The range of gasoline hydrocarbons is typically from C4 to C12 (State of California 1989) with the majority of the compounds within C5 to C10. In the absence of benzene (discussed separately) and potentially ethylbenzene (see discussion in Section 8.6), gasoline is unlikely to be carcinogenic and its primary toxic effects are related to central nervous system depression (ATSDR 1999). Long-term effects from exposure to weathered product in the environment are not known. For fresh product, intermittent gasoline vapor exposure is common among gas station attendants and mechanics and appears to result in generally little to no toxic effect (Andrews and Snyder 1991).

1.1.1 Aliphatic Fraction Toxicity Criteria

Both the oral RfD of 5 mg/kg-day and the RfC of 18 mg/m³ that TPHCWG recommends for the C5 to C8 fraction (note that Alaska DEC’s GRO analyses span a different chain length group than this) are based on studies of exposure to commercial hexane (<53 percent) by rodents (TPHCWG 1999a, 1999b). The inhalation value was derived from several rodent studies applying a NOAEL of 3,000 ppm (adjusted to 1,840 mg/m³) and an uncertainty factor of 100 (for animal to human extrapolation and intrahuman variability). The oral RfD was calculated using the inhalation RfC (assuming an inhalation rate for a 70kg human of 20 m³/day and 100% absorption). The critical effect for the both oral and inhalation RfC is neurotoxicity.

1.1.2 Aromatic Fraction Toxicity Criteria

TPHCWG’s recommended reference dose (RfD) and reference concentration (RfC) for this group (C5 to C8) are based on EPA’s criteria for toluene of 0.2 mg/kg-day and 0.4 mg/m³ for the oral and inhalation values, respectively. The toluene criteria are based on a rat study that reported changes in liver and kidney weights (USEPA 2002).

1.2 DRO (ALASKA DEC CARBON CHAIN LENGTH C10–C25)

Unweathered diesel has toxic effects similar to gasoline, although diesel is less volatile, and less toxic. Like gasoline, diesel is a complex mixture of aliphatic and aromatic hydrocarbons. Generally diesel fuels contain 80 to 90 percent aliphatic hydrocarbons and 10 to 20 percent aromatic hydrocarbons (ATSDR 1999). Central nervous system depression appears to be the
principal toxic effect in humans from inhalation of diesel vapors, but limited evidence indicates there might be other systemic problems (ATSDR 1999).

1.2.1 Aliphatic Fraction Toxicity Criteria

The Alaska DEC DRO carbon chain length range does not exactly match the carbon chain length fraction upon which the TPHCWG toxicity criteria are based. Alaska DEC guidance recommends using the TPHCWG value for DRO as the closest match available. The TPHCWG oral RfD recommended for the aliphatic portion of the C9 – C16 fraction (closest to Alaska’s DRO range) is 0.1 mg/kg-day and is derived from several studies of petroleum mixtures containing branched, straight, and cyclic alkanes, and JP-8 within the carbon range of C7–C18. The studies noted above were also used to derive TPHCWG’s recommended RfC of 1 mg/m³. The studies are mostly unpublished from industry research using rodents (TPHCWG 1999b). EPA’s review of TPHCWG’s proposed surrogates found the selection of 0.1 mg/kg-day for aliphatic DRO compounds a reasonable one and likely to overestimate the toxicity of this fuel (USEPA 2000).

1.2.2 Aromatic Fraction Toxicity Criteria

There are a number of aromatic compounds in this C9 – C16 carbon range for which EPA has derived RfDs. The majority of the possible RfDs for individual constituents in this TPH fraction are in the 10^{-2} range. TPHGWC recommended 0.04 mg/kg-day as an RfD for this fraction range, the EPA’s RfD for fluorene and fluoranthene (TPHCWG 1999a,b). The same study was used to derive the RfDs for these two compounds, a subchronic mouse study (USEPA 2002). EPA’s confidence in the RfD is rated as low and they assign an uncertainty factor of 3,000 to the RfD. TPHCWG’s recommended RfC of 0.2 mg/m³ is derived from a rodent study where mice were exposed to high flash aromatic naphthalene which is composed primarily of C9 compounds (TPHCWG 1999b; ATSDR 1999).
REFERENCES


