ATSDR
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

Public Health Assessment for

BEAR CREEK CHEMICAL AREA
BUTLER AND ARMSTRONG COUNTIES, PENNSYLVANIA
AUGUST 1, 2005

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
Agency for Toxic Substances and Disease Registry

THE ATSDR PUBLIC HEALTH ASSESSMENT: A NOTE OF EXPLANATION

This Public Health Assessment was prepared by ATSDR pursuant to the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA or Superfund) section 104 (i)(6) (42 U.S.C. 9604 (i)(6)), and in accordance with our implementing regulations (42 C.F.R. Part 90). In preparing this document, ATSDR has collected relevant health data, environmental data, and community health concerns from the Environmental Protection Agency (EPA), state and local health and environmental agencies, the community, and potentially responsible parties, where appropriate.

In addition, this document has previously been provided to EPA and the affected states in an initial release, as required by CERCLA section 104 (i)(6)(H) for their information and review. The revised document was released for a 30-day public comment period. Subsequent to the public comment period, ATSDR addressed all public comments and revised or appended the document as appropriate. The public health assessment has now been reissued. This concludes the public health assessment process for this site, unless additional information is obtained by ATSDR which, in the agency's opinion, indicates a need to revise or append the conclusions previously issued.

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PUBLIC HEALTH ASSESSMENT

BEAR CREEK CHEMICAL AREA
BUTLER AND ARMSTRONG COUNTIES, PENNSYLVANIA

Prepared by:

U.S. Department of Health and Human Services
Public Health Service
Agency for Toxic Substances and Disease Registry
Division of Health Assessment and Consultation
Atlanta, Georgia

Executive Summary

The Agency for Toxic Substances and Disease Registry (ATSDR) has prepared this public health assessment (PHA) in response to a request from the Pennsylvania Department of Health (PADOH), a participant in ATSDR's State Cooperative Agreement Program. PADOH received this request originally from the Pennsylvania Department of Environmental Protection (PADEP), the agency leading the remediation of the Bear Creek Chemical Area. The data available for the Bear Creek Chemical Area has been reviewed and summarized in this document. The purpose of this PHA is to evaluate and present information on the question of whether exposures to site-related contaminants are occurring, and whether health effects could result from these exposures.

The Bear Creek Chemical Area consists of 26 disposal areas where industrial waste is suspected or known to have been disposed from the 1950s until the 1970s. It is suspected or known that prior to 1979, industrial waste was hauled for disposal from some of the nearby industrial facilities to several private properties located in northeastern Butler County and northwestern Armstrong County in Pennsylvania. In many cases, the waste was disposed of on land that had been previously strip-mined or deep-mined for coal and may include underground tunnels.

Groundwater in the vicinity of the Bear Creek Chemical Area is contaminated with several chemicals. Based on the available data, the main contaminants of concern in groundwater are resorcinol and several sulfonic acids. In the past, residents likely used contaminated water for drinking, showering, bathing, and other household uses. It is unknown for how long this exposure may have occurred because data for this time period is unavailable. Beginning in mid-2001, bottled water was supplied to residents with drinking water that contained detectable levels of site-related contaminants. Therefore, these residents are no longer ingesting chemicals in their drinking water. However, contaminated water is currently used for showering, bathing, cooking, laundering, and other household purposes.

Past disposal activities resulted in large quantities of wastes being deposited on and into the ground in the Bear Creek Chemical Area. These wastes are still present at several locations. Access to most of the waste disposal areas appears to be unrestricted, although some disposal areas are fenced and on private property. The waste that was deposited onto the ground is referred to as surface deposit materials in this document. Calcium petronates and other contaminants have been detected in surface deposit material of some disposal areas.

Using the evaluation conducted in this PHA, ATSDR concludes the following:

Before the preparation of this PHA, neither ATSDR nor the U.S. Environmental Protection Agency (EPA) had developed health guidelines for resorcinol, sulfonic acids, and calcium petronates. To address the potential exposures, a team of toxicologists with ATSDR's Division of Toxicology prepared a toxicological report for the contaminants of concern associated with the Bear Creek Chemical Area. The document was then externally peer-reviewed by consultant toxicologists. This toxicological information was used in the evaluation conducted as part of this PHA.

ATSDR concludes that past exposure to contaminants in drinking water posed an ***Indeterminate Public Health Hazard***. Domestic water supplies, consisting of private wells, domestic springs, and commercial/public water supplies, were sampled between September 2000 and January 2003. No data is available for these wells prior to this time period. Therefore, the actual concentrations of contaminants that individuals may have been exposed to in their drinking water in the past (prior to 2000) are unknown. In addition, limited cancer and non-cancer toxicological data is available for the contaminants of concern, particularly sulfonic acids. The available toxicity information is inadequate to determine if the estimated doses for past exposures posed a public health hazard.

Currently, individuals with contaminated water supplies are receiving bottled water for drinking water purposes. These individuals continue to use water containing resorcinol and sulfonic acids for non-drinking purposes, such as showering and bathing. Using the available data and information provided by ATSDR's toxicological evaluation, current exposures from showering and bathing are not likely to result in adverse health effects and pose ***No Apparent Public Health Hazard***.

Using data available from the Apple Road Site, Hemlock Road Site, and Kelly Farm, exposure to major contaminants in surface deposit materials, including soil and sediment, by residents (child and adult) and trespassers is not expected to result in adverse health effects. Therefore, the surface deposit exposure pathway poses ***No Apparent Public Health Hazard***.

According to the information contained in the Pennsylvania Cancer Registry for the combined ZIP codes selected for review, it appears that there is not a pattern of elevated cancer within the Bear Creek Chemical Area.

The recommendations of the PHA for the Bear Creek Chemical Area include

- Continue to supply bottled water to homes with contaminated water supplies as an interim measure until the public water supply system is constructed.
- Adequately characterize groundwater contamination associated with the Bear Creek Chemical Area. PADEP should conduct more comprehensive, full-scan sampling (also referred to as analyses for the EPA Target Compound List and EPA Target Analyte List) along the perimeter and outside the proposed public water supply service area. This will ensure that all residents whose private wells are contaminated will be provided with public water and future exposure will be prevented. Full-scan sampling includes laboratory analysis of the site-related contaminants of concern, volatile organic compounds (i.e., benzene and related compounds), semi-volatile organic compounds (i.e., polyaromatic hydrocarbons or PAHs), and metals.

Private wells were primarily sampled for the presence of the contaminants of concern associated with the site (resorcinol and sulfonic acids). However, other contaminants may have been deposited in the disposal areas. Therefore, ATSDR further recommends

- PADEP should conduct more comprehensive, full-scan analyses of some of the private wells to determine whether they have been affected by other contaminants.

- PADEP should conduct comprehensive, full-scan surface water sampling in areas used by individuals for recreational activities (e.g., swimming and fishing) that may have been affected by site activities. If surface water used for fishing has been contaminated with chemicals known to bioaccumulate, fish data should be collected to evaluate the exposure potential.
- To prevent exposure to contaminants, PADEP should restrict the installation of new residential and commercial private wells in the area of groundwater contamination.

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Purpose and Health Issues

The Agency for Toxic Substances and Disease Registry (ATSDR) has prepared this public health assessment (PHA) in response to a request from the Pennsylvania Department of Health (PADOH), a participant in ATSDR's State Cooperative Agreement Program. PADOH received this request originally from the Pennsylvania Department of Environmental Protection (PADEP), the agency leading the remediation of the Bear Creek Chemical Area. ATSDR became involved with the Bear Creek Chemical Area in the summer 2003. The data available for the Bear Creek Chemical Area has been reviewed and summarized in this document. This PHA evaluates and presents information pertaining to whether exposures to site-related contaminants are occurring at the Bear Creek Chemical Area, and if so, whether health effects could result from those exposures. This PHA has been conducted in accordance with the ATSDR Public Health Assessment Guidance Manual [1].

Background

Description

The Bear Creek Chemical Area comprises 26 disposal areas, which includes three plant sites, located in northeastern Butler and northwestern Armstrong Counties in Pennsylvania. It is suspected or known that industrial waste was hauled for disposal from some of the nearby industrial facilities to several private properties before 1979. In many cases, the waste was disposed of on land that previously had been strip-mined or deep-mined for coal and which could include underground tunnels. The chemicals known or suspected to be associated with some of the nearby facilities include resorcinol, several sulfonic acids, and calcium petronates.

The identification of the suspected disposal sites began in March 1980. A preliminary investigation of the suspected disposal areas was conducted by representatives of the Pennsylvania Department of Environmental Resources (PADER) with the assistance of a former employee of Koppers Company, Inc. (Koppers), now known as Beazer East, Inc., (Beazer). A PADER memorandum states that much of the information was gathered from the memory of the former employee. The locations of 13 sites were confirmed during the investigation conducted in 1980 [2]. Since that time, additional sites have been investigated and included on the list of disposal units.

Groundwater Conditions and the Establishment of Site Boundaries

Hydrogeologists with PADEP, formerly PADER, believe that some constituents of the waste materials in the disposal areas were able to move, with little or no obstruction, from soil to drinking water aquifers used by numerous residents throughout the site area[(a)]. The result has been contamination of drinking wells in the two counties. Because the wastes were disposed of at multiple locations, there is no single contaminant plume or single, distinct area of groundwater contamination. Instead, multiple, discontinuous areas of groundwater contamination exist within the site. In addition to the disposal areas, groundwater contamination in the area may also exist from over 100 years of oil and gas well development, as well as from coal mining.

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[a] Mark Ansell, Hydrogeologist, PADEP, personal communciation.

In the Bear Creek Chemical Area, most of the available groundwater comes from water contained within the fractures in sandstones, shales, limestones, and coal beds. Such fractures vary greatly in extent, direction and interconnection with other fractures. Defining distinctive zones of contaminated groundwater is a difficult and resource-intensive process in fractured controlled aquifers. Therefore, PADEP scientists defined the boundaries of the Bear Creek Chemical Area by identifying common drainage areas toward which contaminated groundwater would most likely flow. This effort provides a more timely approach to addressing groundwater in the area rather than spending limited resources on identifying each of the many individual zones of contaminated groundwater. For example, the majority of contaminated groundwater beneath abandoned coal mines adjacent to Bear Creek would tend to flow by various fractures into Bear Creek. Some of the private wells located between the area of waste disposal and Bear Creek are likely to intercept fractures with contaminated groundwater. Still, not all private wells in the same area necessarily intercept contaminated fractures. Rather than spend time and resources to identify which private drinking water wells have or could intercept contaminated fractures, PADEP scientists determined that connecting all residences in the area to a safe water supply was a more cost-effective action.

In mid-2001, Beazer began supplying bottled water to approximately 130 homes and businesses whose water supply had been affected by contamination. Upon discovery of the contamination of the Petrolia public water supply in February 2002, PADEP began supplying bottled water to additional homes. Beazer agreed to a Consent Order in which it was to pay PADEP $18.1 million for its involvement in the contamination of selected Bear Creek Chemical Area disposal sites [3]. PADEP then began providing bottled water to those previously receiving bottled water from Beazer. PADEP currently provides bottled water to over 900 homes. Thirty homes with contaminated water supplies refused the offer for bottled water. The settlement from Beazer is intended to pay for investigation of the disposal areas and the long-term solution to groundwater contamination in the area, which is the construction of a public water supply. In September 2003, Crompton Corporation also entered into a Consent Order with PADEP that provided a settlement of $4.5 million [4].

Description of Contaminants of Concern

Drinking water in the vicinity of the Bear Creek Chemical Area is known to have been affected by several contaminants. Using the available data, the main contaminants of concern in groundwater are resorcinol and several sulfonic acids. Calcium petronates, suspected or known to be associated with some nearby industrial facilities, have been detected in surface deposit material of some disposal areas. Limited published data is available on health effects resulting from exposure to the identified contaminants of concern. Before the preparation of this PHA, neither ATSDR nor the U.S. Environmental Protection Agency (EPA) had developed health guidelines for resorcinol, sulfonic acids, and calcium petronates.

To address the potential exposures, ATSDR's Division of Toxicology prepared a toxicological report for the contaminants of concern associated with the Bear Creek Chemical Area [5]. The report was prepared by a team of ATSDR toxicologists and externally peer-reviewed by consultant toxicologists. The final toxicological report is provided in Appendix A. A brief discussion of each of the contaminants of concern is

provided below. It should be noted that other contaminants have been detected at the disposal units, but the majority of the available environmental data that has been collected focuses on these selected contaminants of concern:

- Resorcinol (also known as m-dihydroxybenzene) is used in pharmaceutical products for skin conditions such as acne, dermatitis, eczema, psoriasis, calluses, and warts. Resorcinol is also an active ingredient in several types of hair dyes and is also used as an adhesive in tire manufacturing [6].
- Meta-Benzene Disulfonic Acid (m-BDSA) is generated during the manufacturing process of oil detergents and other chemicals [5].
- Benzene Sulfonic Acid (BSA) is a used in the manufacture of resorcinol, as well as tanning agents, resins, and pharmaceuticals [6].
- Para-Phenol Sulfonic Acid (p-PSA) is used primarily as an additive in electroplating baths [5] and in the manufacture of dyes and plasticizers. The zinc salt of p-PSA (or zinc phenolsulfonate) is commonly used in antiperspirant products.
- Calcium petronates are very insoluble compounds that are used as rust inhibitors and as lubricating oil additives.

In addition to addressing potential exposures associated with the contaminants of concern, ATSDR also includes in this PHA an evaluation of other contaminants that have been detected at the disposal units.

Description of Disposal Areas

The suspected or known disposal units include a landfill, waste lagoons, drum sites, three plant sites (Indspec Plant, Crompton Plant, and Penreco Plant), and two former EPA National Priorities List (NPL) sites. Currently, the site in its entirety is not listed on EPA's NPL. PADEP leads the investigation and cleanup. A brief description of the disposal areas follows. The locations of the disposal units are depicted in Appendix B, Figure 1.

Kelly Farm is located approximately 1 mile northwest of Karns City in Fairview Township, Butler County. Strip mining was conducted on this 3.5 acre property until about 1950. A total volume of 68,000 tons of industrial waste was estimated to have been deposited on the Kelly Farm Site [6].

Hemlock Road Site is located approximately 1-mile north of Fairview Borough and east of Township Road 632 (also known as Hemlock Road). It is suspected that waste material was deposited on this site, which was previously strip-mined [7].

Apple Road Site is located ¼-mile west of Fairview and north of Township Road 625, also known as Apple Road. Contractors hired by PADEP have performed cleanup activities at the site, which includes the construction of a multi-layer cap on top of the waste disposal areas [8].

Unnamed Apple Road Site, previously known as Site #10, is located approximately ½-mile west of Fairview in an area previously strip-mined and deep-mined [9].

Bruin Lagoon/Shaler is located along the western bank of the South Branch of Bear Creek in Bruin, Butler County. A mineral oil refinery, which began operations in the

1930s, was located on the Shaler property. Bruin Lagoon was an adjacent disposal area that received refinery waste for approximately 40 years. The Bruin Lagoon was placed on the EPA's NPL and designated a Superfund site in 1993. EPA has conducted investigations and cleanup at Bruin Lagoon. The site was removed from the NPL in September 1997, upon completion of the selected remediation [10].

Craig Farm is a 117-acre site located in Armstrong County. From 1958 to 1963, approximately 8,000 tons of resorcinol production waste material was deposited in two strip mines on the property. Craig Farm was added to EPA's NPL in September 1983. Cleanup activities at Craig Farm were completed in December 1995 [11].

Craig #3B was used as a coal refuse disposal area from approximately 1965 to 1967. According to a former Koppers employee, the site was primarily used for the disposal of various chemicals, including hydroxyl diphenyl, sodium sulfite, and sodium sulfate [2,12].

Craig #3C was stated to be a disposal site for hydroxyl diphenyl, according to a former Kopper's employee. The site could not be located during PADEP's 1980 investigation [2,13].

Craig Lagoon, also referred to as Craig Farm #5, is a clay-lined lagoon reportedly containing various waste materials. In 1973, the lagoon was drained and waste material was incinerated at the Koppers plant. At that time, the lagoon was filled with dirt and capped with clay and soil [2,14].

Unnamed Craig was listed on a map provided to Beazer by PADEP. There is no information regarding the types, location, and time period of waste disposal [15].

Wade Armstrong, previously referred to as Craig Site #3A, was strip-mined and was reportedly used for the disposal of hydroxyl diphenyl. In the 1980s the site also operated as a permitted municipal waste landfill [16].

DEP-NO-1 is located approximately ½-mile north of Aspen Road from the Haynesville-Hooker Road intersection. The area has been previously strip-mined. No information is available on the material and time period during which dumping may have occurred [17].

DEP-NO-2 is located near the intersection of Campbell Hollow Road and Birckbickler Road and was formerly known as Spitzer Hollow. The location of DEP-NO-2 indicates the intersection closest to the impacted area. The actual site is located in the area identified as DEP-NO-2A [18].

DEP-NO-2A is a suspected waste area that has been previously strip-mined. Currently, several mobile homes are present in the area [18].

DEP-NO-3 is a strip-cut area located behind a new house on Hemlock Road and approximately ¾-mile from the Hemlock Road disposal area. It is estimated that mining activities were conducted in this area in the 1950s [19].

DEP-NO-4 is a large ravine located north of the Bear Creek Cemetery. The area contains several pits suspected of having been used for waste disposal [20].

DEP-NO-5 is currently an abandoned baseball field and is located east of Bear Creek Cemetery. Reportedly, drums have been deposited on the site [21].

DEP-NO-6 is located approximately 1 mile north of Petrolia, on the east side of Route 268. The site contains several old deep mines where drums and liquid waste have reportedly been disposed [22].

DEP-NO-7 consists of two strip-mined pits located east of Knox Road and approximately ½-mile north of Shakley Road. These areas are suspected of having received liquid and drummed waste. One of the pits reportedly contains 10 to 20 feet of water [23].

DEP-NO-8 is also referred to as the Old Rosebud Mine Site and is located along Magnolia Road. Specific information regarding the type, location, and time period for waste disposal at the site is unavailable [24].

Indspec Plant - Beazer, formerly known as Koppers, operates a plant in Petrolia, Butler County. Beazer manufactures organic materials, including but not limited to resorcinol. In 1988, Indspec Chemical Corporation bought Beazer's operations and the plant in Petrolia. Beazer has, however, retained ownership of portions of the property [25].

Crompton/Witco Plant - Operations began at the plant in the early 1900s when it was operated by Daughtery and Sons. L. Sonneborn Sons, Inc. owned the facility from 1933 through 1962. Witco Corporation took over operation of plant in the early 1960s. Currently, Crompton Corporation, formerly Witco Corporation owns and operates the white oil manufacturing plant in Petrolia [25].

Penreco Plant - Penreco Co., formerly Pennsylvania Refining Company, operates a white oil refining and manufacturing complex in Karns City, Butler County, Pennsylvania. The plant has been in operation since 1878 [25].

Jameson Site, previously referred to as Site #11, is located less than 1 mile southeast of Karns City. The area had been previously strip-mined and was also used as a garbage dump. Industrial waste from the Koppers plant was deposited at the site from 1953 to 1956. The site has since been covered and naturally revegetated [2,26].

Wade Eldorado is located on Eldorado Road, approximately 2 miles north of Bruin. The site was previously used as a residential and commercial landfill. Incinerated cardboard drums and office refuse from the Koppers plant were disposed of at the site [2].

Wade Parsonville was listed on a map provided to Beazer by PADEP in May 2002. No information regarding the types, location, and time period for which waste may have been disposed of on site [27].

Demographics

According to U.S. 2000 Census data, 3,614 persons live within the defined site boundary. Approximately 99% of this population, or 3,580 are white. Also, 324 are children age 6 and under, and 468 are adults over age 65. A total of 1,468 housing units are in the site area. Additional demographic information for the community within the Bear Creek Chemical Area is presented in Appendix B, Figure 2.

Site Visit

On July 14, 2003, ATSDR representatives[b] visited seven of the major disposal areas including Kelly Farm, Apple Road, DEP No. 4, DEP No. 5, Craig Farm, Wade Landfill, and Bruin Lagoon/Shaler. The site visit was led by a PADEP representative[c]. A representative[d] from the PADOH (Southwest District) also participated in the site visit. The purpose of the site visit was to assess site conditions and observe the proximity of residents to the disposal units. According to PADEP, the seven sites that were visited represent the various types of disposal units in the area. Additionally, the visit focused on sites that were most affected by industrial waste disposal, based on environmental sampling data.

ATSDR also met with a representative of Citizens for Pennsylvania's Future (Penn Futures) and the president of the local community group known as Small Towns Opposed to Polluted Sites (STOPS). In addition, ATSDR held a public availability session at the Petrolia Fire Hall on Tuesday, July 15, 2003 from 4:00 PM to 8:00 PM to gather health concerns from the community. These concerns are discussed in the Community Concerns section of this document.

The following observations were made during the site visit:

- In general, a small number of homes are located in close proximity to the disposal units.
- The impact of past strip and deep mining activities was observed at many of the disposal units.
- The two former EPA NPL sites, Bruin Lagoon/Shaler and Craig Farm, were located in remote areas. No homes were observed in the immediate vicinity.
- At the time of the site visit, the chain link fence around the perimeter of the Bruin Lagoon/Shaler was in disrepair. Therefore, access to the Bruin Lagoon/Shaler disposal unit was unrestricted.
- Some of the disposal areas are located on the private property of nearby homeowners. "No Trespassing" signage was not observed on any of the disposal units during the site visit. In an attempt to limit trespassing, Kelly Farm has an electrified fence at the entrance of the disposal area. According to the property owner, trespassing still occurs on the property, particularly by dirt-bikers and all-terrain vehicle (ATV) users who drive through the contaminated areas to access other property.

Environmental Contamination

This section of the PHA describes environmental sampling conducted at the Bear Creek Chemical Area and identifies contaminants of concern found in specific media associated with the site (i.e., groundwater, surface deposit material, surface water deposits). ATSDR

[b] ATSDR representatives included Annmarie DePasquale, Teresa Foster, Debra Joseph, Sandra Lopez, and Aditi Vaidya.

[c] PADEP Bear Creek Chemical Area Project Manager, Chuck Tordella

[d] PADOH (Southwest District)representative, Perry Fox

selects contaminants of concern on the basis of whether they exceed applicable comparison values (CVs). CVs are not available for the major contaminants of concern and other contaminants detected in site media. Therefore, these chemicals are retained in the evaluation and further considered.

In the following sections, concentrations of chemicals in each of the media are compared with appropriate CVs, if available, to select chemicals for further evaluation. A contaminant found to exceed a CV indicates that a more detailed analysis is necessary for that chemical. CVs are used only to screen for chemicals that require further evaluation. Levels of contamination greater than CVs do not necessarily mean that adverse health effects will occur. The amount of the chemical, the duration of exposure, the route of exposure, and the health status of exposed individuals are also important factors in determining the potential for adverse health effects.

The environmental data contained in this PHA were acquired as a result of various investigations conducted by consultants on behalf of Beazer and PADEP or by PADEP personnel directly. The data were analyzed by PADEP's in-house laboratory or by third-party subcontracted laboratories [28].

Environmental Data Quality

Data validation is used to evaluate the quality of field and laboratory-generated analytical data. Validation of data requires that appropriate quality assurance and quality control (QA/QC) procedures are followed, and that adequate documentation is included for all data generated both in the laboratory and in the field. The purpose of the validation is to check for inadequacies, insufficiencies, and discrepancies in the data or in the sampling and analytical techniques used to obtain the data.

To prepare this PHA, ATSDR used existing environmental data. These data were collected by Beazer and PADEP. ATSDR acknowledges that there are uncertainties and limitations regarding the validity of some of the data in the current data sets. Nevertheless, because environmental data generally have an inherent degree of variability that may affect overall data quality, ATSDR decided to include the data in our analyses. ATSDR recognizes that use of the environmental data collected by the PADEP likely overestimates the occurrence of sulfonates and resorcinol in domestic water supplies.

Private Wells, Springs, and other Drinking Water Supplies

Domestic (or household) water supplies, consisting of private wells, domestic springs, and commercial/public water supplies, were sampled between September 2000 and January 2003. Approximately 441 locations were sampled by Beazer or PADEP. The major site-related contaminants of concern, resorcinol and sulfonic acids, were detected in the domestic water supply. As previously stated, CVs are not available for the contaminants of concern, as well as for lead and phenanthrene. Therefore, exposure to these chemicals is considered further in this PHA. A number of other contaminants including arsenic, polycyclic aromatic hydrocarbons (PAHs) [benzo(a)anthracene, benzo(b)fluoranthene, phenanthrene], bromodichloromethane, dibromochloromethane, and cadmium were detected at concentrations above their applicable CVs and will be evaluated further. These data are presented in Table 1 in Appendix C.

Groundwater (Not Used for Drinking Water Supplies)

Groundwater was sampled from monitoring wells at the Apple Road Site and Kelly Farm. Monitoring wells are not used for drinking purposes; rather, they are used only to evaluate the quality of the groundwater. In August 2001, groundwater samples were collected at the Apple Road Site from two monitoring wells adjacent to the western deposit material, and from four monitoring wells adjacent to the eastern deposit material. Between 1994 and 2003, groundwater samples were collected from the 31 monitoring wells or piezometers at Kelly Farm. The major contaminants of concern (resorcinol, sulfonic acids, and calcium petronates) were detected in groundwater samples.

Surface Deposit Material

Deposit material was sampled at the Apple Road Site, Hemlock Road Site and Kelly Farm via soil borings. To obtain samples, soil borings were advanced from the ground surface through the deposit material. The two soil borings at the Apple Road Site were collected from the ground surface to a depth of 8 and 12 feet below ground surface. The two soil borings at the Hemlock Road Site collected material from the ground surface to a maximum depth of 2 and 4 feet below the ground surface. The soil borings at Kelly Farm included material collected from the ground surface to a maximum depth of 34.9 feet below the ground surface. Surface soil samples were also collected in the vicinity of deposit material at the Kelly Farm. Sediment samples were collected downstream from the Kelly Farm along an unnamed tributary running south-southeast from Kelly Farm. ATSDR evaluated only the samples originating on the ground surface to some specified depth below ground because people are more likely to come into contact with these surface materials or soils. For ATSDR's analysis, surface soils, sediments, and surface deposit materials are grouped together and termed "surface deposit material."

The major contaminants of concern (resorcinol, sulfonic acids, and calcium petronates) were detected in surface deposit materials. As previously stated, no CVs are available for these chemicals. Arsenic, beryllium, iron, and lead were also detected in surface deposit materials at concentrations exceeding their applicable CVs. Therefore, exposure to these chemicals will be evaluated further in this PHA. These data are presented in Table 2 in Appendix C.

Surface Water

Surface water samples were collected at 28 locations on and around Kelly Farm between 1991 and 2003. Additional surface water samples were collected between October 2001 and January 2003 from 12 locations within the Bear Creek Chemical Area. The samples were collected from lagoons, ponds, and other surface water bodies within the Bear Creek Chemical Area. Resorcinol, sulfonic acids, and calcium petronates, for which no CVs are available, were also detected in surface water samples. Arsenic, bis(2-ethylhexyl)phthalate, chromium, lead, manganese, and nickel were detected at concentrations above their applicable CVs.

Data Limitations

As a cost-effective monitoring design, the majority of the environmental samples collected within the site area were analyzed for a limited set of site contaminants. While this approach yields a reasonable and cost-effective understanding of the broad extent of

any contamination, it did not provide enough detail for a public health evaluation of the presence or absence of all possible contaminants in drinking water supplies. For example, chemicals other than the contaminants discussed above may have been disposed in the site area and migrated into drinking water supplies.

Pathways of Human Exposure

ATSDR's pathways analysis determines whether people have come into contact with chemicals from a site and whether those contacts were substantial enough to cause harm. To make this determination, ATSDR identifies exposure pathways or ways in which a chemical could enter a person's body (e.g., ingestion, inhalation, or dermal (skin) contact).

An exposure pathway contains five major elements:

1. a source of contamination,
2. transport through an environmental medium,
3. a point of exposure,
4. a route of exposure, and
5. an exposed population.

If an exposure pathway contains all five elements and exists now or did exist in the past, the pathway is considered complete. Completed exposure pathways are evaluated to determine whether health effects could occur. If one or more of the five elements is not clearly defined but could be present, the exposure pathway is classified as potential. Tables 3 and 4 in Appendix C present the completed and potential exposure pathways for the Bear Creek Chemical Area.

Completed Exposure Pathways

Drinking water

Private wells, springs, and the City of Petrolia's public water supply have been found to be contaminated with resorcinol, sulfonic acids, metals, and polycyclic aromatic hydrocarbons (PAHs) such as benzo(a)anthracene and benzo(b)fluoranthene. The most significant completed exposure pathway is the use of contaminated drinking water for domestic purposes. Many residents in the area have used the water from their private wells, springs, and from the Petrolia public water supply for drinking, showering, bathing, cooking, laundering, and other household purposes.

Beginning in mid-2001, bottled water was supplied to residents whose drinking water contained detectable levels of site-related contaminants. These residents are no longer exposed to chemicals in drinking water via ingestion. Before this time, however, during showering and bathing, individuals could have been exposed to contaminants via drinking and direct skin contact. Residents were likely not exposed via inhalation of contaminated vapors and aerosols while showering or bathing because the compounds of concern do not tend to volatilize readily. Because data for this time period are unavailable, it is unknown for how long this exposure may have occurred. Currently, contaminated water is used for showering, bathing, cooking, laundering, and other

household purposes. Therefore, exposure to chemicals in drinking water could still be occurring via direct skin contact.

Surface deposit materials

Past disposal activities resulted in large quantities of wastes deposited on and in the ground in the Bear Creek Chemical Area. These wastes are still present at several locations. Access to most of the waste disposal areas appears to be unrestricted, although some disposal areas are fenced or on private property. The waste that was deposited onto the ground, referred to as surface deposit materials, may have been transported via flooding, surface water runoff, wind, or soil erosion into nearby yards, lands, and water bodies.

The surface deposit materials contain contaminants that people could have come in contact with in the past, or could come in contact with in the present or future. The individuals likely to have come into contact with the contaminants include past workers involved with disposal of the materials, trespassers, and residents whose property has been used for waste disposal.

In the past, workers who loaded and unloaded the waste would have been at greatest risk for exposure. These workers had a greater opportunity for close contact with the contaminants while handling the waste. They were likely exposed via dermal contact, inhalation of suspended particulates, and accidental ingestion of contaminants contained on their hands. Nevertheless, worker's exposure is unknown because of lack of information on the disposal practices (e.g., the use of personal protective equipment, or the length and duration of exposures). Therefore, workers involved with the disposal efforts have not been evaluated in this PHA.

Presently, those most likely to come into contact with the surface deposit materials are area residents and trespassers. Residents can be exposed via dermal contact, inhalation of fugitive dust, or incidental ingestion of contaminants while working, gardening, or playing outside in areas where wastes are present. Young children are of particular concern for dermal and ingestion exposures because they often play or crawl on the ground surface. Young children are more likely to ingest the contaminants because they engage in more frequent hand-to-mouth activity. Information gathered during the July 2003 site visit indicates trespassers may occasionally use dirt bikes or ATVs in contaminated areas which can result in inhalation of suspended dust particles.