### Table 1

**Fractions, Surrogates and Toxicity Reference Doses for Total Petroleum Hydrocarbon Compounds (ADEC 2000)**

<table>
<thead>
<tr>
<th>Alaska DEC Compound and Carbon-Range Fraction</th>
<th>TPHCWG Surrogate Compound for Alaska DEC Carbon Ranges</th>
<th>Oral RfD (mg/kg-day)</th>
<th>Inhalation RfC (mg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aliphatics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GRO (C₆ – C₁₀)</td>
<td>Commercial hexane</td>
<td>5.0</td>
<td>18.4</td>
</tr>
<tr>
<td>DRO (C₁₀ – C₂₅)</td>
<td>Several studies with compounds ranging from C₇ – C₁₈ and JP-8</td>
<td>0.1</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Aromatics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GRO (C₆ – C₁₀)</td>
<td>Toluene</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>DRO (C₁₀ – C₂₅)</td>
<td>Fluorene, fluoranthene (oral); naphtha (inhalation)</td>
<td>0.04</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Notes:
- DEC - Department of Environmental Conservation
- DRO - diesel-range organics
- GRO - gasoline-range organics
- JP-8 - jet petroleum No. 8
- mg/kg - milligram per kilogram per day
- NA - none available
- RfC - reference concentration
- RfD - reference dose
- TPHCWG - Total Petroleum Hydrocarbon Criteria Working Group
2.0 BENZENE

Benzene is widely used as an industrial solvent, an intermediate in chemical synthesis of commercial products, and a component of gasoline (USEPA 1998b). The potential for human exposure via inhalation, dermal, and oral routes is great under environmental and occupational situations (USEPA 1998b).

The EPA reports an oral RfD for benzene of 0.004 mg/kg-day and an inhalation RfD 0.0086 mg/kg-day (USEPA 2003). The critical study for both the oral and inhalation values was a human occupational study where the toxic endpoint was decreased lymphocyte counts. EPA assigned an uncertainty factor of 300 to both the oral and inhalation values, of which a factor of 3 was for subchronic-to-chronic adjustment. EPA’s confidence in the chronic oral and inhalation RfDs is medium. No adjustment was made to the chronic RfDs to evaluate the construction worker exposure scenario.

Under the proposed revised carcinogen risk assessment guidelines (USEPA 1996), benzene is characterized as a known human carcinogen for all routes of exposure based upon convincing human evidence from occupational epidemiological studies as well as supporting evidence from animal studies (USEPA 2003). Significantly increased risk of leukemia, primarily acute myelogenous leukemia (AML), have been reported in benzene-exposed workers in the chemical industry, shoemaking and oil refineries (USEPA 2003). EPA’s IRIS file on benzene summarizes several key studies that support the weight of evidence classification that exposure to benzene is causally related to an increase in the risk of cancer, specifically leukemia. Included in these studies are the effects of benzene exposure among 28,500 Turkish shoe industry workers; a retrospective cohort mortality study where leukemogenic effects of benzene exposure in 748 white male workers in a rubber products manufacturing plant were examined; and two cohort studies by where an extension and elaboration for the initial analysis done for the rubber plant workers was performed (USEPA 2003). These studies were selected by the EPA as the critical studies for dose-response analysis and for the quantitative estimation of cancer risk to humans (USEPA 2003).

The true cancer risk from exposure to inhaled benzene cannot be ascertained because of uncertainties in the low-dose exposure scenarios and lack of clear understanding of the mode of action. Therefore, “a range of estimates of risk is recommended, each having equal scientific plausibility. The range estimates are maximum likelihood values (i.e., best statistical estimates) and were derived from observable dose responses using a linear extrapolation model to estimate low environmental exposure risks...The use of a linear model is a default public health protective approach and an argument both for and against recognizing supra- and sublinear relationships at low doses and non-threshold or threshold modes of action on exposure to benzene. Therefore,
the risk could be either higher or lower” (USEPA 2003). Thus, the inhalation unit risk estimate for benzene is reported as a range, from 2.2E-06 to 7.8E-06 per ug/m³. The inhalation slope factor can then be derived by applying standard inhalation exposure parameters, an air intake of 20 m³/day and an adult body weight of 70 kg. The benzene slope factor range is calculated as 0.0077 to 0.0273 (mg/kg-day)⁻¹. Risks from benzene inhalation evaluated in this assessment used the higher (more health protective) slope factor of 0.0273 (mg/kg-day)⁻¹. The oral SF for benzene is 0.0055 (mg/kg-day)⁻¹. This value is reported on the EPA’s Region IX PRG tables and is based on human data.

REFERENCES


3.0 ETHYLBENZENE

Ethylbenzene is a colorless liquid that smells like gasoline and has an odor threshold of approximately 2 parts per million (ppm) in air. Ethylbenzene is used primarily in the production of styrene, but is also used as a solvent, a component of asphalt and naphtha, and in fuels (gasoline contains about 2 percent ethylbenzene by weight). Consumer products containing ethylbenzene include pesticides, carpet glues, varnishes and paints, and tobacco products. Acute inhalation exposure of humans to high levels of ethylbenzene has been documented to irritate the eyes and throat and adversely affect the central nervous system (CNS). CNS effects include dizziness, headaches, confusion, and weakness. There are no reliable data on toxic effects in humans following ingestion of or dermal contact with ethylbenzene. Whether or not chronic exposure to ethylbenzene affects human health is not known because little information is available.

EPA has established an oral RfD for ethylbenzene of 0.1 mg/kg-day, based on a study reporting histopathologic changes in liver and kidney tissue in female rats following exposure to 408 or 680 mg/kg ethylbenzene for 5 days/week for 182 days (Wolf et al. 1956). The oral RfD was calculated by applying an uncertainty factor of 1000 (to account for both intraspecies and interspecies variability to the toxicity of ethylbenzene in lieu of specific data, and extrapolation of a subchronic effect level to its chronic equivalent) and a modifying factor of 1 to the reported NOAEL of 136 mg/kg/day. The overall confidence in the RfD is rated low because rats of only one sex were tested and the experiment was not of chronic duration (USEPA 2003). For the construction worker scenario, the uncertainty factor of 10 for subchronic to chronic extrapolation was removed from the oral RfD. A subchronic oral RfD of 1 mg/kg-day was used to evaluate hazards to the construction worker population.

EPA has established an inhalation RfC for ethylbenzene of 1 mg/m$^3$, based on a study reporting reduced numbers of live kits per litter in rabbits and developmental abnormalities in rats with chronic inhalation exposure to ethylbenzene at concentrations as low as 434 mg/m$^3$ (Andrew et al. 1981). The inhalation RfC was calculated by applying an uncertainty factor of 300 (to protect unusually sensitive individuals, adjust for interspecies conversion, and adjust for the absence of multigenerational reproductive and chronic studies) and a modifying factor of 1 to the reported LOAEL of 434 mg/m$^3$. The overall confidence in the RfC is rated low due to the relative lack of information on the potential for maternal toxicity and developmental effects (USEPA 2003). No adjustment was made to the inhalation RfC to evaluate subchronic construction worker exposures, because there was no uncertainty factor specifically for subchronic to chronic extrapolation to remove. Therefore, the chronic inhalation RfC of 1 mg/m$^3$ (or inhalation RfD of 0.29 mg/kg-day) was used to evaluate hazards to construction workers.
The IRIS record for ethylbenzene classifies the chemical as Group D—not classifiable as to its human carcinogenicity—due to lack of animal bioassays and human studies. No association between increased cancer incidence in humans and exposure to ethylbenzene has been reported in current literature. However, recently one animal study has provided clear evidence of carcinogenicity in male rats exposed to 750 ppm ethylbenzene for up to 2 years, citing the incidence of renal and testicular lesions. Evidence for female rats and male and female B6C3F1 mice is suggestive, but not conclusive (NTP 1996). The National Toxicology Program (NTP) and EPA have recently reviewed the 1996 NTP study and have concluded that there is “clear evidence” of the carcinogenicity of ethylbenzene in animals by the inhalation route (NTP 1999; USEPA 1999). USEPA has calculated an inhalation unit risk from the male rat data of 1.16 (ug/m³)-¹ corresponding to an inhalation slope factor of 3.85 x 10⁻³ (mg/kg-day)⁻¹ (USEPA 1999). This slope factor has been incorporated into the latest versions of EPA Region 9’s PRG list and EPA Region 3’s Risk-Based-Concentration list, both of which have been published as revised versions this year and are available on their respective websites.