Potential Exposure Pathways

Surface Water

Site-related contaminants have been detected in surface waters (i.e., lagoons, streams, ponds, and drainage or irrigation ditches) within or adjacent to the Bear Creek Chemical Area. Given the current knowledge of site conditions, it is unlikely that people are engaged in activities which would bring them into contact with contaminated surface water on a long-term basis. Short-term (acute) and intermittent exposures to surface water could occur to a few individuals. These acute, intermittent exposures are not likely to result in significant health effects.

It should be noted that downstream water bodies, including Bear Creek, have not been adequately characterized. Therefore, site-related effects on surface water bodies farther from the site are unknown.

Groundwater (Not Used for Drinking Water Supplies)

As previously discussed, the multiple areas of contaminated groundwater within the site are difficult to identify because of movement through subsurface fractures. As a result of such complex hydrogeology, further contamination of private wells is possible in the future. As the contaminated groundwater plumes migrate, contamination could spread to areas outside the known areas of contamination. Additional private wells could become contaminated. The potential also exists for a resident or business to install a new well in the known contaminated groundwater and use the well for domestic purposes. Restrictions on new well installation in the area of groundwater contamination would eliminate future exposures.

Eliminated Exposure Pathways

Biota

Food chain exposures occur when people consume contaminated plants or other game animals. Game animals and fish become contaminated by ingesting contaminated plants, water, or animals, or, for fish, by living in contaminated water. Plants, including vegetables, become contaminated by growing in contaminated soil or by receiving contaminated runoff water. People then become exposed by ingesting the contamination that bioaccumulates in plants or animals.

After a review of available data, however, no bioaccumulation is expected to occur at this site. Because the contaminants of concern at the site do not tend to bioaccumulate in plants or animals, people are not likely to be exposed to contaminants through food chain uptake.

Discussion

A review of the available environmental data and site conditions indicates the presence of two completed exposure pathways by which people might have be exposed to contaminants in the past, in the present, or in the future: the drinking water pathway and the surface deposit material pathway.

As the first step in the evaluation of possible health effects, ATSDR compared the maximum detected concentrations of chemicals in environmental samples with established CVs. Use of the maximum detected concentration in this evaluation is likely to overestimate actual exposures and is therefore considered a conservative approach for health protectiveness. CVs were not available for some of the chemicals associated with the Bear Creek Chemical Area, including resorcinol, several sulfonic acids, and calcium petronates. Further evaluation of exposure to chemicals without CVs and chemicals detected above established CVs was necessary to determine the likelihood of harmful effects. More detailed evaluation involved the calculation of exposure doses using site-specific information regarding exposures at the site to determine whether health effects are likely to occur. In the event that calculated exposure doses exceed established health guidelines (e.g., ATSDR Minimal Risk Levels, EPA Reference Doses, and those

developed in ATSDR's Toxicology Report for Bear Creek Chemicals), an in-depth toxicological evaluation is necessary to determine the likelihood of health effects.

ATSDR also considered the possibility of additive toxicity from exposure to chemicals structurally similar and which may be associated with similar health effects (i.e., sulfonic acids or calcium petronates). A complete discussion of the process for further evaluation is presented in Appendix D of this PHA. The public health implications of exposures associated with the Bear Creek Chemical Area are discussed in the following sections.

Public Health Issues

Drinking Water Exposure Pathway

The contaminants detected in drinking water that exceed their respective CVs or for which CVs are not available are presented in Appendix C, Table 1. These contaminants will be addressed further in this PHA. No CVs were available for resorcinol, p-PSA, m-BDSA, BSA, and phenanthrene. Concentrations of arsenic, benzo(a)anthracene, benzo(b)fluoroanthene, bromodichloromethane, cadmium, and dibromochloromethane were detected above established CVs.

Currently, residents with affected water supplies are receiving bottled water for drinking purposes. However, they could have been exposed to contaminants in drinking water in the past. Contaminants in drinking water may have entered the body via ingestion of the water or direct skin (or dermal) contact during showering and other household activities. Given their physical and chemical properties, detected chemicals are not expected to volatilize readily (or easily migrate from water to air) during showering. Therefore, exposure to contaminants via inhalation during showering is unlikely to result in health effects.

Residents continue to use contaminated water for showering and other household purposes. Therefore, exposure via direct contact with contaminants during showering may be occurring at the present time and could continue until the municipal public water system is completed. This PHA evaluates past ingestion and past and current direct skin exposure to adult and child residents.

The evaluation of past ingestion of drinking water conservatively assumes that adults consume 2 liters of water per day and children consume 1 liter of water per day. Individuals are expected to be exposed 350 days per year for approximately 50 years (1950 to 2001) for adults and 6 years for children. One of the limitations of evaluating past exposure is that historical data from individual wells, springs, or the Petrolia Water Supply are not available. The majority of the drinking water data has been collected since 2000. Therefore, the actual concentrations of contaminants that individuals may have been exposed to in their drinking water supply prior to this time are unknown. Given the available information, ATSDR assumed that individuals were exposed to the maximum detected concentration of contaminants from all drinking water samples collected for health protectiveness. A complete discussion of the assumptions utilized in this evaluation is presented in Appendix D.

Calculated exposure doses were compared with the available health guidelines to determine whether the potential exists for adverse health effects to result from exposure to contaminants in drinking water. Using these site-specific calculations, exposure doses

for the following contaminants were found to exceed the health guidelines and, therefore, require further evaluation: p-PSA, m-BDSA, BSA, and arsenic. Exposure doses calculated for ingestion and direct skin contact with contaminants have been presented as a combined dose. It should be noted that ingestion is considered a major contributor to the combined doses, while doses associated with direct skin contact are considered minimal.

Resorcinol

The calculated exposure doses for ingestion of drinking water and direct contact with water while showering were 0.0017 milligrams per kilogram per day (mg/kg/day) for adults and 0.0037 mg/kg/day for children. These doses do not exceed a health guideline for resorcinol of 2 mg/kg/day, proposed by the Toxicology Excellence in Risk Assessment, a not-for-profit toxicological organization, and accepted by ATSDR [5]. Additionally, no studies were available that indicate an association with cancer from oral or dermal exposure to resorcinol. ***Therefore, cancer and non-cancer health effects are not expected to be associated with resorcinol exposure in drinking water at this site.***

p-PSA

The calculated exposure doses for ingestion of drinking water and direct contact with water during showering were 13 mg/kg/day for adults and 29 mg/kg/day for children. These doses exceed a provisional health guideline for p-PSA of 0.030 mg/kg/day, calculated by ATSDR [5].

Overall, the existing data on health effects for p-PSA are limited and uncertainties exist among the available studies [5]. In particular, there are few long-term studies available for evaluating long-term exposure to p-PSA in drinking water. In evaluating the available scientific data, the lowest adverse effect level in animal studies may be considered 100 mg/kg/day. This database is, however, considered limited and it remains unclear whether the health effect noted among animal subjects (lower lymphocyte counts in male rats) is considered to be an adverse health effect for humans.

It has been observed that p-PSA is absorbed poorly by skin. Animal studies have indicated only slight irritation to skin at much higher concentrations than those detected in tap water associated with the Bear Creek Chemical Area. Additionally, p-PSA is directly applied to skin at much higher concentrations in deodorant products than are present in drinking water at the Bear Creek Chemical Area [5].

A review of the available information shows that non-cancer health effects are not expected to result from dermal exposure to concentrations of p-PSA associated with the Bear Creek Chemical Area. It is difficult to assess the potential health effects associated with drinking contaminated water in the past due to the limitations and uncertainties associated with the available data. Exposure doses calculated for the Bear Creek Chemical Area exceed a provisional health guideline calculated by ATDSR, but are below the doses associated with minor effects in animal studies. Whether the minor effects reported (reduced lymphocyte counts) could be an adverse health effect for humans is unclear. No studies are available to evaluate exposure to p-PSA and the risk of cancer. The available toxicity information is inadequate to determine if the estimated doses for past exposures posed a public health hazard.

Additional toxicological data for p-PSA is necessary to clarify some of the existing uncertainties regarding human exposure to this chemical.

m-BDSA

The calculated exposure doses for ingestion of drinking water and direct contact with water during showering were 1.1 mg/kg/day for adults and 2.4 mg/kg/day for children. These doses exceed a provisional health guideline for m-BDSA of 0.10 mg/kg/day, calculated by ATSDR [5].

Limited information is available to assess ingestion of m-BDSA in drinking water. Currently, no studies are available of m-BDSA exposure among humans. A few studies of animal exposure to m-BDSA in drinking water were, however, available for consideration. Two studies indicated gastrointestinal irritation, such as loose feces, at exposure doses generally thousands of times greater than those associated with exposure to m-BDSA in drinking water at the Bear Creek Chemical Area [5]. Two additional studies indicated blood chemistry changes in rats exposed to m-BDSA in drinking water for 14 days and 13 weeks. Because of study limitations, the findings of the 13-week study were not considered biologically significant (i.e., effects in males and not in female subjects; increased white blood cell counts and decreased white blood cell counts observed among study subjects).

A limited data base exists for the evaluation of dermal effects from exposure to m-BDSA. Because of its chemical properties, m-BDSA is not likely to be absorbed easily by skin. According to one study of rabbits, only slight irritation to skin was observed after exposure to much higher concentrations (approximately 5,000 milligrams per liter [mg/L]) than those detected in tap water associated with the Bear Creek Chemical Area (approximately 40 mg/L).

Given the available information, non-cancer health effects are not expected to result from dermal exposure to concentrations of m-BDSA associated with the Bear Creek Chemical Area. It is difficult to assess the potential health effects associated with drinking contaminated water in the past, on the basis of the current data available. Although the data is limited, it is indicated that concentrations of m-BDSA associated with health effects are higher than those measured in drinking water at the Bear Creek Chemical Area. No studies are available to evaluate exposure to m-BDSA and the risk of cancer. The available toxicity information is inadequate to determine if the estimated doses for past exposures posed a public health hazard. Additional toxicological data for m-BDSA is needed to address some of the uncertainties among the available scientific data.

BSA

The calculated exposure doses for ingestion of drinking water and direct contact with water during showering were 0.14 mg/kg/day for adults and 0.30 mg/kg/day for children. These doses exceed a provisional health guideline for BSA of 0.030 mg/kg/day, calculated by ATSDR [5].

As with other sulfonic acids, a limited data set is available for assessing exposure to BSA. According to the results of two animal studies, blood chemistry effects (i.e., reduced lymphocyte counts) were the most consistently observed effect resulting from

ingestion of BSA. These studies provide limited information regarding the amount of the chemical exposure (dose) and observed health effects (response), referred to as the dose-response relationship. In addition, it remains unclear whether decreased white blood cell count is an adverse health effect for humans. The lack of unpublished literature on BSA toxicity results in a considerable amount of uncertainty regarding the potential health effects from exposure.

It has been observed that BSA is absorbed poorly by skin. Animal studies have indicated only slight irritation to skin at much higher concentrations than detected in tap water associated with the Bear Creek Chemical Area.

Using available information, non-cancer health effects are not expected to result from dermal exposure to concentrations of BSA associated with the Bear Creek Chemical Area. The current data is limited and contains notable uncertainty. Therefore, it is difficult to assess the potential health effects associated with drinking contaminated water in the past. The limited data available for evaluation indicates that concentrations of BSA associated with health effects in animal studies are higher than those measured in drinking water at the Bear Creek Chemical Area. No studies are available to evaluate exposure to BSA and the risk of cancer. The available toxicity information is inadequate to determine if the estimated doses for past exposures posed a public health hazard. Additional toxicological data for BSA is necessary to address the uncertainties regarding human exposure to this chemical.

Arsenic

The calculated exposure doses for ingestion and direct skin contact with drinking water were 0.00018 mg/kg/day for adults and 0.00039 mg/kg/day for children. The adult exposure dose does not exceed the non-cancer health guideline for arsenic of 0.00030 mg/kg/day, ATSDR's chronic oral Minimal Risk Level (MRL) [29] and EPA's oral Reference Dose (RfD) [30]. The exposure dose for children slightly exceeds the health guideline.

The calculated theoretical excess cancer risk for ingestion and dermal contact with drinking water is 1.1×10^{-4}, equivalent to approximately 2 cancer cases per 10,000 persons exposed. Arsenic was also detected at a low frequency, or in approximately 7% of the drinking water samples analyzed for arsenic at the Bear Creek Chemical Area. Additionally, arsenic concentrations in all drinking water samples were below EPA's Maximum Contaminant Limit of 10 micrograms per liter (µg/L).

The doses of arsenic associated with cancer and non-cancer adverse health effects are hundreds of times greater than those associated with exposure to drinking water in the vicinity of the Bear Creek Chemical Area. ***Therefore, cancer and non-cancer health effects are not likely to occur due to arsenic in drinking water at this site.***

Benzo(a)anthracene

No studies indicate non-cancer health effects from exposure to benzo(a)anthracene, which is part of a group of chemicals referred to as PAHs.

The calculated theoretical excess cancer risk for ingestion and dermal contact with drinking water is equivalent to approximately 1 cancer case per 100,000 individuals exposed, which is considered to be a very minimal risk.

Given the available scientific literature on non-cancer effects and the cancer risks calculated for exposure to benzo(a)anthracene in drinking water, exposure is not likely to result in adverse health effects at this site.

Benzo(b)fluoranthene

No studies indicate non-cancer health effects from exposure to benzo(b)fluoranthene, a PAH compound.

The calculated theoretical excess cancer risk for ingestion and for dermal contact with drinking water is equivalent to approximately 2 cancer cases per 100,000 individuals exposed, which is considered to be a minimal risk.

Given the available scientific literature on non-cancer effects and the cancer risks calculated for exposure to benzo(a)fluoranthene in drinking water, exposure is not likely to result in adverse health effects at this site.

Bromodichloromethane

The calculated exposure doses for ingestion of drinking water were 0.000082 mg/kg/day for adults and 0.00018 mg/kg/day for children. The exposure doses do not exceed the non-cancer health guideline for bromodichloromethane of 0.020 mg/kg/day, ATSDR's chronic oral MRL [31] and EPA's oral RfD [30].

The calculated cancer risk for ingestion and dermal contact with drinking water is equivalent to approximately 4 cancer cases per 1,000,000 individuals exposed, which is considered to be a very minimal risk.

On the basis of the non-cancer and cancer evaluation, adverse health impacts are not likely to occur as a result of exposure to bromodichloromethane in drinking water in the vicinity of the Bear Creek Chemical Area.

Cadmium

The calculated exposure doses for ingestion of drinking water were 0.000055 mg/kg/day for adults and 0.00012 mg/kg/day for children. The exposure doses do not exceed the non-cancer health guideline for cadmium of 0.00020 mg/kg/day, ATSDR's chronic oral MRL [32].

The available scientific literature indicates that exposure to cadmium via ingestion and dermal contact has not been associated with an increased risk of cancer [33].

On the basis of the available cancer data and non-cancer evaluation, concentrations of cadmium in drinking water are not likely to result in adverse health effects at this site.

Dibromochloromethane

The calculated exposure doses for ingestion of drinking water were 0.000047 mg/kg/day for adults and 0.00010 mg/kg/day for children. The exposure doses do not exceed the non-cancer health guideline for dibromochloromethane of 0.090 mg/kg/day, ATSDR's chronic oral MRL [34].

The calculated cancer risk for ingestion and dermal contact with drinking water is equivalent to approximately 3 cancer cases per 1,000,000 individuals exposed, which is considered a very minimal risk.

On the basis of the non-cancer and cancer evaluation, adverse health impacts are not likely to occur as a result of exposure to dibromochloromethane in drinking water in the vicinity of the Bear Creek Chemical Area.

Lead

Lead was detected in 8 of 27 samples collected from drinking water sources. The maximum detected concentration of lead is 25 µg/L. Only one of the samples collected was found to exceed EPA's Action Level of 15 µg/L. ***Therefore, lead in drinking water is not considered a widespread public health concern associated with contamination from the Bear Creek Chemical Area.***

Phenanthrene

No studies indicate non-cancer and cancer health effects from exposure to phenanthrene, a PAH compound.

Surface Deposit Exposure Pathway

Soil, surface deposit material, and sediment from the Apple Road Site, Hemlock Road Site, and Kelly Farm are considered collectively in this PHA and referred to as surface deposit material. The contaminants detected in surface deposit materials that exceed their respective CVs or for which CVs are not available are presented in Appendix C, Table 2. These contaminants will be addressed further in this PHA. No CVs were available for resorcinol, p-PSA, m-BDSA, m-PSA, and calcium petronates. Concentrations of arsenic, beryllium, and iron were detected above established CVs.

The Apple Road Site, Hemlock Road Site, and Kelly Farm are private properties. Therefore, adolescent trespassers as well as adult and child residents are considered to be the most likely to come into contact with contaminants present in surface deposit material. Using the available information, ATSDR conservatively assumed that people were exposed to the maximum detected concentration of contaminants from all surface deposit samples collected. The residential exposure pathway represents the most highly exposed population. Residents are assumed to be exposed to chemicals in surface deposits via incidental ingestion or direct skin (or dermal) contact. Residents are assumed to be exposed to contaminants 350 days per year for approximately 30 years for adults and 6 years for children. Although minimal dust is expected to be generated during playing and gardening activities, inhalation of fugitive dust was considered. Further evaluation of this pathway indicated that potential exposures were insignificant for residents and health effects were not expected. A complete discussion of the assumptions used in the evaluation of residential exposure is presented in Appendix D.

During trespassing activities, such as hunting and hiking, incidental ingestion and dermal contact with surface deposit material could occur. Such exposure is, however, expected to be minimal and infrequent. Trespassers could also be involved with all-terrain vehicles or dirt bike riding, which generate considerably more dust than the residential scenario considers for playing and gardening activities. Therefore, the evaluation of the trespasser scenario focused primarily on exposure via inhalation of fugitive dust by adolescents. Trespassers are assumed to be exposed to contaminants in dust 104 days per year for 10 years. A complete discussion of the assumptions utilized in this evaluation is presented in Appendix D.

As with drinking water exposure, calculated exposure doses for surface deposit material were compared with the available health guidelines to determine the potential for adverse non-cancerous and cancerous health effects as a result of exposure. Using site-specific calculations, none of the exposure doses were found to exceed the established health guidelines. A brief discussion of the comparison of site-specific exposure doses with health guidelines is presented in the following sections.

Resorcinol

The calculated exposure doses for adult and child residents are 0.00000015 mg/kg/day and 0.0000050 mg/kg/day, respectively. These doses do not exceed a provisional health guideline for resorcinol of 2 mg/kg/day [5].

The calculated dose for trespasser exposure to fugitive dust during dirt bike use is 0.0000000020 mg/kg/day. One inhalation study indicated no damage to the respiratory system or other harmful effects from inhalation of high levels of resorcinol [5]. Although a health guideline is unavailable for inhalation exposure, this dose is considered very minimal and is not expected to be associated with adverse health effects.

Several studies have examined resorcinol exposure and the potential for cancerous effects. None of the studies reported cancerous effects from exposure [5].

ATSDR concludes that cancer and non-cancer health effects are not expected to be associated with resorcinol exposure to residents and trespassers from contact with surface deposit material at this site.

p-PSA

The calculated exposure doses for adult and child residents are 0.00046 mg/kg/day and 0.015 mg/kg/day, respectively. These doses do not exceed a provisional health guideline for p-PSA of 0.030 mg/kg/day, calculated by ATSDR [5].

The calculated dose for trespasser exposure to fugitive dust during dirt bike use is 0.0000063 mg/kg/day. The available inhalation studies indicate respiratory effects in animals exposed to very high concentrations of aerosolized zinc phenolsulfonate (a zinc salt of p-PSA) [5]. Although a health guideline is unavailable for inhalation exposure, this dose is considered very minimal and is not expected to be associated with adverse health effects.

Using the available scientific literature, non-cancer health effects are not expected to be associated with p-PSA exposure to residents and trespassers from contact with surface deposit material at this site. No studies were available to evaluate exposure to p-PSA and cancer.

m-PSA

The calculated exposure doses for adult and children residents are 0.00034 mg/kg/day and 0.011 mg/kg/day, respectively. These doses do not exceed a provisional health guideline for p-PSA of 0.030 mg/kg/day, which was calculated by ATSDR [5]. Note, however, that although a minor difference appears in the arrangement of the p-PSA and m-PSA structure, this is not expected to affect toxicity.

The calculated dose for trespasser exposure to fugitive dust during dirt bike use is 0.0000047 mg/kg/day. In a single animal study inhalation of very high concentrations of

aerosolized zinc phenolsulfate was associated with respiratory impacts [5]. Still, this dose is considered small and not expected to be associated with adverse health effects.

In summary, non-cancer health effects are not expected to be associated with m-PSA exposure to residents and trespassers from contact with surface deposit material at this site. No studies were available to evaluate exposure to m-PSA and the likelihood of cancer.

m-BDSA

The calculated exposure doses are 0.0020 mg/kg/day for adults and 0.0067 mg/kg/day for children. These doses do not exceed a provisional health guideline for m-BDSA of 0.10 mg/kg/day, calculated by ATSDR [5].

The calculated dose for trespasser exposure to fugitive dust during dirt bike use is 0.0000028 mg/kg/day. No data regarding inhalation exposure to m-BDSA are available [5]. Although a health guideline is unavailable for inhalation exposure, this dose is considered very minimal and it would be unlikely to be associated with adverse health effects.

Using the available scientific literature, non-cancer health effects are not expected to be associated with m-BDSA exposure to residents and trespassers from contact with surface deposit material at this site. No studies were available to evaluate exposure to m-BDSA and the development of cancer.

Calcium Petronates

The calculated exposure doses are 0.32 mg/kg/day for adult residents and 8.4 mg/kg/day for child residents. The calculated dose for trespasser exposure to fugitive dust during dirt bike use is 0.0033 mg/kg/day. No health guideline exists for the evaluation of calcium petronates. Very limited general information was located during the toxicological data evaluation of these chemicals conducted by ATSDR [5]. ***As a result, the potential for cancer and non-cancer health effects associated with exposure to calcium petronates in surface deposit material at this site is unknown.***

Arsenic

The calculated exposure dose for adult residents is 0.0000011 mg/kg/day and for child residents is 0.000047 mg/kg/day. These doses do not exceed the health guideline for arsenic of 0.00030 mg/kg/day, ATSDR's MRL [29] and EPA's Reference Dose [30].

The calculated dose for trespasser exposure to fugitive dust during dirt bike use is 0.000000040 mg/kg/day. Inhalation of very high concentrations of arsenic is associated with several health effects, including cardiovascular and skin conditions [29]. Arsenic exposure to Bear Creek trespassers is, however, considered insignificant and not associated with adverse health effects.

The calculated cancer risk for the resident is equivalent to approximately 6 cancer cases per 1,000,000 individuals exposed. For trespassers, the cancer risk from exposure to surface deposits associated with the Bear Creek Chemical Area is equal to 2 cases per 1,000,000 individuals exposed. Both of these cancer estimates are considered to be very minimal.

In summary, cancer and non-cancer health effects are not expected to be associated with arsenic exposure to residents and trespassers from contact with surface deposit material at this site.

Beryllium

The calculated exposure dose for the adult residents is 0.00000020 mg/kg/day and for child residents is 0.000010 mg/kg/day. These doses do not exceed the health guideline for beryllium of 0.0020 mg/kg/day, ATSDR's MRL [34], or EPA's Reference Dose [30].

The calculated dose for trespasser exposure to fugitive dust during dirt bike use is 0.0000000083 mg/kg/day, which does not exceed EPA's RfD of 0.0000057 mg/kg/day. Exposure to very high concentrations of beryllium via inhalation has been associated with chronic beryllium disease and other respiratory effects [30]. The inhalation dose associated with contact with Bear Creek Chemical Area surface deposits is significantly lower than the study doses associated with health effects, and health effects are unlikely to occur.

The calculated cancer risk for the resident is equivalent to approximately 6 cancer cases per 1,000,000,000 individuals exposed. For trespassers, the cancer risk from exposure to surface deposits associated with the Bear Creek Chemical Area is equal to 3 cases per 100,000 individuals exposed. Both of these cancer estimates are considered to be minimal.

In summary, cancer and non-cancer health effects are not expected to be associated with beryllium exposure to residents and trespassers from contact with surface deposit material at this site.

Iron

The calculated exposure dose for the adult residents is 0.080 mg/kg/day and child residents is 3.5 mg/kg/day. The calculated dose for trespasser exposure to fugitive dust during dirt bike use is 0.0028 mg/kg/day. Although no health guidelines are available for the evaluation of iron exposure, iron is an essential nutrient that is consumed orally. It is also poorly absorbed through the skin. ***Iron concentrations in surface deposits are expected to be naturally occurring and are not expected to be associated with contamination at the Bear Creek Chemical Area. Cancer and non-cancer health effects are not expected from iron exposure at the site.***

Health Outcome Data

Health outcome data may help determine whether the incidence rates of certain adverse health effects are higher than expected in the area potentially affected by the site. ATSDR conducts a review of health outcome data when the toxicological evaluation of a completed exposure pathway indicates the likelihood of adverse health outcomes. The evaluation of health outcome data may give a general picture of the health of a community, or it may confirm the presence of excess disease or illness in a community. Elevated rates of a particular disease may not, however, necessarily be caused by hazardous substances in the environment. Other factors, such as personal habits (e.g., diet, smoking, exercise) socioeconomic status, and occupation can also influence the development of disease [35].

The Superfund law requires consideration of health outcome data in a PHA [36]. These data can include morbidity (or illness) and mortality (death) information. The main requirements for evaluating health outcome data are the presence of a completed exposure pathway, sufficiently high contaminant levels to result in measurable health effects, and a sufficiently large population of individuals included in that completed exposure pathway. Additionally, an important factor for health outcome data evaluation is a database(s) in which disease rates for the population of concern can be identified.

The public has requested that ATSDR evaluate whether cancer is happening at a higher occurrence than would be expected within the Bear Creek Chemical Area. In addition, there are some toxicological and environmental data uncertainties regarding the potential for Area-related chemicals to cause cancer. Therefore, PADOH and ATSDR reviewed the information contained in the Pennsylvania Cancer Registry.

The Pennsylvania Cancer Registry, managed by PADOH, records the diagnosis (or incidence) of cancer that occurs in citizens of the Commonwealth of Pennsylvania and provides data to help physicians, researchers, and other health professionals plan and evaluate cancer programs. Established in 1996, hospitals and laboratories that treat or provide health services to citizens of the Commonwealth are required to report cancer cases to the Pennsylvania Cancer Registry. As a population-based cancer incidence registry, the Pennsylvania Cancer Registry collects demographic, diagnostic, and first course treatment information on all Pennsylvania residents diagnosed with cancer. All information collected and maintained in the Pennsylvania Cancer Registry database is strictly confidential. So to maintain confidentiality, only summary statistical information is published for general distribution and public knowledge.

It is important to know that information from the Pennsylvania Cancer Registry can not be used to determine whether a specific cancer is caused by any particular chemical or other risk factors. The information only gives a limited understanding as to whether or not more cancer is occurring than what would be expected within a particular region of the Commonwealth. If an elevation is found, a health study or some type of formal investigation would be needed to try and determine whether the elevation is real or what may be the potential cause of the cancer. A single health study can not, however, determine the cause of a particular cancer.

To evaluate whether more cancer is occurring, PADOH and ATSDR reviewed the 1996-2002 information contained in the Pennsylvania Cancer Registry for the four ZIP code areas that are primarily within the Bear Creek Chemical Area. Experience has shown that ZIP code information is the most accurate geographic reference collected by the Registry for this type of evaluation. Only 1996–2002 information was used because PADOH is still collecting and confirming information for cancer cases diagnosed since 2002. Therefore, the Registry is not considered to be complete after 2002.

As shown in Figure 3, ZIP codes 16022 (Burin), 16041 (Karns City), 16049 (Parker), and 16050 (Petrolia) make up most, but not all, of the Bear Creek Chemical Area. Because the ZIP code areas are not a perfect match, this review will not be completely accurate. Several of the chosen ZIP codes are not totally within the Bear Creek Chemical Area. Therefore, it is possible that this review may not identify an on-going elevation of cancer occurrence (i.e., cancer cluster). In addition, it is possible that an elevation could be reported by this type of investigation that has nothing to do with the Bear Creek

Chemical Area (e.g., the people with cancer were not exposed to any site-related chemicals).

According to the information contained in the Pennsylvania Cancer Registry for the combined ZIP codes selected for review, it appears that no pattern of elevated cancer is found within the Bear Creek Chemical Area. A more complete presentation of the data and information is in Appendix E.

The only cancer that may be slightly elevated is leukemia; which is a cancer of the blood-forming cells. Within the four ZIP codes, women have been diagnosed with leukemia about twice as often as would be expected when compared with the Commonwealth of Pennsylvania as a whole. The population size and the number of leukemia cases within the ZIP codes used in this analysis is, however, relatively small, and any fluctuation of cancer cases within a small population can result in perceived elevation. The occurrence of cancer fluctuates over time; the same amount of cancer does not continuously occur. In addition, ATSDR was only able to evaluate 7 years of information — a relatively short period of time for this type of investigation. Taking these limitations into consideration, it appears that the reported occurrence of leukemia in women is not out of the ordinary. A review of the available data shows that leukemia has not been associated with exposure to resorcinol. No information exists regarding the cancer-causing potential of sulfonic acids (m-BDSA, BSA, and p-PSA).

Community Health Concerns

As part of ATSDR's process of gathering community health concerns, ATSDR representatives met with the president of a local community group known as Small Towns Opposed to Polluted Sites (STOPS). A representative from Citizen's for Pennsylvania's Future (Penn Futures) was also present at the meeting. Currently, some members of the STOPS group are involved in litigation regarding the Bear Creek Chemical Area. Penn Futures is representing these individuals in the lawsuits.

ATSDR representatives held a public availability session on Tuesday, July 15, 2003 to gather health concerns from the community. The public availability session was held at the Petrolia Fire Hall from 4:00 PM. to 8 PM. A media availability session was held from 3:00 PM. to 4:00 PM. at the same location. Representatives from ATSDR, PADEP, and PADOH (Southwest district) attended the sessions. The public availability session was announced in local newspapers and on the radio. In addition, fliers were sent to approximately 1,050 homes in the vicinity of the site. About 100 individuals attended the session to discuss the PHA process and to communicate their health concerns regarding the Bear Creek Chemical Area. ATSDR representatives met with individuals one-on-one to record their health concerns. Many of the health concerns received by ATSDR have been summarized and addressed in the following questions and responses.

Our household is receiving bottled water for drinking, but we are still showering and bathing in the contaminated water. Is my family going to get sick?

Response: Using the current data for private wells and for the City of Petrolia public water supply, individuals who shower or bathe in household water containing the concentrations of resorcinol, sulfonic acids, and other contaminants considered in this PHA are not likely to experience adverse health effects. In general, the contaminants are

not very likely to be easily inhaled during showering, and dermal contact is considered to be minimal.

Are there elevated rates of breast, uterine, bladder, and colon cancers in my community?

Response: PADOH and ATSDR reviewed the information contained in the Pennsylvania Cancer Registry. The Pennsylvania Cancer Registry, managed by PADOH, records the diagnosis and incidence of cancer that occurs in citizens of the Commonwealth of Pennsylvania and provides data to help physicians, researchers, and other health professionals plan and evaluate cancer programs. According to the information contained in the Pennsylvania Cancer Registry for the combined ZIP codes selected for review, it appears that there is not a pattern of elevated breast, uterine, bladder, and colon cancer within the Bear Creek Chemical Area. A complete discussion of this review is provided in the Health Outcome Data Section of this PHA.

The water contamination investigation seems to be focused on the presence of the identified contaminants of concern, which include resorcinol and sulfonic acids. Has my private well been sampled for other chemicals? Are there other chemicals in my drinking water?

Response: A review of the information that ATSDR has received shows that the majority of private wells have only been sampled for the presence of resorcinol and sulfonic acids PADEP did, however, sample approximately 37 domestic wells for the presence of volatile organic compounds (VOCs) and semi-volatile compounds (SVOCs) between March 2001 and June 2002. These limited samples did not indicate the presence of VOCs or SVOCs at levels of concern. Still, because of the limited extent of this additional sampling, it is still unknown whether other contaminants are present in any given resident's private water supply. Therefore, one of the recommendations of this PHA is for PADEP to collect and analyze samples additional chemicals, including a complete list of volatile organic compounds, semi-volatile organic compounds, and metals.

Have the chemicals detected in private wells been associated with skin effects, such as dermatitis, warts, dermal discoloration, or eczema?

Response: Studies have indicated that exposure to very high concentrations of resorcinol and sulfonic acids have been associated with skin effects and irritation, including eczema and dermatitis. The concentrations of these chemicals measured in private wells in the vicinity of the Bear Creek Chemical Area are significantly lower than exposures from the available studies. Therefore, skin irritations are not expected to occur among Bear Creek Chemical Area residents who currently use their private well water for showering and bathing.

Do chemicals found in private wells cause gastrointestinal effects, such as ulcers, irritable bowel, or Crohn's Disease?

Response: The scientific literature indicates that exposure to very high concentrations of BSA and m-BDSA has been associated with gastrointestinal effects, such as loose feces. The concentrations of these contaminants measured in recently collected drinking water (September 2000 through January 2003) are significantly lower. Using available data, ATSDR does not expect (but can not conclude with certainty) that these conditions will occur or, if they do occur, will be exacerbated by the contaminants at this site.

Have bladder and kidney infections been associated with resorcinol, sulfonic acids, or calcium petronates?

Response: None of the available data indicates an association between bladder and kidney infections and exposure to resorcinol, sulfonic acids, or calcium petronates.

It is possible that I may have ingested contaminated drinking water from my private well during my pregnancy. Have any harmful effects been associated with the site chemicals and in utero exposure?

Response: No scientific research on human exposure was found regarding adverse health effects of resorcinol and sulfonic acids from ingestion during pregnancy.

Public Comments

The Bear Creek Chemical Area PHA was available for public review and comment from July 29, 2004 through October 14, 2004 at the following repositories:

Butler Area Public Library
218 North McKean Street
Butler, PA 16001
(724) 287-1715

John A. Beck Jr. Library
Butler County Community College
Butler, PA 16003
(724) 287-8711

A public meeting was held by ATSDR at the Petrolia Fire Hall on Wednesday, September 8, 2004 at 6:30 PM to discuss the findings of the PHA. Representatives from ATSDR and other officials were available for 2 hours before the meeting to address individual questions and concerns.

A summary of the written comments received on the Public Comment version of the PHA and ATSDR's responses to these comments is provided in Appendix F.

ATSDR Child Health Initiative

In communities faced with air, water, or food contamination, the many physical differences between children and adults demand special emphasis. Children could be at greater risk than are adults from certain kinds of exposure to hazardous substances. Children play outdoors and sometimes engage in hand-to-mouth behaviors that increase their exposure potential. Children are shorter than are adults; this means they breathe dust, soil, and vapors close to the ground. A child's lower body weight and higher intake rate results in a greater dose of hazardous substance per unit of body weight. If toxic exposure levels are high enough during critical growth stages, the developing body systems of children can sustain permanent damage. Finally, children are dependent on adults for access to housing, for access to medical care, and for risk identification. Thus adults need as much information as possible to make informed decisions regarding their children's health. ATSDR is committed to evaluating the special interests of children at sites such as the Bear Creek Chemical Area.

As part of this PHA, ATSDR considered the concentrations of chemicals that children could be exposed to and the likelihood of adverse effects resulting from their exposure. Using U.S. Census 2000 information, about 324 children (age 6 and under) reside within the site boundary.

Because no data are available for this period of time, actual past exposure to drinking water via ingestion is unknown. An evaluation of exposure to drinking water via ingestion and direct skin contact based on the available data (2000–2002) indicates that harmful effects among children are not likely to occur. Additionally, health impacts are not expected among child residents exposed to surface material deposits at the Bear Creek Chemical Area disposal areas for which data are available.

Conclusions

After reviewing the available data, ATSDR assigned a public health hazard category for each of the completed exposure pathways evaluated in this PHA. Appendix G presents a description of each of the public health hazard categories considered during the classification process. Additional conclusions of the PHA for the Bear Creek Chemical Area are presented below.

Before the preparation of this PHA, neither ATSDR nor EPA had developed health guidelines for resorcinol, sulfonic acids, and calcium petronates. To address the potential exposures associated with the Bear Creek Chemical Area, a team of toxicologists with ATSDR's Division of Toxicology prepared a toxicological report for the contaminants of concern associated with the Bear Creek Chemical Area [5]. The document was then externally peer-reviewed by consultant toxicologists. This toxicological information was used in the evaluation conducted as part of this PHA.

ATSDR concludes that past exposure to contaminants in drinking water posed an ***Indeterminate Public Health Hazard***. Domestic water supplies, consisting of private wells, domestic springs, and commercial/public water supplies, were sampled between September 2000 and January 2003. No data is available for these wells prior to this time period. Therefore, the actual concentrations of contaminants to which individuals might have been exposed to in their drinking water in the past (prior to 2000) are unknown. In addition, limited cancer and non-cancer toxicological data is available for the contaminants of concern, particularly sulfonic acids. The available toxicity information is inadequate to determine if the estimated doses for past exposures posed a public health hazard.

Currently, individuals with contaminated water supplies are receiving bottled water for drinking water purposes. These individuals continue to use water containing resorcinol and sulfonic acids for non-drinking purposes, such as showering and bathing. Using the available data and information provided by ATSDR's toxicological evaluation, current exposures from showering and bathing are not likely to result in adverse health effects and pose ***No Apparent Public Health Hazard***.

Using the data available from the Apple Road Site, Hemlock Road Site, and Kelly Farm, exposure to contaminants in surface deposit materials, including soil and sediment, by residents (child and adult) and trespassers is not expected to result in adverse health

effects. Therefore, the surface deposit exposure pathway poses ***No Apparent Public Health Hazard***.

According to the information contained in the Pennsylvania Cancer Registry for the combined ZIP codes selected for review, no pattern of elevated cancer is apparent within the Bear Creek Chemical Area.

Recommendations

The recommendations of the PHA for the Bear Creek Chemical Area are

1. PADEP should continue to supply bottled water to homes with contaminated water supplies as an interim measure until the public water supply system is constructed.
2. PADEP should conduct a more comprehensive, full-scan sampling (also referred to as analyses for the EPA Target Compound List and EPA Target Analyte List) along the perimeter and outside the proposed public water supply service area to ensure that all individuals with contaminated private wells are provided with public water, and future exposure is prevented. Because groundwater contamination associated with the Bear Creek Chemical Area has not been adequately characterized, full-scan sampling should include laboratory analysis of the site-related contaminants of concern, volatile organic compounds (i.e., benzene and related compounds), semi-volatile organic compounds (i.e., polyaromatic hydrocarbons or PAHs), and metals.
3. PADEP should conduct more comprehensive, full-scan analyses of some of the private wells to determine whether they have been impacted by other contaminants. Private wells were primarily sampled for the presence of the contaminants of concern associated with the site (resorcinol and sulfonic acids). Other contaminants may, however, have been deposited in the disposal areas.
4. PADEP should conduct comprehensive, full-scan surface water sampling in areas used by individuals for recreational activities (e.g., swimming and fishing) that might have been impacted by site activities. In the event that surface water used for fishing has been contaminated by chemicals known to bioaccumulate, it is recommended that fish data be collected in order to evaluate the potential for exposure.
5. PADEP should restrict the installation of new residential and commercial private wells in the area of groundwater contamination to prevent exposure to contaminants.

Public Health Action Plan

A Public Health Action Plan describes the actions designed to mitigate or prevent adverse human health effects that might result from exposure to hazardous substances associated with site contamination. A summary of the public health actions that have been taken and those to be completed for the Bear Creek Chemical Area are provided below.

Actions Taken

ATSDR conducted a public availability session on Tuesday, July 15, 2003 to gather health concerns from the community. The public availability session was held at the

Petrolia Fire Hall from 4:00 PM to 8 PM ATSDR representatives discussed the PHA process and gathered community health concerns.

In February 2004, Bear Creek Chemical Area Fact Sheets were sent to over 1,100 residents to provide an update on the progress of ATSDR's PHA and to provide ATSDR with contact information for residents with additional questions or concerns about the site.

ATSDR conducted a public meeting to present the findings of the PHA at the Petrolia Fire Hall on Wednesday, September 8, 2004 at 6:30 PM. Representatives from ATSDR and other officials were available for 2 hours before the meeting to address individual questions and concerns.

ATSDR has been involved with an education program to increase awareness among residents' physicians on site issues and on health effects associated with chemical exposures. In April 2004, ATSDR included such information in a letter coordinated and distributed by the Butler Medical Society. ATSDR provided physicians with site background information, explained what the agency is doing at the site, and shared contact information.

In November 2004, ATSDR conducted three grand rounds at the Armstrong County Memorial Hospital and the Butler County Medical Society, for approximately 40 physicians. Keith K. Burkhart, MD, FACMT, FAACT, FACEP, Regional Medical Toxicologist in ATSDR/Region 3, was the main speaker. Topics included Bear Creek Chemical Area issues and health effects associated with resorcinol exposure. Continued medical education credits, along with an informational packet, were provided to physicians.

Actions to be Completed

ATSDR will continue to collaborate with the appropriate federal, state, local agencies, and other stakeholders. ATSDR will review new environmental data associated with the Bear Creek Chemical Area and will include results in future updates of this PHA, if deemed necessary.

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References

1. Agency for Toxic Substances and Disease Registry. Public health assessment guidance manual. Atlanta: US Department of Health and Human Services; 2005 January.
2. Hursh C. Memorandum from Carl Hursh, Solid Waste Specialist with Pennsylvania Department of Environmental Resources, Region V to Charles A. Duritsa, Regional Solid Waste Manager with Pennsylvania Department of Environmental Resources, Region V; 1980 March 14.
3. Commonwealth of Pennsylvania, Department of Environmental Protection. Consent Order and Agreement with Beazer East, Inc; 2003 May 27.
4. Commonwealth of Pennsylvania, Department of Environmental Protection. Consent Order and Agreement with Crompton Corporation; 2003 September 21.
5. Agency for Toxic Substances and Disease Registry. Toxicological informatinon re: resorcinol and Sselected benzene sulfonic acids (Bear Creek, PA). Atlanta: US Department of Health and Human Services; 2004 April.
6. Malcolm Pirnie, Inc. Environmental fate and transport mechanism of chemicals of interest, remedial investigation support, Kelly Farm Site; 2001 July.
7. Environmental Protection Agency. Current site information fact sheet for the Craig Farm Drum Site. EPA Region 3, Hazardous Site Cleanup Division. Updated 2002 August. Last accessed 2005 21 July. Available at: http://epa.gov/reg3hwmd/super/PA/craig-farm/pad.htm.
8. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, Craig Site No. 3B. Armstrong County, Pennsylvania; 2002 November.
9. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, former Craig Lagoon. Armstrong County, Pennsylvania; 2002 October.
10. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area. Craig Site No. 3C. Armstrong County, Pennsylvania; 2002 November.
11. Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, unnamed Craig Site. Armstrong County, Pennsylvania; 2002 October.
12. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, Craig Site No. 3B. Armstrong County, Pennsylvania; 2002 November.
13. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, Craig Site No. 3C. Armstrong County, Pennsylvania; 2002 November.
14. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, former Craig Lagoon. Armstrong County, Pennsylvania; 2002 October.
15. Key Environmental, Inc. Preliminary (Phase I) investigation Report. Suspected Waste Disposal Area. Unnamed Craig Site. Armstrong County, Pennsylvania. October 2002.
16. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, Wade Armstrong. Armstrong County, Pennsylvania; 2002 October.
17. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, DEP Site No. 1. Butler County, Pennsylvania; 2002 December.

18. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, DEP Site No. 2. Butler County, Pennsylvania; 2002 December.
19. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, DEP Site No. 3. Butler County, Pennsylvania; 2003 February.
20. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area, DEP Site No. 4. Butler County, Pennsylvania; 2002 October.
21. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area. DEP Site No. 5. Butler County, Pennsylvania; 2002 October.
22. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area. DEP Site No. 6. Butler County, Pennsylvania; 2002 November.
23. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area. DEP Site No. 7. Armstrong County, Pennsylvania; 2002October.
24. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area. DEP Site No. 8. Butler County, Pennsylvania; 2002 November.
25. Beazer East, Inc. Consent Order and Agreement between the Commonwealth of Pennsylvania, Department of Environmental Protection and Beazer East, Inc; 2003 May 6.
26. Key Environmental, Inc. Preliminary (Phase I) investigation report, suspected waste disposal area. Jameson Site. Butler County, Pennsylvania; 2003 February.
27. Key Environmental, Inc. Prelimimary (Phase I) investigation report, suspected waste disposal area. Wade-Parsonville. Butler County, Pennsylvania; 2002 December.
28. Key Environmental, Inc. Compilation of data, Bear Creek Chemical Site. Butler and Armstrong Counties, Pennsylvania; 2003 August.
29. Agency for Toxic Substances and Disease Registry. Toxicological profile for arsenic. Atlanta: US Department of Health and Human Services; 2002 September.
30. United States Environmental Protection Agency. Integrated Risk Information System. Last updated 2005 July 21. Last accessed 2005 July 21. Available at: http://www.epa.gov/iris.
31. Agency for Toxic Substances and Disease Registry. Toxicological profile for bromodichloromethane. Atlanta: US Department of Health and Human Services; 1989 December.
32. Agency for Toxic Substances and Disease Registry. Toxicological profile for cadmium. Atlanta: US Department of Health and Human Services; 1999 July.
33. Agency for Toxic Substances and Disease Registry. Toxicological profile for chlorodibromomethane. Atlanta: US Department of Health and Human Services; 2003 September.
34. Agency for Toxic Substances and Disease Registry. Toxicological profile for beryllium. Atlanta: US Department of Health and Human Services; 2002 September.
35. United States Environmental Protection Agency. Exposure factors handbook Volume III; 1997 August.
36. Comprehensive Environmental Response, Compensation, and Liability Act of 1980, Pub. L. No. 95-510 (Dec. 11, 1980), as amended by the Superfund Amendments and

Reauthorization Act of 1986, Pub. L. No. 99-499 (Oct. 17, 1986), codified together at 42 U.S.C. 9601, et seq. Subchapter I-Hazardous Substances Releases, Liability, Compensation. 9604(i)(6)(F).

Appendix A: Toxicological Information on Resorcinol and Selected Benzene Sulfonic Acids

(Bear Creek, PA)

April, 2004

Prepared by:

U. S. Department of Health and Human Services

Agency for Toxic Substances and Disease Registry, Division of Toxicology

Atlanta, Georgia

Executive Summary

The Division of Health Assessment and Consultation (DHAC) has requested the Division of Toxicology (DT) to perform an independent toxicological review of contaminants found in the drinking water at Bear Creek in Pennsylvania. DHAC is advising the PADOH and the public on whether it is safe for people to shower with the contaminated water (bottled water is currently being provided to the population). In addition to a determination of whether dermal and inhalation exposure to the contaminated water is a concern, DHAC has requested a review of oral exposure to the contaminated drinking water for the purpose of evaluating past oral exposures.

The chemical contaminants include resorcinol, which has an extensive data base for oral and dermal exposure, and some information for inhalation exposure. The toxicological summary for resorcinol in this document focuses on the toxicity of dermal and inhalation exposure. Oral exposure to resorcinol was not evaluated in this summary because the proposed reference dose (RfD) of 2 mg/kg/day reviewed by Toxicology Excellence for Risk Assessment (TERA 2004) is acceptable to DHAC.

The other contaminants are meta-benzene disulfonic acid (m-BDSA), benzene sulfonic acid (BSA), para-phenol sulfonic acid (p-PSA), and calcium petronate, for all of which only very limited data bases exist. Unpublished studies recently performed by independent laboratories are available for oral and dermal exposure to m-BDSA, BSA, and p-PSA. Unpublished studies for inhalation exposure to the zinc salt of p-PSA are also available. Data on chemical and physical properties of calcium petronate are available, but no toxicity studies were found in the published literature or in the package of unpublished studies.

Whereas the DT reviewers found that the unpublished studies of these contaminants generally were conducted in compliance with Good Laboratory Practice standards, independent peer review in accord with ATSDR policy was conducted. The three independent peer reviewers (Dr. Finis Cavender, Dr. Kannan Krishnan, and Dr. James Withey) have generally agreed with DT's assessment of the unpublished studies and the conclusions in "Toxicological Information on Resorcinol and Selected Benzene Sulfonic Acids." This document has been revised in response to their specific comments.

On the basis of the review of available unpublished studies, DT has concluded that dermal exposure to m-BDSA, BSA, and p-PSA in tap water is not a concern because at most, only slight irritation to skin has been observed in dermally exposed animals at much higher concentrations than would be present in contaminated water. Application of pharmaceutical creams containing high concentrations of resorcinol on the skin of humans has resulted in thyroid effects in the past, but the exposure scenarios are not relevant to dermal exposure to contaminated tap water. These chemicals are poorly absorbed by the dermal route.

Data regarding the toxicity of the chemicals by inhalation is very limited, but the low volatility suggests that inhalation exposure to tap water containing these compounds during such activities as cooking, bathing, or showering is not likely to be of concern.

For evaluation of oral exposure, the DT reviewers also examined the proposed reference doses that were suggested by AMEC Earth and Environmental, Inc., an independent consultant for the PA DOH regarding the presence of these chemicals at another site (Kelly Farm). AMEC used standard EPA methodology to derive the proposed reference doses. The values proposed by AMEC were 0.4 mg/kg/day for m-BDSA, 0.03 mg/kg/day for BSA, and 0.1 mg/kg/day for p-PSA.

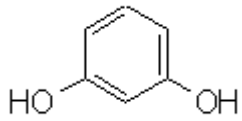
In the identification of no-observed-adverse-effect-levels (NOAELs) and lowest-observed-adverse-effect-levels (LOAELs), AMEC dismissed the reduction of lymphocytes observed in rats treated with these chemicals because other biochemical and histological tests failed to identify an etiology for the hematological effects. The DT reviewers noted that reductions in lymphocytes were observed for all these phenolic sulfonic derivatives, and in the absence of other studies, DT reviewers considered it prudent to identify LOAEL and NOAEL values for the hematological endpoints. The DT reviewers, therefore, suggested appropriate uncertainty factors for the NOAEL and LOAEL values that would result in interim guidance values of 0.1 mg/kg/day for m-BDSA, 0.03 mg/kg/day for BSA, and 0.03 mg/kg/day for p-PSA. These values have not undergone evaluation by the DT minimal risk level (MRL) committee.

Because of the lack of information on the toxicological potential of calcium petronates (CPs), the only conclusion is that these chemicals are unlikely to be a concern for inhalation exposure from water use in bathing, boiling, or cleaning, because CPs are not likely to volatilize from the water.

DT emphasizes the incompleteness of the toxicological database for the selected benzene sulfonic acids (e.g., the lack of reproductive/developmental studies, chronic/cancer bioassays, and subchronic studies in more than one species). The possibility of additive/interactive effects should also be kept in mind.

Resorcinol

CAS 108-46-3



Resorcinol is a natural crystalline solid phenolic compound with a low vapor pressure of 0.000489 mm Hg at 25 ºC, so that it is not likely to exist in ambient air at high concentrations, but it can volatilize slightly with steam. Thus, some inhalation exposure to contaminated tap water during such activities as showering may occur. Resorcinol is very soluble in water (71,700 mg/L at 25 ºC), so that dermal contact with contaminated tap water is likely to occur during bathing or showering. Exposure is also likely form drinking contaminated drinking water.

Resorcinol is used mainly in hair dyes and such skin care products as cold creams and lotions. Thus, it may come in contact with the skin, eyes, hair, nails, and mucous membranes several times a day. Such use and exposure may extend over many years. Resorcinol is considered by the Cosmetic Ingredient Review Expert Panel (CIR) to be safe as a cosmetic ingredient in the present practice of use and concentrations (CIR 1985). Resorcinol has been used for many years in pharmaceutical preparations for topical skin conditions such as acne, dermatitis, eczema, psoriasis, corns, calluses, ring worm, and fungal infections. Industrially, it is used in the rubber and lumber industries and in resin and wood adhesives.

Effects in Humans

Use of resorcinol in pharmaceuticals, hair dyes, and skin care products:

In its use as a component in pharmaceutical preparations, resorcinol has been associated with thyroid effects in a number of case reports. Hypothyroidism and goiter have been described in patients who repeatedly applied ointments containing resorcinol (4% to 12%) to ulcerated varicose veins for several years (Berthezene et al. 1973; Bull and Fraser 1950; March 1951; Young 1951; Hobson 1951; Thomas and Gisburn 1961). On the basis of body weight and details of the frequency of applications, doses of resorcinol in such applications were estimated to range from about 27 to 73 mg/kg/day. Katin et al. (1971) described a case of hypothyroidism in a dialysis patient who had been applying three 2.5 g tubes/day of Lanacane® that contained 2% resorcinol (about 2 mg/kg/day) to relieve persistent itching. The hyperthyroidism disappeared when the patient was denied the use of Lanacane®. In contrast to the cases in which ointments were applied to ulcerated skin, Katin et al (1971) concluded that this case involved intact skin, although the skin could have been abraded because of scratching.

Infants and young children appear to be especially susceptible to toxic effects of resorcinol in therapeutic preparations. Resorcinol-containing creams and lotions applied to the skin of young children for diaper rash or eczema have been found to be very toxic, resulting in cyanosis, hemoglobinemia and hemoglobinuria, hemolytic anemia, convulsions, and death, as reviewed by Cunningham (1956). Methemoglobinemia has also been reported in children for whom resorcinol-containing creams were applied for diaper rash, but its occurrence is rare. Cyanosis and methemoglobinemia occurred in a 6-week-old boy given two applications of Castellani's solution (5% resorcinol), an antimicrobial medicine, for the treatment of eczema (Lundell and Nordman 1973). A case of methemoglobinemia was also reported in the 2-year-old girl who accidentally ingested 10 mL of Nestosyl®, which is used for dental pain (Autret et al. 1989). In addition to resorcinol, Nestosyl® also contains benzocaine and 8-hydroquinoline, chemicals known to be associated with methemoglobinemia. The doses of resorcinol received by these children cannot be estimated from the available data. However, in another case in which a 6-day-old boy treated by his mother with Vagisil® cream for diaper rash developed methemoglobinemia (Tush and Kuhn 1996), AMEC (2004) estimated a dose of resorcinol of 108 mg/kg/day. It should be noted that the Vagisil® cream contained 5 % benzocaine and 2% resorcinol. In an experimental study of healthy women who applied a vaginal antiitch cream containing 20% benzocaine and 3% resorcinol, no increase in methemoglobinemia was observed (Currie et al. 1997), but these authors cautioned that

these results should not be extrapolated to young children or to larger areas of application.

Resorcinol in hair dyes, cosmetic skin care products, and therapeutic agents may produce contact dermatitis in sensitized people. A woman who worked in a hair salon and had been dyeing her hair with the same dye for four years developed intense itching of the scalp with erythema and edema (Vilaplana et al. 1991). After treatment with corticosteroids and cessation of dyeing her hair, the condition improved. After she returned to work, she developed itchy erythematous papules on her hands on contact with certain hair dyes. The results of patch tests with various dye ingredients revealed a positive reaction only to resorcinol. Allergic contact dermatitis as a result of the use of Castellani's paint (5% resorcinol) as a radiotherapy marker occurred in a man with squamous cell carcinoma (Marks and West 1978) and a woman with breast cancer (Pecegueiro 1992) who were being evaluated for radiotherapy. Allergic contact dermatitis has been reported in several case reports of people treated with therapeutic resorcinol preparations for acne (Nakagawa et al. 1992), eczema (Langeland and Braathen 1987), psoriasis (Waddell and Finn 1981), blepharitis (Massone et al. 1993) and other skin disorders (Fisher 1982).

In a prospective study of 179,800 patients of dermatologists, 487 cases of contact dermatitis due to cosmetic sensitivity were identified (Eiermann et al. 1982). Patch testing with various cosmetic ingredients was performed on 149 of the 487 cases. Resorcinol caused a cutaneous reaction in only one subject. In other studies submitted to the Cosmetic Ingredient Review Expert Panel (CIR) by the Cosmetic, Toiletry and Fragrance Association (CTFA), patch testing of 102 or 49 subjects with a 1.4% resorcinol cosmetic product resulted in no irritation, sensitization, or photosensitization (CIR 1985). Fisher (1982) noted that allergic reactions to resorcinol in eye drops, skin fresheners, freckle creams, hair tonics, lipstick, and acne preparations are very rare. In addition, resorcinol produced no or very low occurrences of contact dermatitis in hairdressers (Frosch et al. 1993; Guerra et al. 1992a), hairdressers' clients (Guerra et al. 1992b), people with allergic reactions to cosmetics (Goossens et al. 1999) or plastics and glues (Tarvainen 1995), or people treated with creams for leg ulcers (Kokelj and Cantarutti 1986).

Occupational Exposure

No evidence of hypothyroidism, altered thyroid hormone levels, or death from cancer, circulatory disease, respiratory disease, or digestive diseases was found in workers from the Koppers Company plants in North Carolina and Pennsylvania (TOMA 1980; 1981; Lynch et al. 2002). The plants in Pennsylvania made resorcinol for use in rubber production, where exposure also included formaldehyde, by-products of sulfonation, and benzene. The plant in North Carolina produced laminated beams, where the major concern was pentachlorophenol, organic solvents, and resorcinol. Exposure levels to resorcinol were not provided in these studies.

The finding of 4 cases of overt hypothyroidism over a period of 6 years in a textile factory in the United Kingdom employing 539 workers prompted a follow-up survey of 189 men and 48 women who agreed to participate (Roberts et al. 1990). Of these workers, 115 were process workers, and 122 were employed as managers and office and

laboratory staff. The processes in the textile plant included the use of resorcinol and thiourea, both compounds associated with thyroid effects. Blood was collected for assays for thyroid stimulation hormone (TSH), antithyroglobulin antibodies, and antimicrosomal antibodies. Levels at the inlet of the local exhaust ventilation of stenters (finishing machines) were 5 $\mu g/m^3$ for thiourea and <20 $\mu g/m^3$ for resorcinol. The results of the testing found 15 new cases of thyroid function disturbance, but 3 of the subjects were eliminated from analysis because one was hyperthyroid, one had inherited pituitary hypothyroidism and the third had had partial thyroidectomy. Of the remaining 12 workers, 3 had raised TSH levels with non-specific symptoms, 1 was asymptomatic with raised TSH levels, and 8 had only raised circulating thyroid antibodies. Although these results are difficult to interpret because an appropriate control group was not included and some of the affected individuals were non-process workers, Roberts et al. (1990) were unable to rule out the possibility that the thyroid effects were due to occupational exposure to these chemicals.

Dermatitis was studied in 42 tire makers in a motorcycle factory in Italy (Abbate et al. 1989). The workers were questioned for dermatology history and work history, and given medical examinations, special dermatological examinations, and skin tests. All the workers had a rusty red pigmentation on the fingers, and some also had the pigmentation on the palms. Half of the workers reported slight burning sensation and slight itch. Some displayed desquamation. Skin or allergic reactions occurred in 19% of the workers, all of whom had used a “new compound” lately. Chemical analysis of the compounds indicated an increased use of resorcinol, whereas the levels of other compounds were the same as used previously. Patch testing was negative in all subjects.

Animal Studies.

Dermal/Ocular

Some of the dermal studies described below do not state the area of skin to which the dose of resorcinol was applied. The descriptions will note the area of skin only for those studies that state the area of the skin in the methods. In addition, many of the studies in animals examined the effects of hair dyes, many of which contain resorcinol, along with other chemicals, such as, phenylenediamines, p-toluenediamine sulfate, 2,4-diaminoanisole sulfate, and aminonitrophenols.

General Toxicity

In a dermal study, groups of 4 male albino rabbits had abraded or intact skin in contact with resorcinol for 24 hours (Flickinger 1976). The doses were 1,000, 2,000, 3,980 and 7,950 mg/kg. Based on mortality data during a 14-day observation period, the dermal LD_{50} value was 3,350 mg/kg, with 95% confidence limits of 1,980 to 5,710 mg/kg. Necrosis of the skin was found in all rabbits treated with the 3,980 and 7,950 mg/kg dose and in 3 of 4 rabbits treated with 2,000 mg/kg. Rabbits treated with 1,000 mg/kg had moderate to severe irritation after the 24-hour contact, followed by slight hyperkeratosis. A dose-related decrease in body weight was observed in the rabbits that survived. In the primary skin irritation test, the rabbits had contact with 500 mg of resorcinol moistened with saline on the intact and abraded skin for 24 hours. For the intact skin areas, severity of erythema or edema varied from non-perceptible to moderate, whereas the abraded

areas showed necrosis, which was more marked at 72 hours than at 24 hours and which was still present at 14 days. Resorcinol was classified to be not a primary skin irritant. Resorcinol was, however, found to be an eye irritant. The rabbits received an application of 100 mg of resorcinol in the eyes. Conjunctivitis, corneal opacity and corneal ulcerations were observed at 24 hours, and keratoconus and pannus formation were evident at 14 days after exposure.

In a toxicity study of 12 hair dye composite formulations, 6 of which contained resorcinol, groups of 6 male and 6 female adult New Zealand rabbits received topical applications of 1 mL/kg of preparations of equal volumes of the dyes and 6% hydrogen peroxide, twice a week for 13 weeks (Burnett et al. 1976). The dye formulations contained about 1%–2% resorcinol. (1 mL/kg x 0.02 x 1.2717 g/mL [density] = 25.4 mg/kg for 2 days/week or 7.3 mg/kg/day) The application site was to the shaved back and sides. There were three independent negative control groups. No compound-related overt toxicity or body weight changes and no treatment-related effects on hematological, blood chemistry, or urinalysis parameters were observed. Gross and histological examination of 25 tissues and organs revealed no treatment-related pathology.