REFERENCES


———. 1996. Toxicology and carcinogenesis studies of ethylbenzene in F344/N rats and B6C3F1 mice. Inhalation studies TR-466.


2-Methylnaphthalene, also called beta methylnaphthalene, is a naphthalene-related compound. It is a solid like naphthalene. 2-Methylnaphthalene has an odor threshold in air of 10 parts per billion (ppb), which remains approximately the same when water is applied. Along with naphthalene, it is present in cigarette smoke, wood smoke, fossil fuels, tar, and asphalt, and at some hazardous waste sites. Products containing 2-methylnaphthalene include dyes, resins, and vitamin K (ATSDR 2000).

EPA has established an oral RfD for 2-methylnaphthalene of 0.009 mg/kg-day, based on a study reporting increased incidence of pulmonary alveolar proteinosis in lung tissue of mice following exposure to 50.3 or 54.3 mg/kg-day 2-methylnaphthalene for 81 weeks (Murata et al. 1997). The oral RfD was calculated by applying an uncertainty factor of 1000 (a factor of 10 each to account for both intraspecies and interspecies variability to the toxicity of 2-methylnaphthalene, and a third factor of 10 to account for deficiencies in the database and a modifying factor of 1. The overall confidence in the RfD is rated low because of confidence in the database (USEPA 2003).

Because no uncertainty factor was applied for subchronic-to-chronic exposures, the chronic value was not adjusted to derive a subchronic value for the construction worker scenario.

No inhalation RfD is available for this chemical and EPA specifically states that route-to-route extrapolation is not appropriate because there is limited evidence which suggests that the toxicity associated with the toxic endpoint (pulmonary alveolar proteinosis) may vary with route of exposure (USEPA 2003).

In addition, there is a lack of evidence for human carcinogenicity of 2-methylnaphthalene. The EPA considers the data as inadequate to assess the human carcinogenic potential (USEPA 2003).

REFERENCES


5.0 NAPHTHALENE

Naphthalene is a white solid that evaporates easily. Naphthalene has an odor threshold in air of 84 ppb; that threshold is lowered to 21 ppb when water is applied. Naphthalene is present in cigarette smoke, wood smoke, fossil fuels, tar, and asphalt, and at some hazardous waste sites. Products containing naphthalene include moth repellents, toilet deodorant blocks, dyes, resins, leather tanning agents, and the insecticide, carbaryl (ATSDR 2000).

In humans, exposure to high concentrations of naphthalene is known to cause hemolytic anemia, nausea, vomiting, diarrhea, blood in the urine, and a yellow color to the skin. In animals, ingestion of naphthalene has been shown to cause rats to develop cataracts, and chronic inhalation has been shown to cause respiratory inflammation and irritation in mice. Evidence of naphthalene-induced reproductive toxicity is inconclusive. Evidence that naphthalene is a carcinogen is also inconclusive: female mice with daily lifetime exposures to naphthalene developed lung cancer, but a significant association between tumor development and naphthalene exposure was not established (ATSDR 2000).