Thyroid effects

The production of thyroid effects and goiter has been studied in rats. In one study, Wistar rats were exposed dermally to various preparations containing resorcinol: resorcinol ointment (12.5 g or 12.5%); resorcinol in peanut oil (2 g or 2%; 1 cc = 0.18 mM of resorcinol); resorcinol in beeswax (8 g of 8%, 0.5cc = 0.36 mM of resorcinol); resorcinol diacetate undiluted (0.08 cc.) in glycerin and egg albumin (15.5 %); and resorcinol diacetate in peanut oil (31%) (Samuel 1955). In the experiment with resorcinol ointment, resorcinol ointment was rubbed thoroughly for two periods of 10 minutes each for 28 days to 6 shaved and 4 scarified and shaved skins (to simulate ulceration) of the ventral surfaces of 10 rats. Controls consisted of 4 rats that received only the ointment base without resorcinol on scarified skin. Thyroid weight was increased by 3.3 times in both groups of rats that received the resorcinol, compared with that of controls. The histological examination of the enlarged thyroids revealed uniform diffuse hyperplasia, with acini of variable size and shape and almost complete loss of colloid. Histological effects were also noted in the adrenal glands and the anterior pituitary bodies. The application of resorcinol in these experiments (repeated thorough rubbing ointment on the skin) was designed to mimic human application of ointment containing resorcinol for therapeutic reasons.

The other preparations of resorcinol were administered subcutaneously in order to study the progression of histopathological changes in the enlarged thyroids of the rats that received the resorcinol preparation compared to controls (Samuel 1955). Other studies, in which resorcinol was administered to rats subcutaneously, found that resorcinol was goiterogenic and inhibited the uptake of iodide into the thyroid (Doniach and Fraser 1950; Arnott and Doniach 1951; Doniach and Logothertopoulos 1952). These applications of resorcinol are not relevant to humans exposed dermally to water contaminated with resorcinol.

Reproductive-Developmental Effects

In a two-generation reproduction study, resorcinol was among the dyes contained in four of the six oxidative hair-coloring formulations applied topically to groups of 40 male and 40 female Sprague-Dawley rats (Burnett and Goldenthal 1988). The hair on the back of the rats was clipped short, and the dye solutions, mixed in equal volumes in 6% hydrogen peroxide, were applied twice a week at a dose of 0.5 mL per application to the shaved area (1-inch diameter). Again, the dyes contained about 1%–2% resorcinol (0.5 mL/kg x 0.02 x 1.2717 g/mL [density] = 12.7 mg/kg for 2 days/week or 3.6 mg/kg/day). In the reproduction study, the dyes were applied until the rats were 100 days old (application began at 6–8 weeks of age) before mating and during mating for 15 days, gestation, and lactation. The females were allowed to deliver naturally. Ten days after the weaning of the F_{1a} litters, the F_0 parents were re-mated to produce the F_{1b} litters, some of which were selected to produce the F_2 generation. These F_1 parents were treated the same as the F_0 parents with topical application of the dyes for 100 days before mating and during mating, gestation and lactation to produce the F_{2a} and F_{2b} litters. There were no effects on general health, body weight gains, food consumption, and survival of any rats in any generation. Fertility, gestation, survival and live birth indices, and mean number weaned and mean weaning weights for each litter in each generation did not differ from control groups. Histological examination of tissues of five male and five female F_{1b} parentals revealed no treatment-related lesions. The only difference between controls and rats treated with resorcinol-containing dyes was skin irritation in all treated groups, consisting of mild dermatitis seen intermittently throughout the treatment period in all generations.

In a teratology study of 12 hair dye composite formulations, 6 of which contained resorcinol (0.2%–2%), groups of 20 pregnant Charles River CD rats were treated topically with 2 mL/kg on days 1, 4, 7, 10, 13, 16, and 19 of gestation (2 mL/kg x 0.02 x 1.2717 g/mL =50.8 mg/kg on each day) (Burnett et al. 1976). The treated area was the shaved dorso-scapular area. One positive and three negative control groups were also maintained. The rats were sacrificed on gestational day 20. No overt signs of toxicity or skin irritation were observed during the treatment. No effects on maternal body weight or food consumptions were found. There were no treatment related effects on number of corpora lutea, implantations sites and live fetuses, sex ratio, number of females exhibiting resorption sites, or mean resorptions per pregnancy. The only significant fetal anomaly was an increase in skeletal anomalies (9 of 169 fetuses) in rats receiving one of the six dyes that contained resorcinol. The investigators did not consider the minor skeletal changes (notched ribs, short ribs) to be biologically significant. For the positive control (acetylsalicyclic acid) group, effects consisted of increased teratogenicity, increased embryo death, and decreased fetal weight.

Chronic Toxicity and Carcinogenicity

Groups of 5 New Zealand rabbits of both sexes received 0.02 mL of resorcinol in methanol applied dermally to the interior of the left ear twice a week for up to180 weeks at concentrations of 5%, 10% or 50% (0.02 mL x 1.2717 g/mL x 0.5 x 2/7 ÷ 3.8 kg = 1 mg/kg/day). There were no effects on survival and no skin tumors (Stenbäck 1977).

In a skin painting study of several cutaneous agents used as solvents, insect repellents, fixatives, sun screens, and other applications, groups of 50 female Swiss mice received

0.02 mL of resorcinol in acetone dropped on the dorsal shaved skin (1-inch square area) twice a week until they died spontaneously or were killed when moribund (Stenbäck and Shubik 1974). The concentrations were 5%, 25% and 50% (0.02 mL x 1.2717 g/mL x 0.5 x 2/7 ÷ 0.03 kg = 0.12 mg/kg/day). Negative controls consisted of 150 untreated mice and 50 mice treated with acetone alone. The positive control group consisted of 50 mice treated with 7,12-dimethylbenzathracene (DMBA). There were no effects on survival. Skin lesions with ulceration, inflammation, and hyperplasia were seen in mice treated with resorcinol. In the mice treated with resorcinol, no skin tumors were observed in the mice treated at 50%, but one mouse at 5% had two squamous cell papillomas on the dorsal skin, and one mouse at 25% had a squamous cell carcinoma on the ear. These occurrences did not differ from that of negative controls, whereas the 50 positive control mice had 31 squamous cell papillomas and 26 squamous cell carcinomas on the dorsal skin.

In a chronic toxicity-carcinogenicity study, groups of 50 male and 50 female Sprague-Dawley rats were treated dermally with a mixture of 3% *p*-toluenediamine, 0.75% resorcinol, and 0.75% *m*-diaminoanisole or with *p*-toluenediamine alone (Kinkel and Holzmann 1973). A group of 50 males and 50 females received no treatment, and a group of 25 males and 25 females received the control vehicle (a colorless jelly prepared with carboxymethylcellulose). The solutions were applied to a shaved dorsal skin area measuring 3 x 3 cm^2 and left on the skin for 30 minutes. The treated skin area was then washed with water and dried. This treatment was repeated twice a week for 2 years, and surviving rats were observed for an additional 6 months. There were no treatment effects on behavior, feed intake, body weight changes, blood counts, blood chemistries, or mortality. Gross and histological examinations revealed no treatment-related increased incidence of tumors nor histopathological lesions in liver, kidneys, or lungs. No skin tumors or other skin reactions were found at the site of application.

A chronic toxicity-carcinogenicity study was included in the two-generation reproduction study by Burnett and Goldenthal (1988). Groups of 60 male and 60 female weanling rats selected from the F_{1a} rats received topical application of the dyes to a 1-inch diameter of skin for 2 years. Three separate non-treated control groups, each consisting of 60 males and 60 females, were used for statistical analysis. No treatment-related effects were observed on body weight gain, survival, hematological parameters, clinical chemistry parameters, or urinalyses. No treatment-related increases in non-neoplastic or neoplastic lesions were observed.

In a similar study, groups of 50 male and 50 female Swiss-Webster mice received dermal application of three individual dyes that contained resorcinol (0.40%) weekly or every other week for 18 months at doses of 0.05 mL of the dyes in a 1:1 mixture of the formulation and 6% hydrogen peroxide (0.025 mL of dye) (Burnett et al. 1975). Each application, therefore, was equal to about 4 mg/kg (0.025 mL x 0.004 x 1.2171 g/mL ÷ 0.03 kg). Controls consisted of 250 untreated mice and two groups of 100 mice treated with hydrogen peroxide only weekly or every other week. The positive control received DMBA weekly. No overt signs of toxicity or effects on survival, body weight, or organ weights were observed. Moderate alopecia occurred in about half the mice of each sex in the weekly dye-treated groups during the first 5 months, but this diminished with time. Hematological values were within normal limits. Gross and histological examination of

skin, thyroid, lung, gastrointestinal tract, spleen, pancreas, liver, kidneys, adrenals, urinary bladder, ureter, mesenteric lymph nodes, sternal bone marrow, and gonads revealed no treatment-related pathology.

In another study, resorcinol was found to inhibit the carcinogenicity of benzo[a]pyrene (B[a]P) when co-applied to the skin of mice (Van Duuren and Goldschmidt 1976). Groups of 50 female ICR/Ha Swiss mice received the chemicals that were applied in acetone by micropipette or dimethyl sulfoxide by paintbrush three times a week for 368 days on test. Mice that received resorcinol (10 mg/application or 333 mg/kg) alone did not develop skin tumors. Mice that received both resorcinol and B[a]P developed 6 papillomas in 5 mice (2 had squamous cell carcinoma). Mice treated with B[a]P alone developed 95 papillomas in 40 mice, 33 of which had squamous cell carcinoma. Resorcinol was also tested as a tumor promoter. Groups of 50 mice received 150 µg B[a]P/0.1 mL acetone applied to the dorsal skin once by micropipette. Resorcinol (10 mg/0.1mL acetone) was similarly applied to the dorsal skin 3 times a week beginning 14 days after the initiator. Resorcinol did not show any promoting activity.

In a similar study of cocarcinogenicity, 2,4-toluenediamine alone or in combination with a dye containing resorcinol (0.4% by weight) was tested (Giles et al. 1976). Groups of 28 male and 28 female Swiss-Webster mice received dermal applications to shaved intrascapular regions of 0.05 mL of the test solutions weekly. There were no indications of treatment-related toxicity or carcinogenicity in any groups.

Genotoxicity

Resorcinol did not induce sister chromatid exchange in male or female Sprague-Dawley rats that were treated orally or intraperitoneally at doses up to 100 mg/kg or dermally at doses up to 300 mg/kg (Bracher et al. 1981).

Inhalation

In an acute study, groups of six Harlan-Wistar rats were exposed to aerosols of resorcinol in distilled water at concentrations of 2,230 or 7,800 mg/m^3 for 1 hour or 2,000, 2,480, or 2,800 mg/m^3 for 8 hours (Flickinger 1976). There were no deaths, no effects on body weights, and no treatment-related lesions upon gross necropsy at 14 days after exposure. No damage to lungs and trachea and no evidence of allergic reactions in the respiratory tract were noted in rats, rabbits, and guinea pigs exposed to 34 mg/m^3, 6 hours/day for 2 weeks and maintained for several months. Further details were not reported.

Oral

Oral exposure to resorcinol is not being evaluated in this summary. A reference dose (RfD) for oral exposure of 2 mg/kg/day has been proposed in an evaluation prepared by AMEC Earth and Environmental, Inc., (AMEC 2004) and has been reviewed by a Resorcinol Expert Panel (TERA 2004). DHAC has indicated that this evaluation and proposed RfD are acceptable.

Pharmacokinetics

The absorption, metabolism, and excretion of resorcinol after dermal exposure have been studied in humans. Three healthy men with normal skin were treated with 20 mL of 2% resorcinol in a hydroalcoholic vehicle, 2 times/day 6 days/week for 4 weeks (about

12 mg/kg/day) (Yeung et al. 1983). One control subject was treated only with the vehicle. The solutions were uniformly delivered to the face, shoulders, upper chest, and upper back areas (2,600 cm^2) at a daily dose equivalent to 12 mg resorcinol/kg/day. These exposures were considered to represent the maximal level that would be used as an acne medication containing resorcinol. Blood samples were collected on day 0 and at 1, 2, 3, and 4 weeks after treatment began for analysis of free resorcinol, conjugates, metabolites, blood chemistries and thyroid hormones (T_3, T_4, T_7), and thyroid stimulating hormone (TSH). Urine samples were collected at weeks 2 and 4. No free resorcinol was detected in the plasma when it was assayed for resorcinol or after enzymatic hydrolysis with β-glucuronidase, indicating that the plasma was free of resorcinol and its conjugates (detection limits were 0.1 µg/mL). No free resorcinol was detected in the urine samples, but a resorcinol-conjugate was detected in urine. The urinary levels of the resorcinol-conjugate were 4.8, 33.7, and. 24.3 µg/mL after two weeks, corresponding to total daily urinary excretion of 0.47%, 1.58%, and 2.87% of the applied dose, respectively for the three subjects. After 4 weeks, the levels were 7.0, 8.4, and 1.6 µg/mL, but because the urine collections were incomplete, accurate determinations of the 24-hour urinary excretion were precluded. No conjugates were found in the urine of the control. There were no significant changes in T_3, T_4, T_7, or TSH. All blood chemistries and hemograms were within normal limits. The skin penetration rate of resorcinol was also tested in vitro in excised full-thickness human skin in skin permeation cells, in which preparations of radio-labeled resorcinol were applied to the skin surface. A topical dosage similar to that in the human in vivo study was used. The flux rate was 0.86 µg/cm^2/hour, which was considered to be in good agreement with the flux rate of 0.37 µg/cm^2/hour that was calculated from the 24-hour urinary excretion values obtained in the in vivo experiments. Thus, the dermal absorption of resorcinol was low (<3% of the applied dose). Resorcinol did not persist in the blood, but was excreted as glucuronide- or sulfate-conjugates. The treatments did not result in any effects on thyroid function or blood chemistries.

The scalp penetration of hair dyes, including one containing resorcinol, was studied in humans and monkeys (Wolfram and Maibach 1985). The dyes were enriched with the radio-labeled substance of interest, and urinary excretion of radio-label was measured. For resorcinol, the total excretion in % of dose was 0.076% for humans and 0.177% for Rhesus monkeys, with half-times of 31 hours for both species. The flux of the hair dye containing resorcinol through human scalp was 2.2×10^{-10} (mol/cm^2/hr). The authors reported partition coefficients for resorcinol for guinea pigs: the octanol/water partition coefficient for resorcinol is 7.0, the intact stratum corneum/water coefficient is 3.6, and the delipidized stratum corneum/water coefficient is 7.7. Scalp penetration of resorcinol-containing dye is low.

The pharmacokinetics of resorcinol has also been studied in rats treated either subcutaneously or orally. In the subcutaneous study, groups of male Sprague-Dawley rats were injected with a single dose of 10, 50, or 100 mg/kg resorcinol in water containing a trace amount of ^{14}C-resorcinol (Merker et al. 1982). At 1, 3, 6, and 24 hours after injection, groups of 2 or 3 of the rats were sacrificed, and blood, urine, and feces and specimens of kidney, liver, thyroid, brain, intestine, spleen, spinal cord, urinary bladder and muscle were collected. At dose levels of 50 and 100 mg/kg, resorcinol in the blood reached peak concentrations at 15 minutes, with 90% of resorcinol equivalents eliminated

within the first 2 hours. The half-lives ($t_{1/2}$) for biphasic elimination from the plasma in the 50 mg/kg groups were 21 minutes for the α-phase and 8.6 hours for the β-phase. For the 100 mg/kg dose group, the $t_{1/2}$s were18 minutes for the α-phase and 10.5 hours for the β-phase. Resorcinol distributed mainly to the liver, kidney, and urinary bladder, with peak values at 1 hour, but measurable levels of radioactivity were also found in the thyroid, brain spleen, and spinal cord. After 24 hours, only trace amounts were found in all tissues examined. The excretion in urine and feces was reported only for the 10 mg/kg group. These rats excreted 93.6% of the administered dose in the urine by 24 hours (24-hour urine contained 98% of the recovered radioactivity). A peak level of 7% of the dose was found in the gastrointestinal tract at one hour. By 24 hours, intestinal contents contained less than 0.5%. In the plasma, the glucuronide conjugate of resorcinol accounted for 64% of the radioactivity, and resorcinol was excreted in the urine mainly as the glucuronide conjugate.

In another part of the same study, male Sprague-Dawley rats received a total daily subcutaneous dose of 100 mg/kg/day of unlabeled resorcinol in two divided doses of 50 mg/kg given 6 hours apart for 14 or 30 days (Merker et al. 1982). On days 14 and 30, the rats were injected with a single 50 mg/kg dose of ^{14}C-resorcinol. After injection of the radiolabel, groups of 3 rats were sacrificed at 1, 3, 6, and 24 hours, and tissues (brain, spinal cord, kidneys, liver, spleen, thyroid, testes, intestinal contents, and urinary bladder), blood, feces and urine were collected. Blood samples from the retro-orbital sinus were also collected at intervals of 15 minutes for the first hour and then at 2, 3, and 6 hours. The plasma curves for resorcinol equivalent levels were similar at 14 and 30 days. These levels declined rapidly during the first 2 hours. $T_{1/2}$s for the 14-day treatment were 31 minutes for the α-phase and 5 hours for the β-phase. $T_{1/2}$s for the 30-day treatment were 32 minutes of the α-phase and 7.3 hours for the β-phase. As in the single dose experiments, resorcinol distributed mainly to the liver and kidney, with peak values at 1 hour; only trace amounts were found in all tissues examined after 24 hours. Gastrointestinal contents of resorcinol peaked at about 6% to 12% within 1–3 hours for the 14- and 30-day radioactivity injected rats, with decline to about 0.5% by 24 hours.

In an oral study, groups of male and female Fischer 344 rats were treated with 112 mg/kg ^{14}C-labeled resorcinol (Kim and Matthews 1987). At 24 hours after dosing, only 0.03–48 % of the dose was found in the blood, liver, skin, fat, and muscle. The urine contained 90.77% (male) and 92.8% (female), and the feces contained 2.10% (male) and 1.5% (female) of the dose. The large intestine contained 1.35% (male) and 1.33% (female) of the dose. Thus, total excretory recovery was >90%, with major elimination in the urine. To examine the possibility of biliary excretion, Kim and Matthews (1987) cannulated the bile ducts of anesthetized rats and then introduced an intravenous dose of 11.2 mg/kg ^{14}C-labeled resorcinol. Biliary excretion of resorcinol equivalents was nearly complete within 2 hours and did not account for a major percentage of the dose. Comparison with fecal excretion levels supported the conclusion that enterohepatic recycling occurred, with eventual excretion in the urine. Analysis of the urine for metabolites revealed that resorcinol was excreted mainly as the glucuronide conjugate, with minor metabolites tentatively identified as a sulfate conjugate and a diconjugate of resorcinol with glucuronide and sulfate. When the rats were dosed orally with 225 mg/kg/day for 5 days, no apparent difference in the rate of excretion was noted.

Summary

The repeated, long-term use of resorcinol in pharmaceutical applications in the past has resulted in hypothyroidism and goiter in humans who have applied 27 to 73 mg/kg/day to ulcerated varicose veins or 2 mg/kg/day to intact skin.

Infants and young children were especially susceptible to toxic effects of resorcinol in therapeutic preparations that were applied for diaper rash or eczema, resulting in cyanosis hemoglobinemia, hemolytic anemia, hemoglobinuria, methemoglobinemia, convulsions, and death. Doses were not available in most cases, but a dose of resorcinol received by an infant was estimated to be 108 mg/kg/day in one case.

Resorcinol in hair dyes, cosmetic skin care products, and therapeutic agents may produce contact dermatitis in sensitized people, but allergic reactions are rare. At low concentrations of environmental relevance, allergic reactions to resorcinol would be even more rare.

Resorcinol is considered safe as a cosmetic ingredient in the present practice of use and concentrations by the Cosmetic Ingredient Review Expert Panel.

Occupational exposure to high levels of resorcinol may result in skin irritation and thyroid effects, but the studies are difficult to interpret because of co-exposure to other agents or the lack of appropriate controls.

Animals exposed dermally to resorcinol in applications designed to mimic repeated application such as therapeutic use in the past may develop skin irritation and thyroid effects. These applications of resorcinol are not relevant to humans exposed dermally to water contaminated with resorcinol because the exposure scenarios are very different.

In animals exposed to hair dyes containing resorcinol, no overt toxicity; body weight changes; treatment-related effects on hematological, blood chemistry, or urinalysis parameters; or gross or histopathological lesions in major organs and tissues were seen in rabbits at doses as high as 7.3 mg/kg/day for 13 weeks or to 1 mg/kg/day for 180 weeks, in mice at 4 mg/kg/day for 18 months, or in rats 3.6 mg/kg/day for 2 years.

No reproductive effects in a two-generation study and no developmental effects in a teratology study were found in rats exposed to hair dyes containing resorcinol at calculated doses of 3.6 mg/kg/day for 2 generations or 50.8 mg/kg/day during gestation.

Resorcinol exposure for chronic durations did not result in skin tumors in rabbits exposed dermally to1 mg/kg/day or in mice exposed to 0.12 mg/kg/day. Furthermore, no treatment-related increase in neoplastic lesions in any organ or tissue was found in rats at 3.6 mg/kg/day exposed for 2 years or in mice at 4 mg/kg/day exposed for 18 months.

Inhalation exposure of rats, rabbits, and guinea pigs to 24 mg/m^3, 6 hours/day, for 2 weeks did not result in damage or allergic reactions to the respiratory tract. Exposure of rats to concentrations as high as 7,800 mg/m^3 for 1 hour or 2,800 mg/m^3 for 8 hours did not result in body weight effects or treatment-related lesions upon gross necropsy 14 days later.

Resorcinol is poorly absorbed by the dermal route, and that which is absorbed is conjugated as a glucuronide and is eliminated in the urine in less than a day.

Conclusion

Resorcinol is minimally toxic by the dermal and inhalation routes. Dermal exposure to resorcinol in contaminated water is not likely to result in the thyroid effects that have been found in people who used pharmaceutical preparations of cream and ointments repeatedly for long periods because the exposure scenarios are not equivalent. Thus, individuals tend to experience health effects only if a product contains a very high level of resorcinol and is used over a period of many years. Resorcinol is poorly absorbed by the dermal route. An allergic reaction is possible in sensitized people, but such allergic reactions are rare. In addition, young children are more sensitive than adults to resorcinol. Although resorcinol can volatilize slightly with steam, inhalation exposure to tap water containing resorcinol during such activities as cooking, bathing, or showering is not likely to cause toxic effects on the basis of low exposure concentrations and the limited inhalation data in animals.

References

Abbate C, Polito I, Puglisi A, Brecciaroli R, Tanzariello A, Germano D. 1989. Dermatoses from resorcinol in tyre makers. Br J Industr Med 46:212-214.

Arnott DG, Doniach I. 1952. The effect of compounds allied to resorcinol upon the uptake of radioactive iodine (^{131}I) by the thyroid of the rat. Biochem J 50: 473-479.

AMEC Earth and Environmental, Inc. 2004 Description of a Proposed Reference Dose Resorcinol. Prepared by AMEC Earth and Environmental, Inc. Westford, Massachusetts, September 2004. Prepared for review by the Resorcinol Peer Review Panel, Toxicology Excellence for Risk Assessment.

Autret E, Forveille-Fournier E, Marchand S, Jonville, AP, Ramponi N. 1989. [Méthémoglobinémie après ingestion accidnetelle de Nestosyl®] Arch Fr Pediatr 46:271-272. (French)

Berthezene F, Fournier M, Bernier E, Mornex R. 1973. L'hyothyroïdie induite par la resorcine. Apropos de deux observations [Hypothyroidism induced by resorcinol. Report of two cases]. Lyon Médical 230:319-323.

Bracher MJ, Swistak J, Noser F. 1981. Studies on the potential in vivo induction of sister-chromatid exchanges in rat bone marrow by resorcinol. Mutation Research 91:363-391.

Bull GM, Fraser R. 1950. Myxoedema from resorcinol ointment applied to leg ulcers. Lancet May 6:851-855.

Burnett CM, Goldenthal EI. 1988. Multigenerational reproduction and carcinogenicity studies in Sprague-Dawley rats exposed topically to oxidative hair-colouring formulations containing *p*-phenyenediamine and other aromatic amines. Food and Chemical Toxicology 26:467-474.

Burnett C, Goldenthal EI, Harris SB, Wazeter FX, Strausburg J, Kapp R, Voelker R. 1976. Teratology and percutaneous toxicity studies on hair dyes. J Toxicol Environ Health 1:1027-1040.

Burnett C, Lanman B, Giovacchini R, Wolcott G, Scala R, Keplinger M. 1975. Long-term toxicity studies on oxidation hair dyes. Food Cosmet Toxicol 13:353-357.

Cosmetic Ingredient Review (CIR). 1985. Final report of the safety assessment of 2-methyl resorcinol and resorcinol. Prepared by Cosmetic Ingredient Review Expert Panel, June. 44 pages.

Cunningham, AA. 1956. Resorcin poisoning. Archives of Diseases in Childhood 31: 173-176.

Currie JL, Mott L, Pennisi S, Smith BD, Smith RG. 1997. Potential of external vaginal antiitch cream containing benzocaine to cause methemoglobinemia in healthy women. Am J Obstetrics and Gynecology 176:1006-108..

Doniach I, Fraser R. 1950. Effect of resorcinol on the thyroid uptake of I^{131} in rats. Lancet (May 6):855-856.

Doniach I, Logothetopoulos J. 1953. The goitrogenic action of resorcinol in rats. Brit J Exp Pathol 34:146-151.

Eiermann HJ, Larsen W, Maibach HI, Taylor JS. 1982. Prospective study of cosmetic reactions: 1977-1980. Journal of the American Academy of Dermatology 6:909-917.

Fisher AA. 1982. Resorcinol—a rare sensitizer. Cutis. 29:331-338.

Flickinger CW. 1976. The benzenediols: catechol, resorcinol and hydroquinone — a review of the industrial toxicology and current industrial exposure limits. Am Ind Hyg Assoc J 37:596-606.

Frosch PJ, Burrows D, Camarasa JG, et al. 1993. Allergic reactions to a hairdressers' series: results form 9 European centres. Contact Dermatitis 28:180-183.

Giles AL, Chung CW, Kommineni C. 1976. Dermal carcinogenicity study by mouse-skin painting with 2,4-toluenediamine alone in representative hair dye formulations. J Toxicol Environ Health 1:433-440.

Goossens A, Beck MH, Haneke E, et al. 1999. Adverse cutaneous reaction to cosmetic allergens. Contact Dermatitis 40:112-113.

Guerra L, Tosti A, Bardazzi F, et al. 1992a. Contact dermatitis in hairdressers: the Italian experience. Contact Dermatitis 26: 101-107.

Guerra L, Bardassi F, Tosti A. 1992b. Contact dermatitis in hairdressers' clients. Contact Dermatitis 26: 108-111.

Hobson QJG. 1951. Varicose ulceration of the legs and myxoedema and goiter following application of resorcinol ointment. Proceedings of the Royal Society of Medicine 44:164-166.

Katin MJ, Teehan BP, Sigler MH, Schleifer CR, Gilgore GS. 1977. Resorcinol-induced hypothyroidism in a patient on chronic hemodialysis. Ann Intern Med 86:447-449.

Kim YC, Matthews HB. 1987. Comparative metabolism and excretion of resorcinol in male and female F344 rats. Fund Appl Toxicol 9:409-414.

Kinkel HJ, Holzmann S. 1973. Study of long-term percutaneous toxicity and carcinogenicity of hair dyes (oxidizing dyes) in rats. Food Cosmet Toxicol 11:641-648.

Kokelj F, Cantarutti A. 1986. Contact dermatitis in leg ulcers. Contact dermatitis15: 47-49.

Langeland T, Braathen LR. 1987. Allergic contact dermatitis from resorcinol. Contact Dermatitis 17: 126.

Lundell E, Nordman R. 1973. A case of infantile poisoning by topical application of Castellani's solution. Ann Clinical Research 4:404-406.

Lynch BS, Delzell ES, Bechtel DH. 2002. Toxicology review and risk assessment of resorcinol: thyroid effects. Regulatory Toxicology and Pharmacology 36:198-210.

Marks JG, West GW. 1978. Allergic contact dermatitis to radiotherapy dye. Contact Dermatitis 4:1-2

Marsh F. 1951. Myxoedema from resorcinol ointment. The Lancet (April):855.

Massone L, Anonide A, Borghi S, Usiglio D. 1993 Contact dermatitis of the eyelids from resorcinol in a ophthalmic ointment. Contact Dermatitis 28:49.

Merker PC, Yeung D, Doughty D, Nacht S. 1982. Pharmacokinetics of resorcinol in the rat. Research Communications in Chemical Pathology and Pharmacology 38:367-388).

Nakagawa M, Kawai K, Kawai K. 1992. Cross-sensitivity between resorcinol, resorcinol monobenzoate and phenyl salicylate. Contact Dermatitis 27:199-200.

Pecegueiro M. 1992. Contact dermatitis due to resorcinol in a radiotherapy dye. Contact Dermatitis 26:273.

Roberts FP, Wright AL, O'Hagan. 1990. Hypothyroidism in textile workers. J Soc Occup Med 40:153-156.

Samuel KC.1955. Experimental production of goiter in rats with resorcinol and its derivatives. Lab Invest 4:90-105.

Stenbäck F. 1977. Local and systemic effects of commonly used cutaneous agents. Lifetime studies of 16 compounds in mice and rabbits. Acta Pharmacol Toxicol 41:417-431.

Stenbäck F Shubik P. 1974. Lack of toxicity and carcinogenicity of some commonly used cutaneous agents. Toxicol Appl Pharmacol 31:7-13.

Toxicology Excellence for Risk Assessment. 2004. Report of the Peer Review Meeting on Resorcinol. Sponsored by Beazer East, Inc, November 17-18, 2004, Harrisburg, PA. Toxicology Excellence for Risk Assessment (TERA), Cincinnati, OH. December 15, 2004

Tabershaw Occupational Medicine Associates (TOMA). 1980. Final report. Historical prospective mortality study of workers employed at the Petrolia plant. Prepared for Koppers Company, Inc., Pittsburgh, PA. (Unpublished study).

Tabershaw Occupational Medicine Associates (TOMA). 1981. Occupational health evaluation of the Raleigh, North Carolina plant of Koppers Company, Inc. Forest Products group. Final Report. October 2.

Tarvainen K. 1995. Analysis of patients with allergic patch test reactions to a plastics and glues series. Contact Dermatitis 32:346-351.

Thomas AE, Gisburn MS. 1961. Exogenous ochronosis and myxoedema from resorcinol. Br J Dermatol. 73:378-381.

Tush GM, Kuhn RJ. 1996. Methemoglobinemia induced by an over-the counter medication. Annals of Pharmacotherapy 30: 1251-1254.

Van Duuren BL, Goldschmidt BM. 1976. Cocarcinogenic and tumor-promoting agents in tobacco carcinogenesis. J Natl Cancer Inst 56:1237-1242.

Vilaplana J, Romaguera C, Grimalt F. 1991. Contact dermatitis from resorcinol in a hair dye. Contact Dermatitis 24:151-152.

Waddell MM, Finn OA. 1981. Sensitivity to resorcin. Contact Dermatitis 7:216.

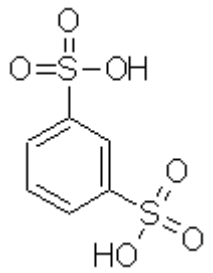
Wolfram LJ, Maibach HI. 1985. Percutaneous penetration of hair dyes. Archs Derm Res 227:235-241.

Yeung D, Kantor S, Nacht S, Gans EH. 1983. Percutaneous absorption, blood levels, and urinary excretion of resorcinol applied topically in humans. Int J Dermatol 22:321-324.

Young S. 1951. Mysoedema from resorcinol ointment. The Lancet. (April): 798-799

Meta-Benzene Disulfonic Acid

CAS 98-48-6



m-Benzenedisulfonic acid (m-BDSA) is a beige to grey powder generated during the manufacturing process of oil detergents and other organic syntheses. m-BDSA has an extremely low vapor pressure of 2.9×10^{-11} mm Hg (25 °C) and is extremely soluble in water, with estimated solubility ranging from 392–1,700 g/L of water (at 25 °C). Additionally, the low Henry's Law constant estimated for m-BDSA, 8.9×10^{-12}, indicates that m-BDSA has a very low affinity to volatilize from the water. Because of these characteristics, m-BDSA is not expected to partition out of wash water and cause an inhalation hazard, even at elevated temperatures that may exist in showering or bathing situations. However, because it is so soluble in water, dermal contact may occur during bathing or showering, or it could be inhaled as an aqueous aerosol (Malcolm Pirnie 2001, Schwab and Anderson 2001).

Effects in Humans

There are currently no reported cases of exposure to the human public or workers and no laboratory studies performed on humans exposed to m-BDSA.

Animal Studies

Dermal

Skin irritation and corrosion potential after single dermal application of m-BDSA for 4 hours were evaluated in groups of 3 New Zealand white rabbits (Tay et al. 2004). The rabbits received 0.5 mL of m-BDSA at 5,000 mg/L or 2,000 mg/L concentrations to the clipped skin under a semi-occlusive gauze patch. There were no effects on body weight and no clinical signs of toxicity. At 5,000 mg/L, irritation (erythema) was very slight in one rabbit and well defined in two rabbits at 1 hour after removal of m-BDSA. After 24 hours, very slight irritation persisted in two rabbits; at 48 hours, very slight irritation persisted in only one rabbit; and no irritation remained after 72 hours. No irritation was noted in rabbits receiving 2,000 mg/L. Thus, m-BDSA is a slight irritant at 5,000 mg/L, but not at 2,000 mg/L (Tay et al. 2004). The mean weight of the rabbits was about 2.2 kg. Therefore, the concentrations of 2,000 and 5,000 mg/L correspond to a dose of approximately 0.5 and 1.1 mg/kg, respectively (e.g., 5000 mg/L = 5 mg/mL; 5mg/mL x 0.5 mL ÷ 2.2 kg = 1.1 mg/kg).

Inhalation

Currently, no reported data exist on inhalation exposures to m-BDSA.

Oral

Groups of 3 male and 3 female healthy, fasted Sprague-Dawley CD rats were given a single oral dose by gavage of m-BDSA at dose levels of 2,000 or 5,000 mg/kg (Blanchard 2002a). The only clinical signs seen throughout the 14 days of observation were loose feces, which were seen in both study groups regardless of sex. No other pre-mortem effects were noted. Postmortem macroscopic examination, which consisted of opening the cranial, thoracic, and abdominal cavities, revealed no abnormalities in the organs. It was determined that the acute lethal dose of m-BDSA was greater than 5,000 mg/kg.

In a palatability study, three male CD rats were administered m-BDSA in drinking water that provided a mean dose level of 21,760 mg/kg/day for 7 days (Geary 2001a). Clinical effects noted were brown staining, wet urogenital regions, and ungroomed appearance and piloerection on day 7. Brown stained urine was noted throughout the study, and loose feces were observed the day after the dosing was completed. From days 2 until 6, lower food consumption was noted, and individual bodyweight losses were also observed in all animals. It was concluded by the authors that the water was palatable to all animals and that water consumption was variable.

m-BDSA was administered to groups of 5 male and 5 female Sprague-Dawley CD rats in drinking water that provided targeted doses of 0, 250, 750, or 2,000 mg/kg daily for 14 days (Geary 2001b). Food consumption was slightly reduced in males at the highest dose, but there was no effect on the other dose groups. Water consumption was higher than for control animals for all groups; therefore, actual intakes of m-BDSA provided doses of 288, 994, or 2,805 mg/kg/day in males and 323, 988, or 3,151 mg/kg/day in females. All treated male groups showed higher white blood cell and lymphocyte counts. The white blood cell counts in the 750 mg/kg/day and 2,000 mg/kg/day male groups and the lymphocyte counts in the 2,000 mg/kg/day male group were significantly higher than control values. Clinical chemistry analysis showed significantly lower potassium and calcium values in females at 750 and 2,000 mg/kg/day, and significantly lower albumin values in females at 2,000 mg/kg/day. The toxicological significance of these effects was not clear. Group mean thymus weights were lower in the 2,000 mg/kg/day groups compared with those of controls. Macroscopic pathology showed pale livers and water content in the cecum of the high-dose males. From the results, NOAELs of 288 mg/kg/day for males and 323 mg/kg/day for females were proposed, based on increased white blood cell and lymphocyte counts. However, since there was an effect noted (higher white blood cell and lymphocyte counts), perhaps this dose could be considered a LOAEL.

In a 13-week study conducted by Huntingdon Life Sciences for AMEC Earth and Environmental, Inc., groups of 10 male and 10 female CD rats were exposed to drinking water that provided nominal doses of m-BDSA of 0, 100, 300 or 1,000 mg/kg/day for 13 weeks (Geary 2003). On the basis of actual drinking water intake, the achieved doses were 100.8, 305.1, and 1,054.7 mg/kg/day for males and 99.7, 291.6, and

1,006.2 mg/kg/day for females. No treatment-related deaths occurred. No significant effects on body weight and no treatment-related clinical signs of toxicity or changes in a neurological functional battery test (startle reflex, tail pinch response, touch response, grip strength, and motor activity) occurred. Statistically significant hematological changes occurred in male rats only. Increased group mean red blood cell count at 1,000 mg/kg/day and increased mean corpuscular hemoglobin levels at 100, 300, and 1,000 mg/kg/day were observed. Although these changes were statistically significant, they were not considered biologically relevant because the magnitude of the changes represented only ≤2% of the values seen in controls. White blood cell counts were also significantly decreased in males at 1,000 mg/kg/day (white blood cell counts were increased in the 14-day study). Prothrombin times were significantly decreased in males at 300 and 1,000 mg/kg/day, representing 7% and 5% changes, respectively, relative to controls, and group mean platelet counts were significantly lower at 1,000 mg/kg/day. Statistically significant blood chemistry changes consisted of increased aspartate amino-transferase activity (AST), decreased total protein, and decreased albumin levels in males at 1,000 mg/kg/day and decreased blood urea in females at 300 and 1,000 mg/kg/day. Gross and histopathological examination of 41 tissues revealed only distended and luminal dilatation of the cecum in females at 1,000 mg/kg/day. In conclusion, a number of other responses were observed, but none were considered to be biologically relevant.

Genotoxicity

In a study of the mutagenic potential of m-BDSA, four strains of *S. typhimurium* and one strain of *E. coli* cultures were incubated with seven concentrations between 50 and 5,000 µg/plate, with and without metabolic activation with S9 (May 2002). The first test was used as a range-finding test. The results of the first test showed no substantial increase in revertant colony counts over the controls in any of the test strains at any concentration. Thus, 5,000 µg/plate was used as the highest concentration in the second test. In the second test, the plates were pre-incubated with the same concentrations as in the first test. There were no visible significant increases or decreases in the number of cells on any treatment plate. It was therefore concluded that, under these specific experimental conditions, m-BDSA did not show a mutagenic potential in bacteria.

A mammalian cell mutation assay was carried out using mouse lymphoma cells to test the mutagenic ability of m-BDSA. Cells were administered m-BDSA at doses ranging from 313–5,000 µg/mL. Cells were exposed to the substance for durations of 3 and 24 hours, with or without (respectively) a supplemented liver fraction (S9 mix) to begin enzyme metabolism of the compound. No significant increase in mutation frequency was detected at any concentration of m-BDSA administered (Clare 2002).

Carcinogenicity

There are currently no known studies that assess the carcinogenicity of m-BDSA.

Pharmacokinetics

The only data regarding the pharmacokinetics of m-BDSA come from an in vitro dermal penetration study carried out by use of male and female human cadaver skin from the National Disease Research Interchange in Philadelphia, PA (Magee et al. 2004). Skin sections were cut into 3 x 3 cm sections, and their thickness was measured. The skin was

placed in Franz diffusion cells and kept at 37°C until dosing. Cells were dosed with 1 mL of 2 mg/mL solution for 24 hours. The diffusion cells were evaluated and the residual liquid was measured after 24 hours. The average recovery of m-BDSA from diffusion cells was 97%. The estimated quantitation limit for m-BSA was defined as the concentration of the lowest non-zero standard in the calibration curve, which was 0.5 ng/µL. It was found that none of the test material was detected in the test cell receptor fluid, so that dermal penetration rate was estimated at half of the quantitation limit of 0.5 ng/µL, or 2 x 10^{-5} cm/hour.

Summary

m-BDSA is irritating to the skin in rabbits at a dermal dose of 1.1 mg/kg, but not at 0.5 mg/kg.

The lethal oral dose of m-BDSA in rats is >5,000 mg/kg.

Loose feces or histologically observed distention and luminal dilatation of the cecum, indicative of gastrointestinal irritation, was the most consistently observed effect in rats exposed orally. Loose feces was observed at single gavage doses of 2,000 or 5,000 mg/kg/day and in drinking water at 21,760 mg/kg/day for 7 days; water in the cecum was observed at 2,000 mg/kg/day in drinking water for 14 days; and distention of the cecum was observed at 1,000 mg/kg/day in drinking water for 13 weeks.

Hematological effects, consisting of changes in white blood cell counts, were observed in male rats given m-BDSA in their drinking water at 750 mg/kg/day for 14 days and at 1,000 mg/kg/day for 13 weeks. The white blood cell counts were increased in the 14-day study but decreased in the 13-week study. Decreased prothrombin times were also observed in the male rats at 300 and 1,000 mg/kg/day in the 13-week study.

No studies were found regarding the toxic effects of m-BDSA for inhalation exposure of humans or animals, but m-BDSA has a very low vapor pressure and is extremely soluble in water, indicating minimal potential for inhalation exposure. It could, however, be inhaled as an aqueous aerosol.

m-BDSA was not mutagenic in bacterial or mammalian cell assays.

m-BDSA was not absorbed by excised human skin.

Conclusions

On the basis of limited information, dermal exposure to m-BDSA in tap water does not appear to be a concern because it was only slightly irritating to the skin of rabbits at 5,000 mg/L (1.1 mg/kg), but not at 2,000 mg/L (0.5 mg/kg), and it does not appear to be absorbed by human skin. No information regarding inhalation exposure to m-BDSA was available, but m-BDSA is not very volatile, so that inhalation exposure to tap water containing m-BDSA during cooking is not likely, but when bathing or showering it could occur as an aqueous aerosol. Oral exposure of rats to m-BDSA resulted in changes in hematological parameters and gastrointestinal effects.

In the 13-week drinking water study in rats, Geary (2003) did not consider any of the responses observed to be biologically significant. Based on this, AMEC (2003) proposed a reference dose of 0.4 mg/kg/day by dividing Geary's highest dose of 1,055 mg/kg/day

by an uncertainty factor of 3,000. The 1,055 mg/kg/day dose was considered a NOAEL. The uncertainty factor consisted of 10 for interspecies extrapolation, 10 for intraspecies extrapolation, 10 for extrapolation from subchronic to chronic, and 10 for the limited database, which would result in a total UF of 10,000. The UF of 10,000 was lowered to 3,000 because a UF of 10,000 was considered to be too conservative, in accordance with standard EPA practice described by Dourson (1994).

However, in the 14-day study, the LOAEL for oral exposures to m-BDSA was 750 mg/kg/day for significantly increased white blood cells in Sprague-Dawley CD rats. The NOAEL was 250 mg/kg/day. In addition, in the 13-week study, males had significantly decreased white blood cells at the 1,000 mg/kg/day dose level and significantly decreased prothrombin times at 300 and 1,000 mg/kg/day dose levels. AMEC discounted the toxicological significance of these effects because the white cell counts were increased in the 14-day study, and histological examination of the bone marrow, thymus, spleen, lymph nodes, and Peyer's patches in the 13-week study revealed no abnormalities to account for a possible etiology of the hematological effects. Nevertheless, because of the limited database, it would be prudent to consider the 100 mg/kg/day dose as the NOAEL and 300 mg/kg/day as a minimal LOAEL. If a value were to be derived from this NOAEL, application of an uncertainty factor of 1,000 (10 for sensitive subpopulations, 10 for extrapolation from animal to humans, and 10 for extrapolation from subchronic to chronic) would result in a chronic oral interim guidance value of 0.1 mg/kg/day.

References

AMEC Earth and Environmental Inc. 2003. Description of a proposed reference dose m-benzene disulfonate. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Blanchard EL. 2002. m-Benzene disulfonate acute oral toxicity to the rat (acute toxic class method). Prepared for AMEC Earth and Environmental, Inc. Westford, MA. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Clare MG. 2002. m-Benzene disulfonate mammalian cell mutation assay. Prepared for AMEC Earth and Environmental , Inc., Westford, MA. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Dourson, M.L. 1994. Methods for establishing oral reference doses (RfDs). In Risk Assessment of Essential Elements. (W. Mertz, C.O. Abernathy, and S.S. Olin, Eds), pp. 51-61. ILSI Press, Washington, D.C. (As cited in AMEC Earth and Environmental 2003).

Geary ME. 2001a. m-Benzene disulfonate—palatability study by drinking water administration to CD rats for 7 days. Huntingdon Life Sciences, Ltd, Cambridge, England. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Geary ME. 2001b. m-Benzene disulfonate—toxicity study by drinking water administration to CD rats for 14 days. Huntingdon Life Sciences, Ltd, Cambridge, England. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Geary ME. 2003. m-Benzene disulfonate–toxicity study by drinking water administration to CD rats for 13 weeks. As cited in AMEC Earth and Environmental, Inc. (2003). Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Malcolm Pirnie, Inc. 2001. Environmental fate and transport mechanisms of chemicals of interest: remedial investigation support, Kelly Farm Site. Prepared for Pennsylvania Department of Environmental Protection. (Unpublished Study).

May C. 2001. m-Benzene disulfonate bacterial reverse mutation test. Prepared for AMEC Earth and Environmental, Inc., Westford, MA. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

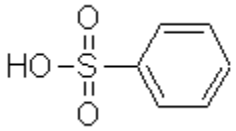
Magee BH, Clough SR, Roy TA. 2004. An i*n vitro* evaluation of human dermal exposure to benzene sulfonate, m-benzene disulfonate and p-phenol sulfonate. Bull Environ Contam Toxicol 73:235-241.

Schwab B, Anderson P. 2001. Potential exposures at central transport. Memorandum to Craig S, Beazer East Inc, Pittsburgh, PA.

Tay CH, Pugh BT, Clough SR, Magee BH. 2004. Dermal irritation assessment of three benzene sulfonate compounds. International Journal of Toxicology 23:11-16.

Benzene Sulfonic Acid

CAS 98-11-3



Benzene sulfonic acid (BSA) is a dull green solid that exists in fine, deliquescent needles or large plates. BSA is a very polar molecule that is likely to dissociate in aqueous media. Thus, in water and soil, the actual chemicals of interest are the sulfonate or ionic forms of these molecules (Schwab and Anderson 2002). It is used as a reagent during the manufacture of phenol, resorcinol, and other synthetic organics. BSA has a very low vapor pressure of 2.4×10^{-5} mm Hg (25°C) and is very soluble in water, with an estimated solubility ranging from 33–68.9 g/L (25°C). Volatilization of BSA is not expected from moist or dry soils. It is also expected to be essentially non-volatile from water, remaining predominantly in the aqueous phase, on the basis of the vapor pressure and a Henry's law constant of 2.52×10^{-9}. Because it is very soluble in water, dermal contact may occur during showering or bathing, or it could be inhaled as an aqueous aerosol. BSA was not found to have skin sensitization potential by QSAR testing (HSDB 2002 and Malcolm Pirnie 2001).

Effects in Humans

No reported current cases of exposure in humans exist, and there are no laboratory studies performed on humans exposed to BSA.

Animal Studies

Dermal

The potential of BSA to produce skin irritation was evaluated in New Zealand White rabbits (Tay et al. 2004). Groups of 3 rabbits (both male and female rabbits were used, but the gender in each group was not specified) weighing between 2.03 and 2.22 kg were exposed to 0.5 mL of solution at concentrations of 500, 1,000, 2,000 or 5,000 mg/L. The application site was covered with 4 layers of gauze held in place with non-irritant tape for 4 hours, after which the tape and gauze was removed. The application sites were investigated after removal of the covering, and very slight erythema was observed in all three rabbits exposed to 5,000 mg/L. After 48 hours, no irritation was observed in that treatment group. In the 2,000 mg/L treatment group, two of three rabbits exhibited mild erythema, but it was resolved within 24 hours. There were no signs of irritation in the 1,000 mg/L and 500 mg/L groups. There were no other clinical signs observed in any of the animals throughout the course of the study. It was concluded that BSA is a slight irritant at 5,000 and 2,000 mg/L, but that it is a non-irritant at doses of 1,000 and 500 mg/L. The mean weight of rabbits was about 2.1 kg. The concentrations of 2,000 and

5,000 mg/L can be converted to doses of approximately 0.5 and 1.1 mg/kg, respectively (e.g., 2,000 mg/L=2 mg/mL, 2 mg/mL x (0.5 mL/ 2.1 kg) = 0.47 mg/kg).

Primary skin irritation from BSA was evaluated by Smyth et al. (1962) in 5 albino rabbits on a 10-grade ordinal series. The grade level was assigned on the basis of the most severe reaction that developed on the clipped skin of the rabbit when 0.01 mL of pure BSA was applied and observed for 24 hours. A grade of 1 indicated no irritation, grade 6 indicated necrosis when undiluted, and a grade of 10 indicated necrosis caused by a 0.01% solution. BSA received a grade of 7 from the results of the experiment. BSA, which is an acid, would be expected to be irritating in its pure, undiluted form.

In the cat, the lowest published lethal dose (LD_{LO}) is 10 g/kg for dermal exposure. This dose caused tremor, muscle weakness, and changes in the structure or function of the salivary glands (JPETAB 1945 as cited in RTECS 2001).

Ocular

In another experiment, corneal injury upon exposure to BSA was evaluated on a 10-grade ordinal scale by Smyth et al. (1962). The grade techniques are described by Carpenter and Smyth (1946). A grade of 1 was assigned to a very small area of necrosis following treatment with 0.5 mL of undiluted chemical, grade 5 to a severe burn following treatment with 0.005 mL, and grade 10 as a severe burn from 0.5 mL of a 1% solution in water or propylene glycol. BSA received a grade of 9. As in the dermal application, the BSA was administered undiluted.

Inhalation

Concentrated vapor inhalation was conducted with a group of six male or female albino rats exposed to a stream of vapor-air mixture at a rate of 2.5 L/min. of air through a fritted glass disc immersed approximately 1” in a gas-washing bottle containing BSA. The concentration of BSA was not listed in the results. The value of 8 hours/day achieved for BSA describes the longest inhalation period that all rats could be exposed each day over a 2-week period with 100% survival (Smyth 1962).

Oral

In an acute oral toxicity study by Saunders (2003), two groups of 3 male and 3 female Sprague-Dawley CD rats of approximately 8–11 weeks of age and weighing between 201 and 238 grams were given single doses of BSA at 2,000 and 5,000 mg/kg. The rats were observed twice daily for mortality, body weights were recorded at days 1, 8, and 15, and all animals were sacrificed on day 15. All animals were macroscopically examined by opening the cranial, thoracic and abdominal cavities.

No deaths were recorded. Loose feces were noted in all rats at both dosages from 30 minutes to 4 hours post-dosage. Full recovery by all rats was observed by day 2. Normal bodyweight gain was observed throughout the study in all rats. No abnormalities were noted upon macroscopic examination at study termination. It was concluded that the acute lethal oral dose was higher than 5,000 mg/kg bodyweight.

From a study of over 300 compounds, the oral toxicity of BSA and other compounds were tested on groups of five male, non-fasted Carworth-Wistar rats. A single dose was administered by gastric intubation, and mortalities were evaluated over 14 days to

determine the oral LD_{50} value for each chemical. The value for BSA was 0.89 mL/kg of 100% BSA, or 0.89 g/kg, assuming the calculated density of 1 g/mL (Smyth et al. 1962).

In a 7-day drinking water study in groups of 8 male and female Sprague-Dawley CD rats weighing between 180 and 250 grams, the palatability of drinking water was measured by adding 30 mg/mL BSA to their drinking water (Blanchard 2002). Achieved doses of BSA ranged between 18,000–44,000 mg/kg/day. No clinical signs were noted. Lower initial food and water consumption was noted in all animals on day 1. It was concluded that 44,000 mg/kg/day (or 30 mg/mL) was palatable for rats, on the basis of drinking water consumption, which remained constant for the duration of the experiment.

In a 14-day drinking water study in CD rats, toxicity of BSA was measured in groups of 20 males and 20 females given varying doses of BSA ad libitum in their drinking water (Saunders 2001). Doses of 0, 300, 1,000, and 3,000 mg/kg/day were administered, and experimental animals were observed for bodyweight gain, food and water consumption patterns, food conversion efficiency, clinical signs, and mortality. The achieved intakes of BSA were higher than the assigned intakes due to increased water consumption, and they ranged from 363–3,584 mg/kg/day. One day after the dosing was completed, lower group mean white blood cell and lymphocyte counts were observed in all treated animals, and a significant difference was observed in all treated males. This trend was not found to be dose-related, however. Significantly longer group average and individual prothrombin (PT) times were noted in males and females receiving the highest dosage, but no clear dose-related relationship was noted. Significantly longer activated partial thromboplastin (APT) times were also noted in all treated females, but no dose-response relationship was evident. Higher adjusted mean kidney weights were noted in all groups receiving 3,000 mg/kg/day compared with controls, but no significant difference was observed. When biochemical parameters were evaluated at day 15, higher group mean alkaline phosphatase values were found in males treated with 3,000 mg/kg/day. Lower phosphorous and calcium values were noted in all treated animals in comparison with controls. Statistical significance was found in all treated groups for phosphorous and for calcium in all treated female groups. No changes were noted after macropathological examination. Final conclusions were that bodyweight gain suppression among animals receiving the highest dose, along with lower mean white blood cell counts, phosphate and calcium levels, and longer PT times, were the most serious effects. Other effects in animals receiving the lower two doses could be coincidental, or they could possibly reflect toxicity with no clear dose-related effect. The dose of 363 mg/kg/day was the NOAEL in this study. However, since there was an effect noted (lower group mean white blood cell and lymphocyte counts), perhaps this dose could be considered a LOAEL.

In a 13-week study, groups of 10 male and 10 female CD rats were given BSA in drinking water that provided doses of 100-1,000 mg/kg/day (Saunders 2003). The control group contained 10 males and 10 females that received untreated drinking water. The rats were between 26 and 30 days old upon arrival, and their body weights ranged from 119–172 grams. No treatment-related deaths, treatment-related weight changes, or treatment-related clinical signs were observed. Higher group mean water consumption was noted in all groups of treated animals and found to be dose-related. In the last week of treatment, statistically-significant lower group mean and individual lymphocyte counts were observed in all groups of treated females and males at the 1,000 mg/kg/day dosage level.

In males receiving 300 or 1,000 mg/kg/day and females receiving 1,000 mg/kg/day, significantly lower group mean basophil counts were noted. Group mean and individual potassium levels in males and females receiving 1,000 mg/kg/day were significantly lower as well. After behavioral screening at week 12, it was observed that females receiving 1,000 mg/kg/day had an increased locomotor activity time. Although these changes were statistically significant, they were not considered biologically or toxicologically relevant. The authors conclude that the lack of microscopic changes in the lymphoid tissues and the lack of any general adverse effects in the study population justify their conclusion of naming 1,000 mg/kg/day the NOAEL.

Genotoxicity

In a study of the mutagenic potential of BSA, four strains of *S. typhimurium* and one of *E. coli* cultures were incubated with seven concentrations between 5 and 5000 µg/plate , with and without metabolic activation with S9 (May 2001). No reverse mutations above control were observed in two round of testing.

A mammalian cell mutation assay was carried out using mouse lymphoma cells to test the mutagenic ability of BSA (Clare 2002). Cells were administered BSA at doses ranging from 313–5000 µg/mL. Cells were exposed to the substance for durations of 3 and 24 hours, with or without (respectively) a supplemental liver fraction (S9 mix) to begin enzyme metabolism of the compound. No significant increase in mutation frequency was detected at any concentration of BSA administered.

Carcinogenicity

There are currently no known studies that assess the carcinogenicity of BSA.

Pharmacokinetics:

Absorption:

There have been no *in vivo* studies found in the literature on BSA, but one *in vitro* study was found in a test using male and female human cadaver skin. Sections of human skin measuring 350 µm thick were mounted on Franz diffusion cells and dosed with 1 mL of a 2 mg/mL solution for 24 hours. The cells were evacuated after this amount of time and the residual liquid was measured. It was found that none of the test material was detected in the test cell receptor fluid, so that dermal penetration rate was estimated at half of the quantitation limit of 0.5 ng/µL, or 2×10^{-5} cm/hour (Magee et al. 2004).

Excretion:

Currently no studies are available on the excretion of BSA. However, the extreme water solubility of BSA would facilitate urinary excretion, and BSA would most likely be excreted unchanged (HSDB 2002, AMEC 2003).

Summary

BSA was found to be a dermal irritant in rabbits at 1.1 and 0.5 mg/kg.

On a scale with a possible high grade of 10 for primary skin irritation, BSA received a grade of 7 for acute dermal irritation.

On a scale with a possible high grade of 10 for corneal injury, BSA received a grade of 9.

The lowest published lethal dose (LD_{LO}) in the cat is 10 g/kg for dermal exposure, with the exposure causing tremor, muscle weakness, and changes in the structure or function of the salivary glands.

Rats exposed to a vapor-air mixture of unknown concentration at 2.5 L/min. for 8 hours a day for two weeks had 100% survival in the experimental population.

The acute lethal oral dose in rats was not identified because no deaths occurred at 5000 mg/kg for BSA.

The single oral dose LD_{50} for a rat exposed to 100% BSA was found to be 0.89 g/kg, and a dose of 44,000 mg/kg/day was found to be palatable for rats in drinking water, during a 7-day study.

Reduced lymphocyte counts were the most consistently observed effect from all oral doses of BSA in both the 14-day and 13-week studies of rats exposed via drinking water. In males receiving 3,000 mg/kg/day and both sexes receiving 1,000 mg/kg/day over 13 weeks, lower mean basophil counts were noted, and in both sexes receiving 1,000 mg/kg/day for 13 weeks, potassium levels were significantly lower. Basophilic counts were not reported in the 14-day study.

BSA was not mutagenic in bacterial or mammalian cell assays.

BSA was not absorbed by excised human skin.

Conclusions

On the basis of the information available, dermal exposure to BSA from tap water may be of concern because it has been found to be a mild irritant at 5,000 mg/L (1.1 mg/kg) and 2,000 mg/L (0.5 mg/kg). However, it appears to be poorly absorbed by human skin, and the doses used in the experiments are much higher than the concentrations of sulfonic acids at the Kelly Farm site (Schwab and Anderson 2001). There was very little information regarding inhalation of BSA in animals or humans, but because BSA is not likely to volatilize, inhalation exposures are not expected to occur from cooking, bathing, or showering except for the inhalation of aqueous aerosols. Oral exposure of rats has resulted in hematological effects.

AMEC (2003) used the 13-week drinking water study to derive a proposed reference dose for BSA. AMEC considered lymphocyte reductions to be an adverse effect by the most conservative evaluation of the data, and therefore indicated the lowest dose in females (achieved dose 99 mg/kg-day) as the LOAEL. An uncertainty factor of 10,000 was applied to the dose to produce an RfD of 0.01 mg/kg/day. The five uncertainty factors applied were 10 for extrapolation from animals to humans, 10 for sensitive populations, 10 for conversion of the LOAEL to a NOAEL, 10 for extrapolation from a subchronic to a chronic experiment, and 10 to account for deficiencies in the data. The uncertainty factor (UF) was reduced from 100,000 to 10,000 as a result of the standard practice of applying an UF of 10,000 when uncertainty exists in five categories. AMEC (2003) does concede that if lymphocyte reduction in females is not considered to be an adverse effect, then either the median (300 mg/kg/day) or the highest (1,000 mg/kg/day) dose may be a more appropriate choice for the LOAEL. The reasoning that AMEC (2003) has presented with regard to the exclusion of lymphocyte reduction as an adverse

effect is that they "had no corollary findings in clinical signs, other measurements, or histopathology that would suggest the clinical significance of the findings." Thus, they concluded, this observation does not clearly lead to an adverse effect level.

In fact, the dose chosen by Saunders (2003) did not cause any external effects indicative of toxicity related to BSA exposure. There was no evidence from microscopic examinations of the primary or secondary lymphoid tissues that lower lymphocyte counts had resulted in any adverse effects. Additionally, the lymphocyte values recorded for females at 100 or 300 mg/kg/day and males at 1,000 mg/kg/day were within concurrent control ranges. The data for females exposed to 100 and 300 mg/kg/day were also very similar compared to the data of controls; therefore, there was little evidence of a dosage-related relationship. Nevertheless, reductions in lymphocyte counts were also observed in rats exposed to m-BDSA and p-PSA in similar 13-week studies conducted by the same laboratory, indicating a consistent finding for these similar phenolic compounds.

The lack of dose response concordance between sexes in the 13-week study and the absence of other signs of immune dysfunction suggest that the assigned LOAEL should be higher than 100 mg/kg/day. However, the lack of data in the published literature on BSA toxicity leaves a considerable amount of uncertainty as to the possible effects of exposure. In the best interest of public health, it would be most prudent to choose the achieved dose of 99 mg/kg/day as the LOAEL. This endpoint can be considered a minimal LOAEL because its precise relevance to human exposure as well as the well-being of the test animals is not clear. Thus, if an interim guidance value were to be derived for BSA, it would result in a chronic oral interim guidance value of 0.03 mg/kg/day after application of the UF of 3,000 (3 for use of minimal LOAEL, 10 for sensitive subpopulations, 10 for extrapolation from animals to humans, 10 for extrapolation from subchronic to chronic).

References

AMEC Earth and Environmental Inc. 2003. Description of a proposed reference dose benzene sulfonate. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study)

Blanchard EL. 2002. Benzene Sulfonate. Acute oral toxicity to the rat (acute toxic class method). Prepared for AMEC Earth and Environmental, Inc. Westford, MA. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Clare MG. 2002. Benzene sulfonate mammalian cell mutation assay. Prepared for AMEC Earth and Environmental Inc., Westford, MA. (Unpublished Study).

Hazardous Substance Databank (HSDB). 2002. Benzene sulfonic acid.