EPA has established an oral RfD for naphthalene of 0.02 mg/kg-day, based on a study reporting decreased mean terminal body weight in rats exposed to 142.9 and 285.7 mg/kg-day naphthalene, 5 days/week for 13 weeks (BCL 1980). The oral RfD was calculated by applying an uncertainty factor of 3,000 (to account for interspecies extrapolation, intraspecies extrapolation to protect sensitive human populations, subchronic to chronic extrapolation, and database deficiencies) and a modifying factor of 1 to the reported NOAEL of 71.4 mg/kg-day. The overall confidence in the RfD is rated low because of inadequate chronic oral data for naphthalene; the lack of any dose-response data for naphthalene-induced hemolytic anemia; and the lack of two-generation reproductive toxicity studies (USEPA 2003). For the construction worker scenario, the uncertainty factor of 10 for subchronic to chronic extrapolation was removed and a subchronic oral RfD of 0.2 mg/kg-day was used to evaluate hazards to the construction population.

EPA has established an inhalation RfD for naphthalene of 0.00086 mg/kg-day, based on a study reporting hyperplasia and metaplasia in respiratory and olfactory epithelium, respectively, in mice exposed to naphthalene concentrations as low as 9.3 mg/m³ (USEPA 2003). The inhalation RfD was calculated by applying an uncertainty factor of 3,000 (to account for interspecies extrapolation, protection of sensitive individuals, and extrapolation from a LOAEL to a NOAEL) and a modifying factor of 3 (to account for database deficiencies) to the reported LOAEL of 9.3 mg/m³. The overall confidence in the RfD is rated low to medium (USEPA 2003). In calculating the inhalation RfD, EPA adjusted the NOAEL for a 7-day exposure from the actual 5-day exposures that occurred during the critical study (USEPA 2003). For the construction
worker scenario, that adjustment was removed and a subchronic inhalation RfD of 0.0043 mg/kg-day) was used in the risk calculations.

EPA has determined that the human carcinogenic potential of naphthalene cannot be determined (Group D) due to the lack of human carcinogenicity data and inadequate animal data. However, there is suggestive evidence that naphthalene is carcinogenic in animals. One study reported observations of benign respiratory tumors and one carcinoma in female mice only exposed to naphthalene by inhalation (NTP 1992). Additional support includes increase in respiratory tumors associated with exposure to 1-methylnaphthalene (Murata 1993).

REFERENCES


6.0 TOLUENE

Toluene is a clear, colorless liquid with a distinctive smell that is produced in the process of making gasoline and other fuels from crude oil, in making coke from coal, and as a byproduct in the manufacture of styrene. Toluene is used in making paints, paint thinners, fingernail polish, lacquers, adhesives, and rubber and in some printing and leather tanning processes. The odor threshold for toluene in air is approximately 8 ppm, while the taste threshold ranges from approximately 0.04 to 1 ppm. In humans, toluene is a known respiratory irritant with central nervous system (CNS) effects. These effects include headaches, confusion, and memory loss, weakness, drunken-type actions, nausea, loss of appetite, dizziness, unconsciousness, loss of muscle control, poor balance, and decreased mental ability. Some of these changes may be permanent, depending on exposure.

EPA has established an oral RfD for toluene of 0.2 mg/kg-day, based on a study reporting liver and kidney weight changes in male rats following exposure to 312, 625, 1250, 2500, or 5000 mg/kg toluene for 5 days/week for 13 weeks (NTP 1989). The oral RfD was calculated by applying an uncertainty factor of 1000 (to account for inter- and intraspecies extrapolations, subchronic-to-chronic extrapolation, and limited reproductive and developmental toxicity data) and a modifying factor of 1 to the reported NOAEL of 223 mg/kg/day. The overall confidence in the RfD is rated medium (USEPA 2003). An oral subchronic RfD of 2 mg/kg-day was obtained from HEAST (USEPA 1997). The subchronic RfD is based on the same critical study as the chronic value.