Journal of Pharmacology and Experimental Therapeutics (JPETAB). 1945. Williams & Wilkins Co., 428 E. Preston St., Baltimore, MD 21202 V.1- 1909/10-84,358,1945. As cited in NIOSH Registry of Toxic Effects of Chemical Substances (RTECS), 1993-2003.

Magee BH, Clough SR, Roy TA. 2004. An *in vitro* evaluation of human dermal exposure to benzene sulfonate, m-benzene disulfonate and p-phenol sulfonate. Bull Environ Contam Toxicol 73:235-241.

Malcolm Pirnie, Inc. 2001. Environmental fate and transport mechanisms of chemicals of interest: remedial investigation support, Kelly Farm Site. Prepared for Pennsylvania Department of Environmental Protection. (Unpublished Study).

May C. 2001. Benzene sulfonate bacterial reverse mutation test. Prepared for AMEC Earth and Environmental, Inc., Westford, MA. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Saunders MD and Geary M. 2001a. Benzene Sulfonate. Palatability study by drinking water administration to CD rats for 7 days. Terminal synopsis. Prepared for AMEC Earth and Environmental, Inc. Westford, MA. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Saunders MD and Geary M. 2001b. Benzene Sulfonate. Palatability study by drinking water administration to CD rats for 14 days. Terminal synopsis. Prepared for AMEC Earth and Environmental, Inc. Westford, MA. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Saunders MD. 2003. Benzene Sulfonate. Toxicity study by drinking water administration to CD rats for 13 weeks. Prepared for AMEC Earth and Environmental, Inc. Westford, MA. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Schwab B, Anderson P. 2001. Potential exposures at central transport. Memorandum to Craig S, Beazer East Inc., Pittsburgh, PA.

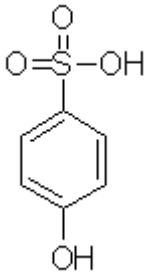
Schwab B. Anderson P. 2002. Discussion of comments: Toxicity assessment and risk-based concentrations for COI, Kelly Farm Site. Letter to Brourman M, Beazer East, Inc. Pittsburgh, PA.

Smyth HF, Carpenter CP, Weil C.S., Pozzani U.C. and Striegel J.A. 1962. Range-finding toxicity data: List VI. American Industrial Hygiene Association Journal. 23:95-107.

Tay CH, Pugh BT, Clough SR, Magee BH. 2004. Dermal irritation assessment of three benzene sulfonate compounds. International Journal of Toxicology 23:11-16.

Para-Phenol Sulfonic Acid

CAS 98-67-9



Para-phenol sulfonic acid (p-PSA) is used primarily as an additive in electroplating baths (HSDB 2003). Another use is as an intermediate in the making of dyes, plasticizers, and emulsifiers. The zinc salt of p-PSA—zinc phenolsulfonate or ZPS—is commonly used as a deodorant, due to its ability to diffuse into the sweat duct and to form an obstructive hydroxide gel (Gilman et al. 1980). The sulfonate and hydroxyl groups of p-PSA contribute to the hydroxide gel.

p-PSA has a very low estimated vapor pressure ($3x10^{-7}$ mm Hg, HSDB 2003) and is very hydrophilic (estimated solubility at 25 °C is at least 300 g/L; Malcolm Pirnie 2001). Because of its high preference for water, it is not expected to volatilize much during activities such as showering, cooking, or cleaning. While showering can create microdroplets that contain p-PSA, due to the facts that the water has low levels of contamination and that p-PSA does not otherwise volatilize appreciably, inhalation exposure to p-PSA is expected to be minimal or negligible. Dermal exposure is likely to occur during bathing or cleaning, however.

Effects in Humans

No oral or inhalation studies were located regarding the effects of p-PSA in humans. However, there is a substantial body of literature concerning the use of ZPS applied topically (dermally). For example, a 1981 review of cosmetic product formulations found it to be in 67 products, including 40 underarm deodorants (FDA 1981). For most of these topical formulations, ZPS's concentration was 1 to 5%. A Cosmetic Ingredient Review (1986) lists dozens of human dermal studies, almost all of which are patch tests. ZPS was found to be a moderate irritant at high concentrations for prolonged times. Such exposures would be far in excess of environmental-contamination scenarios.

Animal Studies

Dermal

Tay et al. (2004) assessed the effect of a single four-hour application of p-PSA on the intact skin of New Zealand White rabbits. The test substance was applied to approximately 6 cm^2 of skin via saturated gauze padding. At 5,000 mg/L, mild irritation (erythema) was noted in all three animals after exposure. By 24 hours, only one animal showed irritation that persisted at 48 hours but was gone by 72 hours. A second group of

three rabbits dosed at 2,000 mg/L showed no signs of irritation. The authors state that no other signs of clinical toxicity were seen, although they did not specify what endpoints were evaluated. For this study, 0.5 mL of solution were applied, and the average weight of the rabbits was 2.2 kg. Thus, the applied high dose is equivalent to 1.1 mg/kg, and the low dose to 0.45 mg/kg.

No further dermal studies for p-PSA were found.

Note that a Cosmetic Ingredient Review has extensively summarized information on the dermal effects of ZPS (CIR 1986). Its effects are expected to be similar to those for p-PSA, for similar exposure scenarios. Pure zinc phenol sulfonate is a mild irritant. However, 2-16% aqueous solutions or powders were not irritating at all. Indeed, it is routinely used in deodorants at concentrations of 1 to 5% (10,000 to 50,000 ppm).

Inhalation

No inhalation studies were located for p-PSA; the absence of such studies might reflect that p-PSA (per se) is almost always used in aqueous solution.

Two studies were provided concerning ZPS:

A 13-week inhalation study by Bio/dynamics (1979) used 20 guinea pigs per treatment group (half sacrificed at 4 weeks). Concentrations were 10 mg/m^3 and 45 mg/m^3 of a 2.84% ZPS aerosol deodorant (equals 0.28 and 1.3 mg ZPS/m^3, respectively) for three one-hour exposures a day, seven days a week. Dose-related effects appeared to be rales (seen at both concentrations) and depressed liver, kidney, and body weights (seen at the high concentration); however, not all effects were significant for both sexes. Terminal necropsy showed chronic respiratory disease in both the treated animals and in controls, which brings the experimental conditions into question and reduces the impact of the study.

Hazleton (1979) studied the effect of aerosolized zinc phenolsulfate on cynomolgus monkeys for 90 days. Nine monkeys per group were exposed to approximately 6 or 35 mg/m^3 of a 2.84% ZPS spray deodorant (equals 0.17 or 0.99 mg ZPS/m^3, respectively) for 13 weeks, three times one hour/day, seven days/week. Various parameters were measured, such as weight gain, lung capacity, hematology, clinical chemistry, organ weights, and histopathology. The only clear treatment effect was respiratory inflammation (accumulation of macrophages).

In addition, further ZPS inhalation studies are summarized in CIR 1986, but they were not available for review. (ZPS is used in spray can underarm deodorants, footsprays, etc.) As the CIR summary shows, inhalation of ZPS aerosol for 13 weeks (e.g. 3 hours/day, 7 days/week) generally resulted in little or no effect. The effects noted in the previous two paragraphs are the only significant inhalation effects seen.

Note that the levels of lung intake attributable to deliberate ZPS aerosolization for purposes of dosing animals undoubtedly results in far higher doses than would be achieved when breathing in humid air whose water droplets have low-ppm concentrations of p-PSA. The effects seen in the animal inhalation studies above may have been due to the high levels inhaled or to the zinc or deodorant vehicle, concerns that are not expected to be present in a p-PSA water contamination scenario.

Oral

Geary (2001a) provided three rats with 30 g/L p-PSA in drinking water (equal to ~30,000 mg/kg/day) for seven days, in a palatability study. Although water consumption was lower the first two days, it returned to consistent levels for the remainder of the study. Body-weight gains were noted over the course of the seven days, but no controls existed (nor was the age of the rats stated), so that this may have been normal weight gain. The author noted no adverse signs and considered the concentration to be palatable.

Geary (2001b) performed a 14-day toxicity study of p-PSA in drinking water to groups of 10 rats (5 male, 5 female) at doses of 0, 300, 1,000 and 3,000 mg/kg/day. Numerous endpoints were studied and several equivocal effects were noted; none was sufficient to be a clear sign of toxicity, but further investigation was recommended by the authors. A significant ($p<0.05$) decrease in bodyweight gain (73% of controls) was seen in males at the highest dose. White blood cell counts were lower for all treated groups; the effect was significant for the highest dose (for male and female rats). Blood alkaline phosphatase was significantly lower for the high-dose female group, and urea, creatinine, and calcium were statistically lower and cholesterol higher for the high-dose male group. All male groups had significantly lower adrenal weight relative to controls. Testes and epididymis weights were significantly higher for high-dose males. Macropathology at termination revealed no treatment changes; no histopathology was performed. Taken together, the findings suggest that 300 mg/kg/day or higher might be a LOAEL, but the small group sizes, various equivocal findings, and lack of histopathology detract from the strength of the study.

Geary (2003) assessed the toxicity of p-PSA in drinking water in a 13-week (91-day) study in rats. Three doses were employed (100, 300, and 1,000 mg/kg/day, and a control group), and each group had 20 rats. The authors studied numerous endpoints, including hematology, blood chemistry, behavioral, opthalmoscopy, organ weights, and organ pathology. Several minor or equivocal effects were noted, such as cell atrophy in the salivary glands of some male rats at all dose levels (achieving statistical significance in the high-dose group), lower blood potassium levels for both sexes at 300 and 1,000 mg/kg/day (with female rats achieving significance at 1,000 mg/kg/day), lower lymphocyte levels in all male treatment groups, and a shorter activated partial thromboplastin time (APTT) in the male 1,000 mg/kg/day group. No serious or gross effects were observed at any dose. On the basis of this study, 100 mg/kg/day might be deemed a minimal LOAEL, due to the statistically-significant lower lymphocyte counts in all male treatment groups. While this appeared to be a clear result ($p>0.05$ for all three treatment groups), it did not show a dose-response effect, was present only in males, and the extent to which it might be adverse (given, for example, no significant change in white blood cell counts) is not immediately apparent. Thus, 100 mg/kg/day could be classified as a minimal LOAEL. Further study could clarify whether it is relevant to humans. Note that Geary did not consider any of the study's results to qualify as a LOAEL (i.e., 1,000 mg/kg/day was considered a NOAEL), but the Discussion in this unpublished study is short and contained little explanation.

Scientific Associates (1973) performed a study of zinc phenolsulfonate administered in food to groups of 40 rats for 91 days at doses of 62.5, 250, and 1,000 mg/kg/day. Animals

showed minor and/or sporadic adverse effects; it is unclear whether these were a treatment effect or unrelated. For example, animals from the week-4 sacrifice group showed testicular tissue abnormalities, but animals from week 8 and week 15 did not (and testicular effects were also seen only for the week-4 group for a different chemical whose results were presented in the same study). This study incorporated little statistical analysis. The author's general conclusions seem sound, however, that there were no gross or readily apparent adverse effects from any of the doses.

Taken together, these studies suggest that a minimal animal LOAEL might be 100 mg/kg/day. However, the existing database is far from ideal; equivocal and minor effects, and problems with controls, plague the studies that exist. Moreover, it is not entirely clear whether this LOAEL (lowered lymphocyte counts in male rats) might indeed be an adverse effect for humans.

Genotoxicity

May (2001) assayed p-PSA for bacterial reverse mutation. Strains of *S. typhimurium* and *E. coli* were employed at doses up to 5 mg/plate (50 g/L), with and without exogenous metabolic activation (S9 mix). Results were uniformly negative; p-PSA showed no evidence of bacterial mutagenicity in this assay.

Clare (2002) assayed p-PSA for mammalian cell mutation. A strain of mouse lymphoma cells was employed at doses up to 5 mg/plate (50 g/L) , with and without exogenous metabolic activation (S9 mix). Results were uniformly negative; p-PSA showed no evidence of mammalian cell mutation in this assay.

Carcinogenicity

There are currently no known studies that assess the carcinogenicity of p-PSA.

Pharmacokinetics

Magee et al. (2004) assessed the dermal permeability of p-PSA by using human skin and found it to be lower than the equipment detection limit (EQL) of 0.5 ppm; these authors recommended a permeability constant at half the EQL, namely, $2x10^{-5}$ cm/hr.

Summary

In an exposure scenario involving contaminated water used for bathing or cleaning, p-PSA is expected to be far below concentrations that might cause dermal irritation. Note that it is applied directly to the skin at concentrations up to 5% in deodorants.

It is unlikely that inhaling humid air during showering might cause exposures of concern. Only particulate aerosols at far higher concentrations have been shown to have effects, and that was with recurring exposure (several hours a day) over the course of months, while also including the potential additional irritant or confounder zinc (as ZPS).

A LOAEL for the oral route is difficult to establish, given the lack of reliability, breadth, or relevance of the few existing studies. However, a tentative minimal LOAEL of 100 mg/kg/day could be used.

p-PSA was not mutagenic in bacterial or mammalian cell assays.

p-PSA was poorly absorbed by excised human skin.

Conclusions

Adverse effects from p-PSA are unlikely to be of concern for the inhalation or dermal routes during showering, cleaning, or cooking with water contaminated with environmental levels of p-PSA. p-PSA (as ZPS) has long been used in deodorants and footsprays in the 1–5% concentration range with no known ill effects (past equivocal dermal irritation, in a few human studies); dermal exposure to water containing far lower concentrations, for considerably shorter duration than, for example, applied deodorant, is thus not expected to have effects. Likewise, inhalation of low, environmental levels of p-PSA in humid air during showering and bathing is very unlikely to approach the high levels used in testing aerosolized ZPS for inclusion in cosmetics. These high levels showed only moderate effects in circumstances that probably greatly exceeded the amount of exposure in the scenario in question.

AMEC (2003) proposed a NOAEL of 288 mg/kg/day (the achieved dose for the 300 mg/kg/day group) from the Geary (2003) 13-week rat study. This NOAEL is below the 1,000 mg/kg/day dose AMEC identified as a LOAEL, due to male salivary-gland atrophy. AMEC thus derived a reference dose of 0.1 mg/kg/day by dividing their NOAEL by an uncertainty factor of 3,000. The uncertainty factor consists of 10 for sensitive subpopulations, 10 for extrapolation from animals, 10 for extrapolation from subchronic to chronic, and 10 for the limited database; this would result in a total UF of 10,000, which AMEC lowered to 3,000 because of the large number of conservative factors (as is common practice with, e.g., the USEPA).

Because there was a statistically-significant lymphocyte reduction at 100 mg/kg/day in the Geary (2003) study, and relevant information is otherwise scarce, it seems prudent to consider this a minimal LOAEL. Further research will be needed to ascertain whether this arguably marginally-adverse effect is relevant to humans. If an interim guidance value were to be derived, application of an uncertainty factor of 3,000 (3 for use of a minimal LOAEL, 10 for sensitive subpopulations, 10 for extrapolation from animals, and 10 for extrapolation from subchronic to chronic) would result in a chronic oral interim guidance value of 0.03 mg/kg/day.

References

AMEC Earth and Environmental. 2003. Description of a proposed reference dose: phenol sulfonate. Westford, MA: AMEC Earth and Environmental, Inc. Draft printed February 9, 2003. Sponsored by Beazer East, Inc. Pittsburgh, PA.

Bio/dynamics. 1979. A thirteen-week inhalation toxicity study of [aerosol deodorant with 2.84% (w/w) ZPS] in the guinea pig. East Millstone, New Jersey: Bio/dynamics. Project No. 78-7058 dated April 12, 1979. Note: Portions of this study were censored. Text in [brackets] was noted by hand on the hardcopy provided.

Blanchard EL. 2002. P-phenol sulfonate acute oral toxicity to the rat (acute toxic class method). Huntingdon, Cambridgeshire, UK: Huntingdon Life Sciences, Ltd. Report MAP 002/003 completed February 20, 2002. 18 pages. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Clare GM. 2002. P-phenol sulfonate mammalian cell mutation assay. Huntingdon, Cambridgeshire, UK: Huntingdon Life Sciences, Ltd. Report MAP 002/022617 issued April 4, 2002. 34 pages. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Cosmetic Ingredient Review (CIR). 1986. Final report on the safety assessment of zinc phenolsulfonate. J Am Coll Toxicol 5: 373-390.

Food and Drug Administration (FDA). 1981. Computer printout of voluntary submission of cosmetic ingredient data. *As cited in* CIR 1986.

Geary M. 2001a. P-phenol sulfonate – Palatability study by drinking water administration to CD rats for 7 days. Huntingdon, Cambridgeshire, UK: Huntingdon Life Sciences, Ltd. Report MAP/018. Prepared for AMEC Earth and Environmental, Inc. Westford, MA. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Geary M. 2001b. P-phenol sulfonate – Toxicity study by drinking water administration to CD rats for 14 days. Huntingdon, Cambridgeshire, UK: Huntingdon Life Sciences, Ltd. Report MAP/004 dated Oct. 10, 2001. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Geary ME. 2003. P-phenol sulfonate toxicity study by drinking water administration to CD rats for 13 weeks. Huntingdon, Cambridgeshire, UK: Huntingdon Life Sciences, Ltd. Report MAP 005/022536 issued Jan. 29, 2003. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Gilman AG, Goodman LS, Gilman A, eds. 1980. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 6th ed. New York: Macmillan Publishing Co., Inc. Page 954. *As cited in* HSDB 2003.

Hazleton. 1979. Subchronic inhalation toxicity study in cynomolgus monkeys. Vienna, VA: Hazelton Laboratories America, Inc. Revised final report submitted August 22, 1979. Note: Handwritten notes on the hardcopy identify the encoded test substance as aerosol deodorant with 2.84% (w/w) ZPS.

HSDB. 2003. Hazardous Substances Data Bank for 4-hydroxyphenylsulfonic acid. Bethesda, MD: U.S. Department of Health and Human Services, U.S. National Library of Medicine. Available at: URL: http://toxnet.nlm.nih.org.

Malcolm Pirnie, Inc. 2001. Environmental fate and transport mechanisms of chemicals of interest: remedial investigation support, Kelly Farm Site. Prepared for Pennsylvania Department of Environmental Protection. Orchard Park, NY: Malcolm Pirnie, Inc. Cover date July 2001.

May K. 2001. P-phenol sulfonate bacterial reverse mutation test. Huntingdon, Cambridgeshire, UK: Huntingdon Life Sciences, Ltd. Report MAP 001/014202 issued Dec. 17, 2001. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study)

Magee BH, Clough SR, Roy TA. 2004. An *in vitro* evaluation of human dermal exposure to benzene sulfonate, m-benzene disulfonate and p-phenol sulfonate. Bull Environ Contam Toxicol 73:235-241.

Saunders M. 2001. P-phenol sulfonate – Palpability study by drinking water administration to CD rats for 7 days. Huntingdon, Cambridgeshire, UK: Huntingdon Life Sciences, Ltd. Report MAP/018. 3 pages. Sponsored by Beazer East, Inc. Pittsburgh, PA. (Unpublished Study).

Scientific Associates. 1973. Final report of 91-day subacute oral administration in rats of [zinc phenolsulfonate]. Scientific Associates, Inc. Note: Portions of this study were censored. Text in [brackets] was noted by hand on the hardcopy provided.

Tay CH, Pugh BT, Clough SR, Magee BH. 2004. Dermal irritation assessment of three benzene sulfonate compounds. International Journal of Toxicology 23:11-16.

Calcium Petronates

(Various CAS Numbers and Structures)

Calcium petronates (CPs) are large molecules with molecular weights ranging from about 950 to1100 atomic mass units. They have extremely high octanol/water coefficient values, suggesting that they tend to partition out of the aqueous phase readily. They also have a high soil/water coefficient, meaning that they are very likely to adsorb to soil particles when they are in water. Because CPs are such large molecules, they are insoluble in water, and they may behave as surfactants. CPs may also form micelles when they are in the aqueous phase, and they are not expected to volatilize from the water phase when they are dissolved (Malcolm Pirnie 2001).

CPs are stable in the environment, and they usually do not leach to groundwater because of their affinity for adsorbing to soil. Also, because they are large molecules, they do not bioaccumulate in aquatic life and cannot be transported through the lipid membranes of organisms that ingest them. When the biodegradability of CPs was measured by use of the surrogates linear alkylbenzene sulfonate (LAS) and alkyl benzene sulfonate (ABS), it was estimated that CPs would biodegrade much slower than LAS and ABS, which have half lives of 9–17 days in soil and 4–17 days in water. CPs have persistence times of 109–238 days, as determined by EPI suite (Malcolm Pirnie 2001).

A QSAR analysis was carried out by the EPA's National Center for Environmental Assessment for a representative CP using TOPKAT®. This was carried out in order to identify probable toxic effects of the chemical on humans and mammals, as well as to estimate the carcinogenic potential. Calcium petronate was outside the model's prediction space for carcinogenic potential. When modeled for mutagenicity and skin sensitization, calcium petronate showed "no probability of mutagenic activity...or potential for skin irritancy." The model was not able to complete a LOAEL prediction for calcium petronate because the chemical had descriptors that were outside the model's optimum prediction space (Califano 2001).

QSAR may have also been attempted by Beazer East, but only three characteristics of the chemical were used in comparing the chemical with the potential surrogates, LAS and ABS. These three characteristics, molecular size, water solubility, and metabolism, make up only a portion of the information that affect a chemical's toxicity. Because of the lack of information on calcium petronates as a group of chemicals, it is difficult to say whether QSAR analysis would accurately predict the toxicological potential of these chemicals (Califano 2001).

Because of the low bioavailability of CPs, it is not likely that they will pose problems with regard to wildlife around the Kelly Farm site. The low solubility and high affinity for adsorption suggest that CPs will not migrate very far from the site via groundwater, and will persist in the environment whether they migrate or not. CPs are not a concern for inhalation exposure from water use in bathing, boiling, or cleaning because CPs are not likely to volatilize from the water. Dermal contact may be of concern because these chemicals will quickly adsorb to soils, or perhaps to other organic material.

Toxicity of CPs has been tested on only one documented occasion, for acute oral toxicity in rats. The oral LD_{50} obtained from that experiment was found to be >20 g/kg (Cited in RTECS online, 1997, no details of experiment provided). As mentioned previously, ABS and LAS have been recommended as potential surrogates for estimating the toxicity of CPs (Beazer East 1998, Califano 2001, Malcolm Pirnie 2001). However, it is difficult to extrapolate a guidance based on surrogate chemicals. It is even more difficult because it was concluded that the relative toxicity of calcium petronate compounds would likely be substantially less than for either ABS or LAS (Beazer East 1998). Although a guidance value is needed, it would be very difficult to derive one from such limited data.

References

Beazer East, Inc. 1998. Toxicological review for purposes of establishing toxicity factors Kelly Farm site. (Unpublished Study).

Califano RJ. 2001. Kelly Farm site, Fairview Township, Butler County, PA. Memorandum to A. Talak, Jr. Pennsylvania Department of Environmental Protection, Meadville, PA.

Malcolm Pirnie, Inc. 2001. Environmental fate and transport mechanisms of chemicals of interest: remedial investigation support, Kelly Farm Site. Prepared for Pennsylvania Department of Environmental Protection. (Unpublished Study).

Registry of Toxic Effects of Chemical Substances (RTECS). 1997. Sulfonic acid, petroleum, calcium salt. National Institute for Occupational Safety and Health (NIOSH).

Appendix B: Figures B-1, B-2 and B-3

Appendix C: Tables

Table C-1: Contaminants of Concern in Domestic Wells, Springs, and Other Potable Water Supplies, Bear Creek Chemical Area

Contaminant	*Concentration Range (ppb)*	*Mean (ppb)*	*Frequency Detected*[1]	*Location of Highest Detection*[2]	*Comparison Value & Source*
Major Site-Related Contaminants of Concern					
resorcinol	ND – 61	17.6	45/638	Haysville Rd.	None
p-PSA	ND- 474,330	1,869.5	197/570	Hemlock Rd.	None
m-BDSA	ND – 40,100	1,089.8	179/638	Hemlock Rd.	None
BSA–total	ND – 4,900	51.2	51/638	Haysville Rd.	None
Other Contaminants of Concern					
Arsenic	ND – 6.4	2.6	5/27	138-PET	0.02 CREG
benzo(a)anthracene	ND – 0.16	0.06	3/26	130-AQU	0.09 RBC
benzo(b)fluoranthene	ND – 0.2	0.07	4/26	130 AQU	0.09 RBC
bromodichloromethane	ND – 2.9	0.23	4/37	SP-3-6-24	0.6 CREG
cadmium	ND – 2.0	0.18	2//27	270 HEM	2 EMEG-chronic
dibromochloromethane	ND – 1.7	0.19	2/37	SP-3-6-24	0.13 RBC
Lead	ND – 24.8	2.0	8/27	301 PET	None
phenanthrene	ND – 0.06	0.05	6/26	130 AQU	None

Notes

[1] The denominator may include samples taken on multiple occasions from the same location or duplicate samples.

[2] According to submitted reports, a total of 441 separate locations were sampled. Not all chemicals were analyzed for at each location.

Key

ppb = parts per billion or micrograms per liter (µg/L)

ND = Not detected

CREG = ATSDR's Cancer Risk Evaluation Guides

RBC = EPA's Region 3 Risk-based Concentrations

EMEG = ATSDR's Environmental Evaluation Guides

Table C-2: Contaminants of Concern in Surface Soil, Sediment, and Surface Deposit Material[1], Bear Creek Chemical Area[2]

Contaminant	*Concentration Range (ppm)*	*Frequency Detected*	*Comparison Value (ppm) & Source*
Major Site-Related Contaminants of Concern			
resorcinol	ND – 0.3	1/29	None
p-PSA	ND – 920	15/41	None
m-BDSA-total	ND – 400	12/39	None
m-PSA	ND – 680	5/14	None
calcium petronates	ND – 480,000	29/31	None
KNT – 451*	ND – 10.8	2/4	None
KNT – 465*	ND – 2.6	2/4	None
KNT – 479*	ND – 1.9	2/4	None
KNT – 493*	ND – 2.7	2/4	None
KNT – 507*	ND – 8.4	2/4	None
KSS – 451[H]	ND – 23.8	2/4	None
KSS – 465[H]	ND – 4.9	2/4	None
KSS – 479[H]	ND – 3.1	2/4	None
KSS – 493[H]	ND – 4.7	2/4	None
KSS – 507[H]	ND – 14.9	2/4	None
KSS - TCSH[H]	ND – 34.6	9/14	None
Other Contaminants of Concern			
arsenic	ND – 5.7	25/43	0.5 CREG
beryllium	ND – 1.2	7/16	0.1 SSL
iron	ND – 421,000	21/22	23,000 SSL

Notes

[1]Surface samples include only those samples originating from the ground surface (0 ft. below ground surface) to some depth below ground.

[2] Includes samples collected from selected locations at the Apple Road Site, Hemlock Road Site, and Kelly Farm

KNT* and KSS[H] are different isomers of calcium petronate compounds

Key

ppm = parts per million or milligrams per liter (mg/L)

ND = not detected

CREG = ATSDR's Cancer Risk Evaluation Guides

SSL = EPA's Soil Screening Level

Table C-3: Completed Exposure Pathways

Pathway Name	***Exposure Pathway Elements***					***Time***
	Source	Environmental Media	Point of Exposure	Route of Exposure	Exposed Population	
Drinking water	Past waste disposal	Groundwater contamination	Water faucets, indoor plumbing	Ingestion Inhalation Dermal	Residents with contaminated water supplies	Past
Showering/ Bathing	Past waste disposal	Groundwater contamination	Water faucets, indoor plumbing	Inhalation Dermal	Residents with contaminated water supplies	Past Present Future
Surface Deposit Material (including soil and sediment)	Past waste disposal	Surface soil	Residential properties & other waste disposal areas	Ingestion Inhalation Dermal	Residents, trespassers, or workers who come into contact with waste	Past Present Future

Table C-4: Potential Exposure Pathways

Pathway Name	***Exposure Elements***					***Time***
	Source	Media	Point of Exposure	Route of Exposure	Exposed Population	
Surface water	Past waste disposal	Surface water	Nearby creeks, ponds, drainage ditches	Ingestion Dermal	Recreational users of area creeks	Past Present Future
Groundwater	Past waste disposal	Groundwater	Residential or commercial wells	Ingestion Dermal	Persons who install wells into contaminated groundwater	Future

Appendix D: ATSDR's Evaluation Process

Step 1 – Comparison Values and the Screening Process

To evaluate the available data, ATSDR used comparison values (CVs) to determine which chemicals to examine more closely. CVs are the contaminant concentrations found in a specific media (for example: air, soil, or water) and are used to select contaminants for further evaluation. CVs incorporate assumptions of daily exposure to the chemical and a standard amount of air, water, and soil that someone may inhale or ingest each day. CVs are generated to be conservative and non-site specific. These values are used only to screen out chemicals that do not need further evaluation; CVs are not intended as environmental clean-up levels or to indicate that health effects occur at concentrations that exceed these values.

CVs can be based on either carcinogenic (cancer-causing) or non-carcinogenic effects. Cancer-based comparison values are calculated from the U.S. Environmental Protection Agency's (EPA) oral cancer slope factor (CSF) or inhalation risk unit. CVs based on cancerous effects account for a lifetime exposure (70 years) with an unacceptable theoretical excess lifetime cancer risk of 1 new case per 1 million exposed people. Non-cancer values are calculated from ATSDR's Minimal Risk Levels (MRLs), EPA's Reference Doses (RfDs), or EPA's Reference Concentrations (RfCs). When a cancer and non-cancer CV exists for the same chemical, the lower of these values is used in the comparison for conservatism. The chemical and media-specific CVs utilized during the preparation of this PHA are listed below:

An **Environmental Media Evaluation Guide (EMEG)** is an estimated comparison concentration for which exposure is unlikely to cause adverse health effects, as determined by ATSDR from its toxicological profiles for a specific chemical.

A **Reference Dose Media Evaluation Guide (RMEG)** is a comparison concentration that is based on EPA's estimate of the daily exposure to a contaminant that is unlikely to cause adverse health effects.

A **Cancer Risk Evaluation Guide (CREG)** is a comparison concentration that is based on an excess cancer rate of one in a million persons and is calculated using EPA's cancer slope factor (CSF).

A **Maximum Contaminant Level (MCL)** is a contaminant concentration that EPA deems protective of public health, and may consider the availability and economics of water treatment technology.

A **Life Time Health Advisory (LTHA)** is developed by EPA and is considered a lifetime exposure level for contaminants specifically in drinking water (assuming 20% of an individual's exposure comes from drinking water) at which adverse, non-carcinogenic health effects would not be expected to occur.

A **Risk-Based Concentration (RBC)** is developed by EPA Region III and used primarily in the initial screening process of a baseline risk assessment. EPA toxicity factors have been combined with standard default assumptions in order to generate these values.

Preliminary Remediation Goal (PRG) is a screening tool, generated by EPA Region IX, which is used at the early stages of human exposure evaluation and clean-up considerations at contaminated sites. PRGs are risk-based concentrations derived from standardized equations, combining exposure assumptions and EPA toxicity data. These values are generic and do not take into account available site-specific information.

Step 2 – Evaluation of Public Health Implications

The next step in the evaluation process is to take those contaminants that are above their respective CVs and further identify which chemicals and exposure situations are likely to be a health hazard. Separate child and adult exposure doses (or the amount of a contaminant that gets into a person's body) are calculated for site-specific exposure scenarios, using assumptions regarding an individual's likelihood of accessing the site and contacting contamination. A brief explanation of the calculation of estimated exposure doses for the site is presented below. Calculated doses are reported in units of milligrams per kilograms per day (mg/kg/day). Separate calculations have been performed to account for non-cancer and cancer health effects for each chemical based on the health impacts reported for each chemical. The same dose equations have been used for non-cancer and cancer calculations with the indicated modifications. Some chemicals are associated with non-cancer effects while the scientific literature many indicate that cancer-related health impacts are not expected from exposure.

Exposure Dose Estimation

When chemical concentrations at the site exceed the established CVs, it is necessary for a more thorough evaluation of the chemical to be conducted. In order to evaluate the potential for human exposure to contaminants present at the site and potential health effects from site-specific activities, ATSDR estimates human exposure to the site contaminant from different environmental media by calculating exposure doses. A brief discussion of the calculations and assumptions is presented below. The equations and the assumptions are based on the EPA Risk Assessment Guidance for Superfund, Part A[5] and the EPA Exposure Factors Handbook[6], unless otherwise specified. A discussion of the cancer and non-cancer evaluation of exposure is presented following the equations for each pathway.

Ingestion of Contaminants Present in Drinking Water

The exposure dose for ingestion of drinking water is

$$Dose\ (mg\ /\ kg\ /\ day) = \frac{C \times IR \times EF \times ED}{BW \times AT}$$

where

C = chemical concentration (mg/L)

IR = ingestion rate (L/day)

[5] U.S. Environmental Protection Agency. Risk Assessment Guidance for Superfund. December 1989.

[6] U.S. Environmental Protection Agency. Exposure Factors Handbook. August 1997.

EF = exposure frequency (days/years)

ED = exposure duration (years)

BW = body weight (kg)

AT = averaging time (days)

Exposure doses were calculated using the maximum detected concentration of a contaminant (C) from the environmental data in milligrams per liter (mg/L). An ingestion rate (IR) of 2 liters per day (L/day) for adults and 1 L/day for children. An exposure frequency (EF) of 350 days per year was assumed (year minus two weeks of vacation or other time spent away from the home). It was assumed that the exposure duration (ED) was 50 and 6 years for adults and children, respectively. A body weight (BW) of 70 kilograms (kg) (or 154 pounds) for adults and 10 kg (or 22 pounds) for children was also assumed. The averaging time (AT) for non-cancer chemicals is equal to the ED multiplied by 365 days, which is 10,950 days for adults and 2,190 days for children. For chemicals associated with cancerous effects, AT of 25,550 days was used to account for lifetime exposure to a particular chemical (365 days per year multiplied by 70 years).

Inhalation of Contaminants Present in Drinking Water

An evaluation of this pathway was not conducted because contaminants detected in drinking water were not considered to be volatile chemicals. Therefore, they are not expected to enter the air from water during showering and result in exposure. Health risks are not likely from this pathway.

Direct Skin (Dermal) Contact with Contaminants Present in Drinking Water

It was assumed that dermal exposure with drinking water occurred primarily during showering and bathing. Dermal absorption depends on numerous factors, including the area of exposed skin, anatomical location of the exposed skin, length of contact, concentration of the chemical in contact with the skin, chemical-specific permeability factors, and other factors. Because chemicals differ greatly in their potential to be absorbed through the skin, each chemical needs to be evaluated separately.

The exposure dose for direct contact with drinking water during showering or bathing is

$$Dose(mg/kg/day) = \frac{C \times SA \times PC \times ET \times EF \times ED}{BW \times AT}$$

where

C = chemical concentration (mg/L)

SA = surface area exposed (cubic centimeters or cm^3)

PC = permeability constant (cm/hour)

ET = exposure time (hours/day)

EF = exposure frequency (days/year)

ED = exposure duration (years)

BW = body weight (kg)

AT = averaging time (days)

Exposure doses were calculated using the maximum detected concentration of a contaminant (C) from the environmental data in milligrams per liter (mg/L). Surface area exposed in assumed to be the entire body (23,000 cm^2 and 10,400 cm^2 for adults and children, respectively). Chemical-specific permeability constants were also incorporated into the dose calculation[7,8]. An exposure time (ET) of 30 minutes (or 0.50 hour) was assumed for showering and bathing. An exposure frequency (EF) of 350 days per year was assumed (year minus two weeks of vacation or other time spent away from the home). It was assumed that the exposure duration (ED) was 50 and 6 years for adults and children, respectively. A body weight (BW) of 70 kilograms (kg) (or 154 pounds) for adults and 10 kg (or 22 pounds) for children was also assumed. The averaging time (AT) for non-cancer chemicals is equal to the ED multiplied by 365 days, which is 10,950 for adults and 2,190 for children. For chemicals associated with cancerous effects, AT of 25,550 days was used to account for lifetime exposure to a particular chemical (365 days per year multiplied by 70 years).

Incidental Ingestion of Contaminants Present in Surface Deposit Material

(Exposure to adults during gardening; Children during playing)

Adult residents may be exposed to contaminants in surface deposit material during gardening via unintentional ingestion. Children residents may also be exposed via this route while playing in the soil. The exposure dose for incidental ingestion of soil is

$$Dose(mg/kg/day) = \frac{C \times IR \times EF \times ED \times CF}{BW \times AT}$$

where

C = chemical concentration (mg/kg)

IR = ingestion rate (mg/day)

EF = exposure frequency (days/years)

ED = exposure duration (years)

CF = conversion factor (kg/mg)

BW = body weight (kg)

AT = averaging time (days)

Exposure doses were calculated using the maximum detected concentration of a contaminant (C) from the environmental data in milligrams per liter (mg/kg). An ingestion rate (IR) of 100 mg/day for adults and 200 mg/day for children. An exposure frequency (EF) of 40 days per year and 212 days per year were assumed for adult and

[7] U.S. Environmental Protection Agency. Dermal Exposure Assessment: Principles and Application. Office of Health and Environmental Assessment. EPA/600/8-91/011/B. January 1992.

[8] U.S. EPA. Risk Assessment Guidance for Superfund Volume I: Human health evaluation manual (Part E, Supplemental guidance for dermal risk assessment). Interim. Washington DC: US EPA, Office of Emergency and Remedial Response. EPA/540/R/99/005. September 2001.

children residents, respectively. It was assumed that the exposure duration (ED) was 30 and 6 years for adults and children, respectively. A body weight (BW) of 70 kilograms (kg) (or 154 pounds) for adults and 10 kg (or 22 pounds) for children was also assumed. The averaging time (AT) for non-cancer chemicals is equal to the ED multiplied by 365 days, which is 10,950 days for adults and 2,190 days for children. For chemicals associated with cancerous effects, AT of 25,550 days was used to account for lifetime exposure to a particular chemical (365 days per year multiplied by 70 years).

Inhalation of Contaminants Present in Fugitive Dust During Trespassing Activities

Adolescent trespassers may ride dirt bikes or ATVs on the site and may be exposed to contaminants present in surface deposit material via inhalation of dust. The exposure dose for inhalation of fugitive dust is

$$Dose(mg/kg/day) = \frac{C \times IR \times ET \times EF \times ED \times DLF}{BW \times AT}$$

where

C = chemical concentration (mg/kg)

IR = inhalation rate (m^3/hour)

ET = exposure time (hours/day)

EF = exposure frequency (days/year)

ED = exposure duration (years)

DLF = dust loading factor (kg/m^3)

BW = body weight (kg)

AT = averaging time (days)

Exposure doses were calculated using the maximum detected concentration of a contaminant (C) from the environmental data in mg/kg. An inhalation rate (IR) of 0.80 m^3/hour. An exposure time of 4 hours/day was assumed, based on best professional judgment. An exposure frequency (EF) of 104 days per year was assumed (to account for year round weekend exposure). An exposure duration of 10 years was assumed. A dust loading factor of 3.80×10^{-7} kg/m^3 for dirt-biking exposure was also incorporated[9]. A body weight (BW) of 50.4 kilograms (kg) was also assumed. The averaging time (AT) for non-cancer chemicals is equal to the ED multiplied by 365 days, which is 3,650 days. For chemicals associated with cancerous effects, AT of 25,550 days was used to account for lifetime exposure to a particular chemical (365 days per year multiplied by 70 years).

Non-Cancer Health Effects

The doses calculated for exposure to each individual chemical are then compared to an established health guideline, such as a MRL or RfD, in order to assess whether adverse health impacts from exposure are expected. These health guidelines, developed by

[9] Value was calculated based on site-specific information and the EPA Soil Screening Guidance (July 1996).

ATSDR and EPA, are chemical-specific values that are based on the available scientific literature and are considered protective of human health. Non-carcinogenic effects, unlike carcinogenic effects, are believed to have a threshold, that is, a dose below which adverse health effects will not occur. As a result, the current practice for deriving health guidelines is to identify, usually from animal toxicology experiments, a No Observed Adverse Effect Level (or NOAEL), which indicates that no effects are observed at a particular exposure level. This is the experimental exposure level in animals (and sometimes humans) at which no adverse toxic effect is observed. The NOAEL is then modified with an uncertainty (or safety) factor, which reflects the degree of uncertainty that exists when experimental animal data are extrapolated to the general human population. The magnitude of the uncertainty factor considers various factors such as sensitive subpopulations (for example; children, pregnant women, and the elderly), extrapolation from animals to humans, and the completeness of available data. Thus, exposure doses at or below the established health guideline are not expected to result in adverse health effects because these values are much lower (and more human health protective) than doses, which do not cause adverse health effects in laboratory animal studies. For non-cancer health effects, the following health guidelines are described below in more detail. It is important to consider that the methodology used to develop these health guidelines does not provide any information on the presence, absence, or level of cancer risk. Therefore, a separate cancer evaluation is necessary for potentially cancer-causing chemicals detected in samples at this site. A more detailed discussion of the evaluation of cancer risks is presented in the following section.

Minimal Risk Levels (MRLs) – developed by ATSDR

ATSDR has developed MRLs for contaminants commonly found at hazardous waste sites. The MRL is an estimate of daily exposure to a contaminant below which non-cancer, adverse health effects are unlikely to occur. MRLs are developed for different routes of exposure, such as inhalation and ingestion, and for lengths of exposure, such as acute (less than 14 days), intermediate (15-364 days), and chronic (365 days or greater). At this time, ATSDR has not developed MRLs for dermal exposure. A complete list of the available MRLs can be found at http://www.atsdr.cdc.gov/mrls.html.

References Doses (RfDs) – developed by EPA

An estimate of the daily, lifetime exposure of human populations to a possible hazard that is not likely to cause non-cancerous health effects. RfDs consider exposures to sensitive sub-populations, such as the elderly, children, and the developing fetus. EPA RfDs have been developed using information from the available scientific literature and have been calculated for oral and inhalation exposures. A complete list of the available RfDs can be found at http://www.epa.gov/iris.

If the estimated exposure dose for a chemical is less than the health guideline value, the exposure is unlikely to result in non-cancer health effects. Non-cancer health effects from dermal exposure were evaluated slightly differently that ingestion and inhalation exposure. Since health guidelines are not available for dermal exposure, the calculated dermal dose was compared with the oral health guideline value (RfD or MRL).

If the calculated exposure dose is greater than the health guideline, the exposure dose is compared to known toxicological values for the particular chemical and is discussed in more detail in the text of the PHA. The known toxicological values are doses derived from human and animal studies that are presented in the ATSDR Toxicological Profiles and EPA's Integrated Information System (IRIS). A direct comparison of site-specific exposure doses to study-derived exposures and doses found to cause adverse health effects is the basis for deciding whether health effects are likely to occur. This in-depth evaluation is performed by comparing calculated exposure doses with known toxicological values, such as the no-observed adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from studies used to derive the MRL or RfD for a chemical. As part of this comparison to toxicological values, a margin of exposure (MOE) is calculated by dividing the NOAEL and/or LOAEL by the site-specific exposure dose. Generally, when the MOE is greater than 1,000, harmful health effects are not expected. When the MOE ranges from approximately 100 to 1,000, further toxicological evaluation is necessary to determine whether harmful effects are likely. This may include a closer look at the studies used to derive the NOAELs and LOAELs. Adverse health effects may occur when the MOE is less than 10.

Cancer Risks

Exposure to a cancer-causing compound, even at low concentrations, is assumed to be associated with some increased risk for evaluation purposes. The estimated excess risk of developing cancer from exposure to contaminants associated with the site was calculated by multiplying the site-specific adult exposure doses, with a slight modification, by EPA's chemical-specific Cancer Slope Factors (CSFs or cancer potency estimates), which are available at http://www.epa.gov/iris. Calculated dermal doses were compared with the oral CSFs.

An increased excess lifetime cancer risk is not a specific estimate of expected cancers. Rather, it is an estimate of the increase in the probability that a person may develop cancer sometime during his or her lifetime following exposure to a particular contaminant. Therefore, the cancer risk calculation incorporates the equations and parameters (including the exposure duration and frequency) used to calculate the dose estimates, but the estimated value is divided by 25,550 days (or the averaging time), which is equal to a lifetime of exposure (70 years) for 365 days/year.

There are varying suggestions among the scientific community regarding an acceptable excess lifetime cancer risk, due to the uncertainties regarding the mechanism of cancer. The recommendations of many scientists and EPA have been in the risk range of 1 in 1 million to 1 in 10,000 (as referred to as 1×10^{-6} to 1×10^{-4}) excess cancer cases. An increased lifetime cancer risk of one in one million or less is generally considered an insignificant increase in cancer risk. Cancer risk less than 1 in 10,000 are not typically considered a health concern. An important consideration when determining cancer risk estimates is that the risk calculations incorporate several very conservative assumptions that are expected to overestimate actual exposure scenarios. For example, the method used to calculate EPA's CSFs assumes that high-dose animal data can be used to estimate the risk for low dose exposures in humans. As previously stated, the method also assumes that there is no safe level for exposure. Lastly, the method computes the 95% upper

bound for the risk, rather than the average risk, suggesting that the cancer risk is actually lower, perhaps by several orders of magnitude.

Because of the uncertainties involved with estimating carcinogenic risk, ATSDR employs a weight-of-evidence approach in evaluating all relevant data. Therefore, the carcinogenic risk is also described in words (qualitatively) rather than giving a numerical risk estimate only. The numerical risk estimate must be considered in the context of the variables and assumptions involved in their derivation and in the broader context of biomedical opinion, host factors, and actual exposure conditions. The actual parameters of environmental exposures have been given careful and thorough consideration in evaluating the assumptions and variables relating to both toxicity and exposure. A complete review of the toxicological data regarding the doses associated with the production of cancer and the site-specific doses for the site is an important element in determining the likelihood of exposed individuals being at a greater risk for cancer.

Appendix E: Cancer Occurrence Information from the Pennsylvania Cancer Registry

The tables that follow presents information from the Pennsylvania Cancer Registry on how often cancer has occurred (incidence) within most of the Bear Creek Chemical Area (G. Bogdan, Pennsylvania State Department of Health, personal communication, 2005). These screening results are based on combining the cancer information for the 7-year time period, 1996-2002 for the following ZIP code areas: 16050 (Petrolia), 16049 (Parker), 16041 (Karns City), and 16022 (Burin). The Pennsylvania State Department of Health has found that ZIP codes make a reliable geographic reference for local area analysis because municipalities assigned to cancer cases by reporting hospitals are frequently in error, while ZIP codes are not.

Appendix F, Tables 1 and 2 provide the results of separate statistical analyses for all cancers and 25 specific cancer sites for males, females, and total (males & females combined) where appropriate, and for polycythemia for 2001-2002. Columns list the cancer site, 2000 census population (POP), the number of cancer cases diagnosed between 1996-2002 (CASES), and the number of cases expected if the area had the average state cancer incidence rate (EXPECTED). The next column is the standardized morbidity ratio (SMR), which is the ratio of observed-to-expected number of cases (observed/expected cases). A ratio of 1.00 implies that a cancer rate is the same as the state rate. The next columns provide the average annual state rate (ST RATE) and ZIP code study area average annual crude rate (CR RATE) and age-adjusted rate (ADJ RATE) per 100,000 population. The last column provides an estimate of the statistical significance (Z-SCORE) of finding the observed number of cancer cases in that area when compared to average statewide cancer incidence rates for the 1996-2002 time period. A more detailed definition of the table variables is provided on the last page of the table.

When conducting cancer risk screening evaluations, a SMR ratio 2.0 or greater is generally regarded as more noteworthy; however, statistical significance should also be found in order to help rule out the possibility of chance variation (z-scores of 1.96 or greater). A z-score of 1.96 equates to a 95 % level of statistical significance or a 1 in 20 chance that the results are due to random variation. Interpreting this kind of data can be confusing because of the number of comparisons that are made, i.e., the more analyses conducted, the greater the likelihood of finding a statistically significant result. Therefore, we look for the presence of a consistent pattern in the cancer rates.

A review cancer incidence data for the following ZIP code areas: 16050 (Petrolia), 16049 (Parker), 16041 (Karns City), and 16022 (Burin) does not show a pattern of elevated cancer incidence rates.

Cancer Occurrence Information

Table 1 – Combined Cancer Incidence 1996-2002 for Pennsylvania ZIP code Areas 16022, 16041, 16049, and 16050

	POP	CASES	EXPECTED	SMR	ST RATE	CR RATE	ADJ RATE	Z-SCORE
All CANCER SITES								
MALE	3681	140	158.15	.89	610.85	543.33	540.76	-1.53
FEMALE	3721	140	129.99	1.08	538.44	537.49	579.90	.91
TOTAL	7402	280	288.14	.97	573.40	540.39	557.21	-.50
BUCCAL CAVITY AND PHARYNX								
MALE	3681	4	4.12	.97	15.53	15.52	15.10	-.06
FEMALE	3721	1	1.70	.59	7.02	3.84	4.12	-.76
TOTAL	7402	5	5.82	.86	11.13	9.65	9.57	-.36
ESOPHAGUS								
MALE	3681	3	2.51	1.20	9.60	11.64	11.48	.28
FEMALE	3721	1	.63	1.58	2.72	3.84	4.30	.41
TOTAL	7402	4	3.14	1.27	6.04	7.72	7.69	.43
STOMACH								
MALE	3681	0	3.01	.00	11.81	.00	.00	-1.74 -
FEMALE	3721	1	1.51	.66	6.78	3.84	4.48	-.60

TOTAL	7402	1	4.52	.22	9.20	1.93	2.04	-3.71 --
COLON AND RECTUM								
MALE	3681	20	19.18	1.04	75.13	77.62	78.33	.18
FEMALE	3721	18	16.35	1.10	71.33	69.11	78.51	.44
TOTAL	7402	38	35.53	1.07	73.16	73.34	78.24	.43
LIVER/INTRAHEPATIC BILE DUCT								
MALE	3681	0	1.91	.00	7.31	.00	.00	-1.37 -
FEMALE	3721	1	.75	1.33	3.23	3.84	4.28	.27
TOTAL	7402	1	2.67	.37	5.20	1.93	1.95	-1.68 -
PANCREAS								
MALE	3681	1	3.36	.30	13.07	3.88	3.89	-2.37 --
FEMALE	3721	3	2.93	1.02	12.71	11.52	13.01	.05
TOTAL	7402	4	6.29	.64	12.89	7.72	8.19	-1.22
LARYNX								
MALE	3681	2	2.33	.86	8.81	7.76	7.55	-.23
FEMALE	3721	1	.55	1.81	2.21	3.84	3.99	.46
TOTAL	7402	3	2.89	1.04	5.39	5.79	5.61	.06

BRONCHUS AND LUNG								
MALE	**3681**	**20**	**25.38**	**.79**	**97.79**	**77.62**	**77.06**	**-1.19**
FEMALE	**3721**	**19**	**16.37**	**1.16**	**67.61**	**72.95**	**78.46**	**.65**
TOTAL	**7402**	**39**	**41.75**	**.93**	**82.18**	**75.27**	**76.76**	**-.45**
MELANOMA OF THE SKIN								
MALE	**3681**	**2**	**4.74**	**.42**	**18.22**	**7.76**	**7.69**	**-1.92 -**
FEMALE	**3721**	**2**	**3.25**	**.61**	**12.96**	**7.68**	**7.97**	**-.92**
TOTAL	**7402**	**4**	**7.99**	**.50**	**15.50**	**7.72**	**7.76**	**-2.01 -**
BREAST								
MALE	**3681**	**0**	**.42**	**.00**	**1.63**	**.00**	**.00**	**-.65 -**
FEMALE	**3721**	**43**	**38.42**	**1.12**	**156.01**	**165.09**	**174.59**	**.74**
TOTAL	**7402**	**43**	**38.84**	**1.11**	**81.47**	**82.99**	**90.19**	**.69**
CERVIX UTERI								
FEMALE	**3721**	**1**	**2.54**	**.39**	**9.85**	**3.84**	**3.89**	**-1.55 -**
CORPUS/UTERUS, NOS								
FEMALE	**3721**	**11**	**8.88**	**1.24**	**35.69**	**42.23**	**44.23**	**.67**
OVARY								
FEMALE	**3721**	**4**	**4.91**	**.81**	**19.92**	**15.36**	**16.23**	**-.48**

PROSTATE								
MALE	**3681**	**45**	**47.16**	**.95**	**180.04**	**174.64**	**171.81**	**-.32**
TESTIS								
MALE	**3681**	**1**	**1.49**	**.67**	**5.86**	**3.88**	**3.94**	**-.49**
URINARY BLADDER								
MALE	**3681**	**14**	**11.28**	**1.24**	**44.33**	**54.33**	**55.01**	**.74**
FEMALE	**3721**	**5**	**3.56**	**1.40**	**15.33**	**19.20**	**21.51**	**.72**
TOTAL	**7402**	**19**	**14.84**	**1.28**	**29.33**	**36.67**	**37.54**	**.98**
KIDNEY AND RENAL PELVIS								
MALE	**3681**	**2**	**4.86**	**.41**	**18.56**	**7.76**	**7.63**	**-1.99 --**
FEMALE	**3721**	**3**	**2.77**	**1.08**	**11.38**	**11.52**	**12.34**	**.14**
TOTAL	**7402**	**5**	**7.63**	**.66**	**14.84**	**9.65**	**9.73**	**-1.19**
BRAIN/OTHER NERVOUS SYSTEM								
MALE	**3681**	**0**	**2.12**	**.00**	**8.16**	**.00**	**.00**	**-1.45 -**
FEMALE	**3721**	**1**	**1.63**	**.61**	**6.49**	**3.84**	**3.99**	**-.65**
TOTAL	**7402**	**1**	**3.75**	**.27**	**7.30**	**1.93**	**1.95**	**-2.77 --**

THYROID								
MALE	**3681**	**2**	**1.22**	**1.64**	**4.61**	**7.76**	**7.57**	**.54**
FEMALE	**3721**	**1**	**3.58**	**.28**	**13.83**	**3.84**	**3.86**	**-2.60 --**
TOTAL	**7402**	**3**	**4.80**	**.62**	**9.38**	**5.79**	**5.86**	**-1.05**
NON-HODGKIN LYMPHOMA								
MALE	**3681**	**8**	**6.26**	**1.28**	**24.31**	**31.05**	**31.06**	**.62**
FEMALE	**3721**	**4**	**5.05**	**.79**	**21.22**	**15.36**	**16.81**	**-.57**
TOTAL	**7402**	**12**	**11.31**	**1.06**	**22.71**	**23.16**	**24.10**	**.21**
HODGKIN LYMPHOMA								
MALE	**3681**	**1**	**.97**	**1.03**	**3.81**	**3.88**	**3.91**	**.03**
FEMALE	**3721**	**0**	**.75**	**.00**	**2.94**	**.00**	**.00**	**-.88 -**
TOTAL	**7402**	**1**	**1.72**	**.58**	**3.36**	**1.93**	**1.95**	**-.73**
MULTIPLE MYELOMA								
MALE	**3681**	**1**	**1.68**	**.60**	**6.56**	**3.88**	**3.91**	**-.68**
FEMALE	**3721**	**3**	**1.38**	**2.17**	**5.92**	**11.52**	**12.84**	**1.04 +**
TOTAL	**7402**	**4**	**3.06**	**1.31**	**6.23**	**7.72**	**8.13**	**.49**
LEUKEMIAS								
MALE	**3681**	**4**	**4.00**	**1.00**	**15.72**	**15.52**	**15.74**	**.00**
FEMALE	**3721**	**6**	**2.78**	**2.16**	**11.67**	**23.04**	**25.19**	**1.44 +**

TOTAL	7402	10	6.78	1.48	13.63	19.30	20.11	1.06
ALL OTHER SITES								
MALE	3681	10	10.44	.96	41.11	38.81	39.38	-.14
FEMALE	3721	11	9.56	1.15	41.15	42.23	47.35	.49
TOTAL	7402	21	20.00	1.05	41.13	40.53	43.19	.23

Table 2 – Combined Cancer Incidence 2001-2002 For Pennsylvania ZIP Code Areas 16022, 16041, 16049, and 16050

	POP	CASES	EXPECTED	SMR	ST RATE	CR RATE	ADJ RATE	Z-SCORE
Polycythemia vera								
MALE	3681	0	.13	.00	1.80	.00	.00	-.36 -
FEMALE	3721	0	.07	.00	1.11	.00	.00	-.29 -
TOTAL	7402	0	.21	.00	1.44	.00	.00	-.46 -

+ Screened Higher Rate (SMR greater than or equal to 2.0 OR Z-SCORE greater than or equal to 1.96)

++ Screened Higher Rate (SMR greater than or equal to 2.0 AND Z-SCORE greater than or equal to 1.96)

- Screened Lower Rate (SMR less than or equal to .50 OR Z-SCORE less than or equal to -1.96)

-- Screened Lower Rate (SMR less than or equal to .50 AND Z-SCORE less than or equal to -1.96)

VARIABLE CODES:

POP	**=**	**2000 Census Population.**
CASES	**=**	**Number of newly diagnosed cases during the reporting period.**
EXPECTED	**=**	**Number of expected cases if study area had experienced average PA state rates during reporting period.**
SMR	**=**	**Standard Morbidity Ratio (observed/expected cases).**
ST RATE	**=**	**Average annual state rate per 100,000 population during reporting period.**
CR RATE	**=**	**Average annual crude rate per 100,000 population for study area during reporting period.**
ADJ RATE	**=**	**Average annual age-adjusted per 100,000 population for study area during reporting period.**
Z-SCORE	**=**	**Statistical significance of study area compared to state during reporting period (a z-score of 1.96 equates to a 95 % level of statistical significance or a 1 in 20 chance that the results are due to random variation).**

Appendix F: Public Comments

The Bear Creek Chemical Area PHA was available for public review and comment from July 29, 2004 through October 14, 2004 at the following repositories:

Butler Area Public Library
218 North McKean Street
Butler, PA 16001
(724) 287-1715

John A. Beck Jr. Library
Butler County Community College
Butler, PA 16003
(724) 287-8711

A paraphrased summary of the comments received and ATSDR's responses to these comments are provided below.

Penreco (Thorp Reed and Armstrong, Attorneys at Law)

Comment: Page 6 of the Draft PHA contains the following statement:

Prior to 1979, industrial waste was hauled for disposal from three nearby industrial facilities to several properties, located in northeastern Butler County and northwestern Armstrong Counties in Pennsylvania."

Penreco proposes that this sentence be revised as follows: "It is suspected or known that prior to 1979, industrial waste was hauled for disposal from some of the nearby industrial facilities to several private properties, located in northeastern Butler County and northwestern Armstrong County in Pennsylvania.

Response: The text has been modified to address this comment.

Comment: The PHA states that "One of the industries is involved with the production of resorcinol, an adhesive used in tire manufacturing. The other two industries are involved with white (or mineral) oil manufacturing and refining. In addition to resorcinol, other chemicals associated with the industries include several sulfonic acids and calcium petronates."

Penreco proposes that this text be revised as follows: "Generally, chemicals known to be or suspected to be associated with certain of the nearby facilities include resorcinol and several sulfonic acids and calcium petronates."

Response: The text has been modified to address this comment.

Comment: Page 7 of the Draft PHA contains the following statement: "Drinking water in the vicinity of the Bear Creek Chemical Area is known to have been impacted by several contaminants. Using the available data, the main contaminants of concern in groundwater are resorcinol and several sulfonic acids. Calcium petronates, utilized by two of the industries, have been detected in surface deposit material of some disposal areas."

Penreco proposes that the last sentence quoted above be revised as follows: "Calcium petronates suspected to be or known to be associated with certain of the nearby industrial facilities have been detected in surface deposit material of some disposal areas."

Response: The text has been modified to address this comment.

Comment: The Executive Summary of the PHA states "Industrial waste was hauled from three nearby industrial facilities to several private properties, located in northeastern Butler County and northwestern Armstrong County in Pennsylvania, for disposal prior to 1979."

Pereco proposes that the last sentence quoted above be revised as follows: "It is known or suspected that industrial waste was hauled from certain of the nearby industrial facilities to several private properties, located in northeastern Butler County and northwestern Armstrong County in Pennsylvania, for disposal prior to 1979."

Response: The text has been modified to address this comment.

Crompton Corporation

Comment: Crompton addresses the toxicology of calcium petronates. It is stated in the surface deposit pathway discussion that there are no health guidelines for CP and that the health effects are unknown. Crompton respectfully submits that there is more than sufficient information to conclude that, as with groundwater, there is no apparent health risk associated with exposure to CP in surface deposit material. The PHA states that there are no applicable comparison values for CP. However, there exists ample information, including supporting literature, to derive a conservatively appropriate interim oral guidance value (or RfD) for CP that is overly protective of human health. Application of the RfD for CP, which ATSDR can and should utilize, demonstrates that CP poses no apparent health risk from the surface deposit exposure pathway.

Response: Because no specific information is available for calcium petronates, Crompton considered toxicity and biodegradability information based on linear alkylbenzene (LAS) and alkyl benzene sulfonate (ABS), which they considered surrogate compounds for calcium petronates. ATSDR does not develop guidance values and Minimal Risk Levels based on surrogate compound information. Therefore, a interim guidance value was not developed for calcium petronates.

Comment: The PHA assumes that the molecular weight of CP is 350-450 atomic mass units (amu), whereas in fact it is materially larger (900-2,000 amu).

Response: The text has been modified to address this comment.

Comment: Available well testing data does not support statements in the PHA that there is "wide-spread contamination" throughout the BCCA. Therefore, ATSDR should revise any language in the PHA which incorrectly suggests that the sampling results to date support evidence of "widespread contamination" of drinking water supplies within the BCCA.

Response: The term "widespread" has been removed from the text.

Comment: The PHA erroneously suggests that the manufacturing facility in Petrolia now owned by Crompton Corporation once deposited in most or all of the disposal areas identified in the PHA when in fact it did not. (Crompton was only involved with disposal at Kelly Farm and perhaps Apple Road and Craig Farm for brief periods).

Response: The PHA does not state that Crompton Corporation once deposited in most or all of the disposal areas identified in the PHA. No change has been made to the text.

Comment: The PHA erroneously suggests that the facility now owned by Crompton used to generate m-MBDSA in its manufacturing process when in fact it did not.