EPA has determined that toluene is not classifiable as to its human carcinogenicity (Group D), as human studies have not reported a statistically-significant increased risk of cancer due to exposure to toluene. Animal studies examining adverse effects of toluene following chronic and sub-chronic exposure have not reported carcinogenic responses following exposure (CIIT 1980; Poel 1963; Coombs et al. 1973; Doak et al. 1976; Lijinsky and Garcia 1972). Toluene was also found to be nonmutagenic in genotoxicity assays using several strains of microorganisms (Mortelmans and Riccio 1980; Nestmann et al. 1980; Bos et al. 1981; Litton Bionetics, Inc.)
1981; Snow et al. 1981). Although Russian studies (Dobrokhotov 1972; Lyapkalo 1973) have reported chromosomal damage in bone marrow cells of rats following toluene exposure, other studies have reported no evidence of chromosomal aberrations in blood lymphocytes of workers exposed to toluene only (Maki-Paakkanen et al. 1980; Forni et al. 1971).

The International Agency for Research on Cancer (IARC) and the Department of Health and Human Services (DHHS) have also not classified toluene for carcinogenic effects.

REFERENCES


Chemical Industry Institute of Toxicology (CIIT). 1980. A twenty-four-month inhalation toxicity study in Fischer-344 rats exposed to atmospheric toluene. Executive Summary and Data Tables, October 15. CIIT, Research Triangle Park, NC.


7.0 XYLENES

Xylene is primarily synthesized from petroleum, although it also occurs naturally in petroleum and coal tar, and is formed during forest fires. It is a colorless, flammable liquid with an odor threshold of approximately 0.08-3.7 ppm. Xylene is one of the top 30 chemicals produced in the U.S. in terms of volume. It is used as a solvent, cleaning agent, and paint thinner. Xylene is also used as a component of materials manufactured in the chemical, plastics, and synthetic fiber industries. Isomers of xylene are used in the manufacture of certain polymers (ATSDR 2000).

In humans, acute exposure to high concentrations of xylene is known to cause irritation of the skin, eyes, nose, and throat; difficulty in breathing; impaired function of the lungs; delayed response to a visual stimulus; impaired memory; stomach discomfort; and possible changes in the liver and kidneys. Both acute and chronic exposure to high concentrations of xylene can also cause a number of effects on the nervous system, such as headaches, lack of muscle coordination, dizziness, confusion, and loss of balance. Most of the information on long-term exposure to xylene is from studies of workers employed in industries that make or use xylene. Animal studies indicate that exposure to high concentrations of xylene can cause harmful effects on the liver, kidneys, lungs, heart, and nervous system. Studies of unborn animals have reported dose-dependent developmental toxicity (i.e., increased numbers of deaths, decreased weight, skeletal changes, delayed skeletal development). In many instances, the same xylene concentrations cause deleterious health effects in the mothers (ATSDR 2000).

EPA has recently re-evaluated the toxicity of mixed xylenes and has revised its previous oral RfD for xylenes to 0.2 mg/kg-day (USEPA 2003). EPA has applied an uncertainty factor of 1,000 to the study NOAEL to account for intra and inter species differences (factor of 10 each), and a factor of 10 for data base uncertainties. In calculating the oral RfD, EPA adjusted the NOAEL for a 7-day exposure from the actual 5-day exposures that occurred during the critical study (USEPA 2003). For the construction worker scenario, the adjustment was removed, giving a subchronic oral RfD of 0.25 mg/kg-day.

The recent re-evaluation also has established a reference concentration for xylenes of 0.1 mg/m³, equivalent to an inhalation RfD of 0.029 mg/kg-day. An uncertainty factor of 300 was applied to the study NOAEL as follows: factor of three applied for interspecies differences, factor of three for subchronic-to-chronic adjustments, a factor of 10 for human variability. For the construction worker scenario, the factor of three for subchronic to chronic extrapolation was removed, giving a subchronic inhalation RfD of 0.09 mg/kg-day.

The critical endpoint for both the RfD and the RfC is neurotoxicity.
EPA has determined that the human carcinogenic potential of xylene cannot be determined (Group D) due to the lack of human carcinogenicity data and inadequate animal data. The NTP study (1986) used to derive the original oral RfD reported no evidence of carcinogenicity (i.e., neoplastic lesions, etc.) in rats exposed orally to 0, 250, 500, or 1,000 mg/kg-day xylene via gavage. However, Maltoni et al. (1985) reported higher incidences (versus controls) of malignant tumors in male and female rats treated by gavage with xylene in olive oil at 500 mg/kg-day, 5 days/week for 104 weeks. Berenblum (1941) reported that “undiluted” xylene applied at weekly intervals produced one tumor-bearing animal out of 40 after 25 weeks in skin-painting experiments in mice.

REFERENCES


8.0 CARCINOGENIC PAHS (BENZO[A]ANTHRACENE)

Toxicity of all carcinogenic polycyclic aromatic hydrocarbons (PAHs) are based on benzo(a)pyrene and all of these chemicals have similar toxic endpoints. Thus, only benzo(a)pyrene is discussed in this profile. The relative toxicity of the carcinogenic PAHs to benzo(a)pyrene is as follows: benzo(a)anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, dibenzo(a,h)anthracene, and indeno(1,2,3-cd)pyrene are 0.1, 0.1, 0.001, 1, and 0.1 times as toxic as benzo(a)pyrene, respectively.

Benzo(a)pyrene, a PAH, is a common and persistent environmental contaminant. It is produced as a mixture of PAHs during combustion reactions, and is a component of tobacco smoke, automobile exhaust and air pollution (Mauderly 1993).

Little or no data is available on the toxicity of benzo(a)pyrene in humans. Because exposure scenarios most commonly involve mixtures of PAHs, it is not possible for epidemiological studies to associate adverse health effects with exposure to benzo(a)pyrene alone. However, benzo(a)pyrene toxicity has been well documented in animals. For instance, benzo(a)pyrene has been identified as a vascular toxicant capable of initiating and/or promoting atherosclerosis (Ou and Ramos 1992). Benzo(a)pyrene has also been shown to affect reproductive function in both male and female animals. Mice fed high levels of benzo(a)pyrene during pregnancy had difficulty reproducing, and so did their offspring. Birth defects and decreased body weight were also observed in the offspring (ORNL 1982). Similar adverse health effects could occur in humans, but no data exists that allow a certain determination to be made (ATSDR 2000).

No non-carcinogenic toxicity values (i.e., reference dose, reference concentration) are listed for benzo(a)pyrene by the U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS) or Oak Ridge National Laboratory (ORNL) Risk Assessment Information System (RAIS) online databases (EPA 2002; ORNL 2002).

The primary health concern associated with benzo(a)pyrene exposure is its ability to induce and/or promote cancer. Animal studies report the formation of DNA adducts and tumors in the liver, lung, and stomach of animals, and human skin cells, exposed to benzo(a)pyrene (Culp and Beland 1994; Zhang et al. 1990). The U.S. Department of Health and Human Services (DHHS) has determined that benzo[a]pyrene is a known animal carcinogen. Both the International Agency for Research on Cancer (IARC) and the U.S. Environmental Protection Agency (EPA) have determined that benzo[a]pyrene is also a probable human carcinogen (ATSDR 2000).

EPA has classified benzo(a)pyrene as a probable human carcinogen (Group B2) based on data from three studies reporting increased incidence of forestomach tumors in mice and rats (Neal
and Rigdon 1967; Rabstein et al. 1973; Brune et al. 1981). This classification is supported by positive results from mutagenicity assays (EPA 2002). The oral slope factor (SF) for benzo(a)pyrene (calculated using data from the previously referenced mouse and rat studies) is 7.3 (mg/kg-day)^-1. A provisional inhalation SF of 3.1 (mg/kg-day)^-1 has been developed for benzo(a)pyrene by the National Center for Environmental Assessment (NCEA 1995).

REFERENCES