Response: The PHA does not state that m-BDSA was produced by Crompton manufacturing processes. No change has been made to the text.

Comment: Appendix C, Table 2 of the PHA lists CP detections ranging from ND to 480,000 ppm. It is stated that it is inappropriate to use this data, which was collected in 1994 using an unsuitable analyses method. More recent data utilizing more sophisticated analyses methods indicates much lower levels of CP, further confirming the inherent unreliability of the 1994 data. The 1994 data should be eliminated all together. The dose estimates should be corrected.

Response: After careful consideration, ATSDR has decided to include the 1994 data collected by the PADEP in our analyses. ATSDR acknowledges that uncertainties and limitations exist regarding the validy of some of the data. ATSDR has included additional text in the document which reflects this uncertainty.

Comment: The PHA should be corrected so that it does not erroneously state that CPs are sulfonate oil surfactants used in the manufacture of resins and pharmaceutical products.

Response: The text has been modified to address this comment.

Comment: The PHA should be corrected in its characterization of plant ownership.

Response: The text has been corrected.

Beazer and AMEC Comments

Comment: It is recommended that ATSDR clarify in the text that the use of a maximum reported concentration of a contaminant to calculate an exposure dose likely results in an overestimation of actual exposure.

Response: The text has been modified to address this comment.

Comment: The discussion regarding uncertainty throughout the PHA should be revised. The PHA indicates in several locations that, according to ATSDR, there is great uncertainty and very limited information available on the constituents of concern (mainly for sulfonate compounds). However, ATSDR does not recognize that the data available for the benzene sulfonate compounds is in fact superior to the database available for many chemicals for which ATSDR and EPA have derived minimum risk levels. Given that current language in the PHA incorrectly suggests that the uncertainties associated with the constituents of concern are greater than the routine uncertainties faced every day in environmental risk assessment, it is suggested that ATSDR revise any language relating to uncertainty. Specifically, ATSDR should recognize that the existing uncertainty associated with the constituents of concern has been adequately managed through the conservative use of uncertainty factors during the derivation of public health guidelines.

Response: The discussion regarding uncertainty refers to the lack of published data on these chemicals. Most of the data comes from unpublished studies which have been sponsored by the potentially responsible party(ies). Beazer states that ATSDR did not explicitly recognize that

they sponsored 7-day, 14-day, 13-week drinking water studies, mutagenicity studies, dermal irritation, and dermal penetration studies on m-BSDA, BSA and PSA. The reference list in Appendix A was revised to indicate who sponsored them. Changes to some of the phrases in the text such as "great uncertainty" and "very limited information" were made to indicate "uncertainty" and "limited" to address this comment.

Comment: ATSDR does not recognize that sulfonates in the environment may be attributable to many sources other than the Suspected Disposal Locations. The BCCA is located within an area sometimes referred to as Petroleum Valley. In addition to petroleum manufacturing facilities, the region has been the location of other industrial activities for well over a century, including oil and gas well development and coal mining. Therefore, it is suggested that ATSDR place language in the PHA acknowledging that the presence of sulfonates in groundwater within the BCCA can be attributable to sources other than the Suspected Disposal Locations.

Response: Information regarding the additional potential sources of sulfonates in groundwater within the site vicinity has been included in the text.

Comment: ATSDR's PHA states on page 13 that "it is assumed that the data were collected and analyzed in accordance with adequate quality assurance and quality control measures." In fact, PADEP's data were not independently validated, and much of the PADEP data are unreliable and of very poor quality. Reported resorcinol detections are not defensible, and the laboratory ultimately issued a memorandum stating that the detections were "subjective." ATSDR should recognize that the environmental data generated by PADEP for resorcinol cannot be used to accurately determine whether resorcinol is actually present in domestic water supplies within the BCCA.

Response: ATSDR has removed the statement regarding the assumption of validity of the data. ATSDR acknowledges that there are uncertainties and limitations regarding the validity of some of the data utilized in the PHA. Because, however, environmental data generally have an inherent degree of variability, ATSDR has decided to include the data in the PHA. It should be noted that the use of the data does not change the conclusions of the PHA. ATSDR recognizes that the use of the data collected by PADEP might overestimate the magnitude and occurrence of the contaminants of concern. The text has been modified to include this statement.

Comment: The proposed oral RfD for resorcinol (0.07 mg/kg/day) that was derived by AMEC and was cited in the PHA has been revised based on considerations of a recent, subchronic dose range finding study of resorcinol in rats. AMEC provided updated information to ATSDR on the new development in the toxicology of resorcinol. ATSDR should revise its provisional health guideline for resorcinol in light of updated toxicological information.

Response: The newly proposed value of 2 mg/kg/day dose is based on thyroid effects in rats in a two-generation reproductive drinking water study performed by WIL Laboratories (2003). This newly proposed underwent a peer review conducted by TERA in November 2004, and the report of Peer Review Meeting was available in December, 2004. ATSDR scientists agreed that the value of 2 mg/kg/day is appropriate.

Comment: ATSDR should indicate that other factors could have contributed to the hyperthyroidism of the patient. It is noted that the patient was using the Lanacane for pruritis, so scratching the skin could have led to abrasion, rather than intact skin and that the patient was taking other medications.

Response: The text has been revised to state that the author of the case report indicated that the skin was intact, but that the skin could have been abraded because of scratching. That the hyperthyroidism disappeared when the patient was denied the use of Lanacane (active ingredient is resorcinol) was also added to the text.

Comment: It is stated that ATSDR relies on a study by Roberts et. al to support a general conclusion that occupational exposure to resorcinol may cause thyroid effects, but the literature provides no evidence that this is the case.

On Page 51, Summary, the PHA could lead the reader to conclude that occupational exposures to resorcinol may cause thyroid effects. Specifically, the PHA states that "Occupational exposure to resorcinol may result in skin irritation and thyroid effects, but the studies are difficult to interpret because of co-exposure to other agents or the lack of appropriate controls." AMEC states that the evidence does not support an association between occupational exposure to resorcinol and thyroid effects.

In addition, the statement about skin irritation is based on an evaluation of the report by Abbate et al. (1989), which describes skin irritation in a self-selected group of individuals who worked with a resorcinol-based adhesive. Resorcinol-based adhesives may contain concentrations of resorcinol as high as several percent. However, at concentrations typical of mild therapeutic treatments, no irritation is seen in human volunteers who are treated with resorcinol at levels as high as 1.4% (CIR, 1985). In summary, AMEC states that the evidence does not support a strong association between occupational exposure to resorcinol and skin irritation and that the language on page 51 should be revised to state: "Certain occupational exposure to resorcinol at high levels may result in skin irritation. Resorcinol has not been shown to be associated with thyroid effects in the available scientific literature."

Response: ATSDR's general conclusion for resorcinol indicates that occupational exposure *may* cause thyroid effects. It is based on a study in textile workers. A number of limitations are provided in the discussion of the study that the results are difficult interpret. Nevertheless, the authors of the study (Roberts et al) were unable to rule out the possibility of thyroid effects, which was added.

Comment: Effects in Humans Section, page 42, ATSDR states that "infants and young children appear to be especially susceptible to toxic effects of resorcinol in therapeutic preparations. Resorcinol-containing creams and lotions applied to the skin of young children for diaper rash or eczema have been found to be very toxic, resulting in cyanosis, hemoglobinemia and hemoglobinuria…" AMEC states that it should be noted that methehemoglobinemia in children using resorcinol medications is rare and that the evidence that children may be especially sensitive to the effects of resorincol is extremely limited. Beazer states that ATSDR presents no evidence that children are especially susceptible to methemoglobinemia, which they say is very rare.

Response: Beazer's contractor, AMEC, states "There are several case studies in the literature, which indicate that children may be particularly sensitive to certain acute toxic effects of resorcinol, such as methemoglobinemia" in Attachment 5, page 60. Additional references are provided on page 18. These studies were added to the review in Appendix A. A statement has also been included which states the occurrence is rare.

Comment: On page 43, the PHA states that resorcinol may produce contact dermatitis in sensitized people and cites several case studies that describe dermatitis in only five individuals. The PHA then goes on to cite three epidemiology studies that demonstrate that the incidence of sensitization to resorcinol is very low. AMEC recommends that ATSDR add a statement such as "Allergic reactions at lower resorcinol concentrations of environmental relevance, such as those in groundwater in the Bear Creek Area, would presumably be more rare." Beazer states that ATSDR does not note that the incidence of allergic sensitization is low.

Response: In the discussion of 487 cases of contact dermatitis due to cosmetic sensitivity, ATSDR notes that resorcinol challenge caused a reaction in only one patient. ATSDR also noted the allergic reactions to resorcinol in eye drops, skin fresheners, freckle creams, etc. are very rare. Also, the summary states that allergic reactions are rare. On page 9 Attachment 1, AMEC acknowledges that ATSDR states that allergic actions are rare, but recommends adding the statement that "Allergic reactions at lower resorcinol concentrations of environmental relevance, such as those in groundwater in the Bear Creek Area, would presumably be more rare." AMEC also provides citations for additional studies that characterize sensitization as a rare event. The additional studies were obtained and included in the discussion, and the summary statement has been changed to read that "at low concentrations of environmental relevance, allergic reactions to resorcinol would be even more rare."

Comment: On page 46 of the PHA, it is stated that mild dermatitis was seen in the animals studies by Burnett and Goldenhtal (1988). AMEC recommends that ATSDR add a statement that no animals in the experiment were given resorcinol only. All animals were given equal volumes of 6% hydrogen peroxide, which is a known skin irritant. AMEC recommends that ATSDR acknowledge in the PHA that other constituents in these dyes may have caused the irritation. Beazer suggest that ATSDR identify other chemical constituents in hair dyes that may cause or contribute to observed health effects.

Response: The other chemicals present in hair dyes have been included in the text.

Comment: Beazer suggests that ATSDR recognize that individuals tend to experience health effects only if the product contains a very high level of resorcinol and is used over a period of many years.

Response: The conclusions of the resorcinol section of Appendix A has been modified to address this comment.

Comment: ATSDR should recognize that the environmental data collected by the Department for sulfonates overstates the occurrence of sulfonates in domestic water supplies within the BCCA. Therefore, Beazer suggests that ATSDR revise the PHA to include language which notifies the public that certain sampling results analyzed by Lancaster Laboratories for sulfonates resulted in false positives and hence cannot be relied upon as a basis for establishing the presence of sulfonates in domestic water supplies within the BCCA. Futhermore, ATSDR should reconsider the effect of including invalid results in any overall data set used to evaluate the presence of sulfonates in domestic water supplies within the BCCA.

Response: ATSDR has removed the statement regarding the assumption of validity of the data. ATSDR acknowledges that there are uncertainties and limitations regarding the validity of some of the data utilized in the PHA. However, because environmental data generally have an inherent degree of variability, ATSDR has decided to include the data in the PHA. It should be noted that

the use of the data does not change the conclusions of the PHA. ATSDR recognizes that the use of the data collected by PADEP might overestimate the magnitude and occurrence of the contaminants of concern. The text has been modified to include this statement.

Comment: The PHA should be revised to indicate that food chain uptake is not likely to pose a significant risk to humans given that the constituents of concern do not bioaccumulate.

Response: The text has been modified to address this comment.

Comment: ATSDR should clarify that aerosol exposures to the constituents of concern do not pose a significant risk to human health.

Response: The text has been modified to address this comment.

Comment: ATSDR should revise any language which suggests that disposal actually occurred at all of the twenty-six Suspected Disposal Locations included within the Site (Page 2, Page 6, Pages 8 through 11).

Response: The text has been modified to address this comment.

Comment: The number of potable water supply sample locations should be revised. (Page 13 and Page 81). On Page 13 of the PHA, ATSDR states that between September 2000 and January 2003, approximately 423 domestic water supplies were sampled by Beazer or the Department for the presence of the constituents of concern (a similar reference is also made in Footnote 2 on Page 81). A review of the spreadsheets provided by Beazer to ATSDR indicates that approximately 441 domestic water supplies were sampled by Beazer or the Department during this time period.

Response: The document has been corrected.

Comment: ATSDR should make clear that the Department did sample some individual wells for constituents other than the constituents of concern (Page 29). In the Response to Question 3 on Page 29 of the Public Comment PHA, ATSDR indicates that the majority of domestic water supplies sampled by Beazer or the Department were only sampled for the presence of the constituents of concern and that as a result it is unknown whether or not other constituents are present in domestic water supplies within the BCCA. However, as the spreadsheets provided by Beazer to ATSDR indicate, the Department did, in fact, sample thirty-seven domestic water supplies for the presence of volatile organic compounds (VOCs) and semi-volatile organic compounds (SVOCs) between March 28, 2001 and June 25, 2002 (a sub-set of these thiry-seven domestic water supplies were also sampled by the Department for the presence of pesticides). Given the fact that the sampling did not show the presence of VOCs, SVOCs or pesticides above levels of concern, the Department elected to focus future sampling efforts on resorcinol and benzene sulfonate compounds only. Therefore, Beazer suggests that the limited sampling efforts to data indicate that it is unlikely that these other constituents are present in domestic water supplies within the BCCA.

Response: The text has been modified to address this comment. the recommendation remains, however, for additional full-scan analyses of private wells in the site area.

Comment: The highest concentration for meta-benzene disulfonic acid in Appendix C, Table 1 should be revised. Appendix C, Table 1 of the PHA contains incorrect information regarding the highest concentration range for meta-benzene disulfonic acid. According to the information

provided in the table, the highest concentration for meta-benzene disulfonic acid is 37,369 ppb collected at Haysville Road. However, based upon a review of the spreadsheets provided by Beazer to ATSDR, the highest reported concentration for meta-benzene disulfonic acid should be 40,100 ppb for a sample collected at 215 Hemlock Road.

Response: The table has been corrected.

Comment: The maximum concentration range for iron in Appendix C, Table 2 should be revised. (Page 82). Appendix C, Table 2 of the PHA contains incorrect information regarding the highest reported concentration for iron. According to the information provided in the table, the highest reported concentration for iron is 412,000 ppm. However, based upon a review of the spreadsheets provided by Beazer to ATSDR, the highest concentration for iron should be 421,000. Therefore, Beazer suggests that ATSDR revise the reported concentration range for iron contained in Appendix C, Table 2 by changing the highest reported concentration from 412,000 ppm to 421,000 ppm.

Response: The table has been corrected.

Comment: For all constituents, the PHA did not evaluate uptake by wildlife (game or fish), because it was stated that there was insufficient information. ATSDR implied that they would evaluate these pathways if additional information were made available. The PHA should, instead, state that these pathways should be excluded for resorincol and benzene sulfonates, because the compounds do not bioaccumulate. The bioconcentration factors for the constituents of concern are far less than 1,000, which is EPA's benchmark for the definition of a bioaccumulative substance. Thus, the PHA should state this fact.

Response: The text has been modified to address this comment.

Comment: The PHA indicates that the doses from exposures to drinking water are based on a 50-year exposure duration for adults when the doses were actually derived by ATSDR for a 30-year exposure duration, which is appropriate.

Response: An exposure duration of 50 years was indicated in the text and used in the dose calculations because many residents indicated that they have resided in the area of the site from childhood. No change has been made to the document.

Comment: The PHA presents data from an unpublished study cited as Tay (2001). This study was designed and managed by AMEC. It has now been published in the peer reviewed journal of International Journal of Toxicology (Tay et al., 2003). AMEC would like to bring several clarifications to ATSDR's attention. For BSA, the PHA states on page 61 that there were 12 rabbits tested. This is true, but the study involved three rabbits per dose tested. The PHA states that mild erythema was observed in all three animals exposed to 5,000 mg/L. In fact, "very slight" erythema was observed. The PHA states that the erythema had subsided by 72 hours. In fact, it was not observed at 24 hours in 2 of the 3 animals and it was not observed in any animals by 48 hours. ATSDR states that the conclusion of the study was that BSA is an irritant at 5,000 mg/L and 2,000 mg/L. In fact, Tay et al. (2003) concludes that BSA is a "slight" irritant at these doses. For m-BDSA, the PHA states that the erythema observed at 5,000 mg/L had subsided by 72 hours. In fact, in two of the three animals, the erythema had subsided by 48 hours. ATSDR states that the conclusion of the study was the m-BDSA is an irritant at this dose.

Response: The published study by Tay et al. (2004) was obtained and evaluated by ATSDR. The text has been modified to address the specific comments regarding this study.

Comment: The PHA also cites skin and eye irritation data by Smyth, et al. (1962) for BSA. AMEC suggests that ATSDR acknowledge that these studies were performed on pure BSA, which is crystalline acid. Such pure acid would be expected to be irritating to the skin and eye. However, if the benzene sulfonates were present in groundwater, they would be present as dilute solutions of sulfonate ions, not dissociated acids. ATSDR stated on page 61 that "in water and soil, the actual chemicals of interest are the sulfonate or ionic forms of these molecules."

In the toxicological evaluation of p-PSA, ATSDR reports from CIR (1986) that ZPS is a "mild irritant at all but the most extreme exposures." This statement needs clarification. In fact, CIR (1986) states that pure zinc phenol sulfonate is a mild skin irritant. However, 2-16% aqueous solutions or powders were not irritating at all.

Response: The text has been modified to address these comments. The PHA text now states "BSA, which is an acid, would be expected to be irritating in its pure, undiluted form." In addition, the following statement was added about p-PSA: "Pure zinc phenol sulfonate is a mild skin irritant. However, 2–16% aqueous solutions or powders were not irritating at all."

Comment: The PHA on page 63 reports an oral LD50 for BSA of 0.89 g/kg and cites Smyth, et al. (1962). AMEC recommends that this study be qualified. Smyth, et al. (1962) conducted a screening of the lethal doses of a number of compounds in Carworth Wistar rats and reported a 50% lethal does (LD50) of 0.89 milliliters benzene sulfonic acid per kilogram body weight (ml/kg). These units of measure are curious because they imply a liquid dose, however, benzene sulfonic acid is a solid at room temperature (Merck Index, 1996). A number of sources (e.g., Lewis, 1992) cite Smyth, et al. (1962) when indicating an acute LD50for benzene sulfonate in units of mass (not volume): 890 milligrams per kilogram bodyweight (mg/kg) in rats. This value would only be correct if benzene sulfonic acid were in fact a liquid and had a density of one gram per milliliter. No reference to the density of benzene sulfonic acid could be found, rendering the Smyth, et al. (1962) LD50 suspect.

In addition, a LD50 of 890 mg/kg is not consistent with the recent toxicological studies performed on BSA, in which doses as high as 44,000 mg/kg/day were tolerated by male and female rats (Blanchard, 2002).

Response: The summary already states that 0.89 mL/kg and (vol) would be equivalent to 0.89 g/kg (wt) if a density of 1 is assumed. The argument that 44 g/kg/day was tolerated by rats in the unpublished Blanchard (2002) study does not take into account that the 89 mL/kg dose reported by Smyth is a bolus dose, whereas the 44 g/kg/day dose in the Blanchard study was calculated from a drinking water concentration.

Comment: On page 58, 64, and 71, the PHA presents data from an unpublished study cited as Ray [sic] (2001) or Petrotec (2001). This study was designed and managed by AMEC. It has now been published in the peer reviewed journal Bulletin of Environmental Contamination and Toxicology (Magee, et al., 2004).

Response: The published study has been obtained and cited.

Comment: The bacterial mutation study for m-BDSA is cited as May (2002). The actual date is 2001. In addition, the PHA did not report the mutagenicity testing that was performed by AMEC on BSA.

Response: The mutagenicity data have been added.

Comment: The PHA states that there is no basis for making statements about the potential of the sulfonic acids to cause cancer because these substances were all shown to be non-genotoxic in bacterial and mammalian systems. Therefore, there is a strong basis for stating that there would be no reason to suspect that the constituents would pose a cancer risk.

Response: There are no studies available to evaluate exposure to these chemicals and risk of cancer. Chemicals can be associated with the development of cancer by non genetic mechanisms. No change was made to the document.

Comment: A lengthy, detailed discussion was presented about the relevance of the hematological endpoints that ATSDR used to derive provisional guidance values and the relationship between the lymphocyte reduction and immunological effects.

Response: The document was peer reviewed by well respected toxicologists (Dr. Finis Cavender, Dr. Kannan Krishnan, and Dr. James Withey), who have generally agreed with ATSDR's assessment of the unpublished studies and the conclusions in "Toxicological Information on Resorcinol and Selected Benzene Sulfonic Acids" (PHA, Appendix A) No changes have been made to the document.

Comment: The PHA states in several places that additional data are needed. AMEC agrees that additional toxicological data would allow one to reduce the use of default Uncertainty Factors and be more certain about the definition of critical toxicological endpoints from the existing studies. However, additional toxicological data are not needed to evaluate human health risks with the Interim Guidance Values given the conservative decisions that ATSDR has made in designating changes in lymphocyte cell counts that are within normal ranges as adverse health effects. AMEC is concerned that the reader of the above statements about the need for more studies may worry that the ATSDR's Interim Guidance Values are not health-protective. However, ATSDR's approach was extremely conservative and health-protective, and additional toxicological studies would not only serve to revise those values upward.

Response: As AMEC agrees that additional toxicological data would allow one to reduce the use of default Uncertainty Factors and be more certain about the definition of critical toxicological endpoints (e.g., developmental effects or cancer), the PHA has retained statements about the need for additional data. No change was made to the document.

Comment: Toxicological Evaluation Summary: In the third bullet on page 58 several effects are lumped together in a manner that loses a certain amount of information. In fact, loose feces were seen at single does of 2,000 or 5,000 mg/kg or in drinking water doses of 21,760 for 14 days. Water in the cecum was seen in drinking water exposures of 2,000 mg/kg/day for 14 days, and distention of the cecum was seen in drinking water exposures at 1,000 mg/kg/day for 13 weeks.

Response: The text has been modified to address this comment.

Comment: In the forth bullet, the statement should be qualified to state "in males only."

Response: The text has been modified to address this comment.

Comment: Toxicological Evaluation Conclusions: On page 58, the PHA states that there is "very limited information" on the effects of dermal exposure to m-BDSA. AMEC believes that a guideline compliant dermal irritation study in rabbits performed in accordance with EPA and OECD guidelines on the compound of interest in the chemical species of interest in the medium of interest provide more that "very limited information." Such a study is entirely adequate for defining the effect and no effect concentrations for skin irritation. The study has, in fact, been published in a peer-reviewed journal. AMEC recommends that ATSDR remove the phrase "very limited information."

Response: The text has been modified to address this comment.

Comment: On page 59, the PHA states that the compound "appears to be poorly absorbed by human skin." As above, a guideline compliant dermal penetration study was performed in accordance with EPA and OECD guidelines. Such a study is entirely adequate for determining that m-BDSA is not absorbed by human skin, which is exactly what one would predict based on its physical-chemical properties. The study has also been published in a peer-reviewed journal. AMEC recommends that ATSDR revise the statement "appears to be poorly absorbed by human skin" to "is not absorbed by human skin."

Response: The text has been modified to address this comment.

Comment: Summary: In the first bullet on page 64, it is stated that BSA was a dermal irritant. In fact, Tay et al. (2003) found that BSA was a "slight irritant" at high doses.

Response: The text of the BSA section of Appendix A regarding the Tay et al. (2003) study has been modified to address this comment. The summary has not been modified because the Smyth et al. (1962) found skin irritation in rabbits exposed to pure BSA.

Comment: In the second and third bullets on page 64, ATSDR should note that these studies were performed on pure, undissociated benzene sulfonic acid and that the study results are suspect due to the use of units of mL/kg, which implies a liquid dose.

Response: The text of the BSA section of Appendix A has been modified to address this comment. The summary has not been modified because summaries are not intended to include all information that is in the main text.

Comment: In the sixth bullet on page 64, ATSDR may wish to add that the lethal dose would be >5,000 mg/kg.

Response: The text already states that there were no deaths at 5000 mg/kg. No change was made to the document.

Comment: In the seventh bullet on page 64, AMEC recommends that ATSDR add that the study from which the 0.89 mL/kg value was derived is suspect due to the use of units of mL/kg, which implies a liquid dose. ATSDR converted the dose from 0.89 mL/kg to 0.89 g/kg but did not explain how the dose of a solid crystalline compound could have been administered in mL.

Response: A previous section of the text explains how exposure doses were estimated. The explanation has not been added to the summary because summaries are not intended to included all information that is in the text.

Comment: In the eighth bullet on page 64, AMEC recommends that the information be clarified. It is stated that: "Reduced lymphocyte counts were the most consistently observed effect from all oral doses of BSA in both the 14-day and 13-week studies of rats exposed via drinking water." In fact, in the 14-day study only the males showed statistically significant decreases in lymphocyte counts and all were within the normal range for this species in this laboratory. In the 13-week study, all females but only high dose males showed statistically significant decreases in lymphocyte counts. However, all were within the normal range for this species in this laboratory.

Response: ATSDR maintains that reduced lymphocyte counts were the most consistently observed effect. The document was peer reviewed by well respected toxicologists (Dr. Finis Cavender, Dr. Kannan Krishnan, and Dr. James Withey), who have generally agreed with ATSDR's assessment of the unpublished studies and the conclusions in "Toxicological Information on Resorcinol and Selected Benzene Sulfonic Acids" (PHA, Appendix A) No change has been made to the document.

Comment: In the ninth bullet on page 64, the PHA reports hematology parameters under the heading of "behavioral effects." AMEC recommends that the PT and APTT effects be moved to the previous bullet. Regarding these effects, AMEC recommends that only statistically significant effects be summarized. The high dose males in the 14-day study did not have statistically significantly different APPT times compared to controls. AMED also recommends that it be noted that these effects were not reproduced in the 13-week study. In the 13-week study, there were no statistically significant differences between treatment groups and control groups for PT and APPT parameters.

Response: The statement has been removed from the text.

Comment: Regarding the increased motor activity time seen in the high dose females, this effect was determined by the toxicology laboratory as having no toxicological significance. AMEC has reviewed the literature and finds that increased motor activity in the absence of any other behavioral effects is viewed by neurotoxicologists as having no biological significance. ATSDR acknowledges this fact on page 64, but the qualification was not carried over to page 65.

Response: The statement has been removed from the text.

Comment: On page 65, ATSDR states that the compound is poorly absorbed by human skin. In fact, it was not absorbed at all, and AMEC recommends that this statement to be revised accordingly.

Response: The statement as been revised to state that BSA is not absorbed by excised human skin.

Comment: On page 65, it is stated: "Oral exposure of rats has resulted in hematological and lymphatic changes, as well as gastrointestinal and locomotor effects." This statement is misleading, and AMEC recommends that the statement be clarified. No gastrointestinal effects are noted in the literature discussed. Lastly, a reference is made to "lymphatic effects." This statement is also in error as can be seen on page 66, where a reference is made to the fact that no macroscopic or histopathological effects were seen in either primary or secondary lymphoid tissues.

Response: The statement has been changed to indicate that oral exposure or rats has resulted in hematological effects."

Appendix G: Levels of Public Health Hazard

ATSDR categorizes exposure pathways at hazardous waste sites according to their level of public health hazard to indicate whether people could be harmed by exposure pathways and site conditions. The categories are:

Urgent Public Health Hazard:	This category applies to exposure pathways and sites that have certain physical features or evidence of short-term (less than 1 year), site-related chemical exposure that could result in adverse health effects and require quick intervention to stop people from being exposed.
Public Health Hazard:	The category applies to exposure pathways and sites that have certain physical features or evidence of chronic (long-term), site-related chemical exposure that could result in adverse health effects.
Indeterminate Public Health Hazard:	The category applies to exposure pathways and sites where important information is lacking about chemical exposures, and a health determination cannot be made.
No Apparent Public Health Hazard:	The category applies to pathways and sites where exposure to site-related chemicals may have occurred in the past or is still occurring, however, the exposure is not at levels expected to cause adverse health effects.
No Public Health Hazard:	The category applies to pathways and sites where there is evidence of an absence of exposure to site-related chemicals.

Appendix H: Glossary of Environmental Health Terms

The Agency for Toxic Substances and Disease Registry (ATSDR) is a federal public health agency with headquarters in Atlanta, Georgia, and 10 regional offices in the United States. ATSDR's mission is to serve the public by using the best science, taking responsive public health actions, and providing trusted health information to prevent harmful exposures and diseases related to toxic substances. ATSDR is not a regulatory agency, unlike the U.S. Environmental Protection Agency (EPA), which is the federal agency that develops and enforces environmental laws to protect the environment and human health.

This glossary defines words used by ATSDR in communications with the public. It is not a complete dictionary of environmental health terms. If you have questions or comments, call ATSDR's toll-free telephone number, 1-888-42-ATSDR (1-888-422-8737).

Absorption

The process of taking in. For a person or animal, absorption is the process of a substance getting into the body through the eyes, skin, stomach, intestines, or lungs.

Acute

Occurring over a short time [compare with chronic].

Acute exposure

Contact with a substance that occurs once or for only a short time (up to 14 days) [compare with intermediate duration exposure and chronic exposure].

Additive effect

A biologic response to exposure to multiple substances that equals the sum of responses of all the individual substances added together [compare with antagonistic effect and synergistic effect].

Adverse health effect

A change in body function or cell structure that might lead to disease or health problems.

Aerobic

Requiring oxygen [compare with anaerobic].

Ambient

Surrounding (for example, *ambient* air).

Anaerobic

Requiring the absence of oxygen [compare with aerobic].

Analyte

A substance measured in the laboratory. A chemical for which a sample (such as water, air, or blood) is tested in a laboratory. For example, if the analyte is mercury, the laboratory test will determine the amount of mercury in the sample.

Analytic epidemiologic study

A study that evaluates the association between exposure to hazardous substances and disease by testing scientific hypotheses.

Antagonistic effect

A biologic response to exposure to multiple substances that is less than would be expected if

the known effects of the individual substances were added together [compare with additive effect and synergistic effect].

Background level

An average or expected amount of a substance or radioactive material in a specific environment, or typical amounts of substances that occur naturally in an environment.

Biodegradation

Decomposition or breakdown of a substance through the action of microorganisms (such as bacteria or fungi) or other natural physical processes (such as sunlight).

Biologic indicators of exposure study

A study that uses (a) biomedical testing or (b) the measurement of a substance [an analyte], its metabolite, or another marker of exposure in human body fluids or tissues to confirm human exposure to a hazardous substance [also see exposure investigation].

Biologic monitoring

Measuring hazardous substances in biologic materials (such as blood, hair, urine, or breath) to determine whether exposure has occurred. A blood test for lead is an example of biologic monitoring.

Biologic uptake

The transfer of substances from the environment to plants, animals, and humans.

Biomedical testing

Testing of persons to find out whether a change in a body function might have occurred because of exposure to a hazardous substance.

Biota

Plants and animals in an environment. Some of these plants and animals might be sources of food, clothing, or medicines for people.

Body burden

The total amount of a substance in the body. Some substances build up in the body because they are stored in fat or bone or because they leave the body very slowly.

CAP

See Community Assistance Panel.

Cancer

Any one of a group of diseases that occurs when cells in the body become abnormal and grow or multiply out of control.

Cancer risk

A theoretical risk of for getting cancer if exposed to a substance every day for 70 years (a lifetime exposure). The true risk might be lower.

Carcinogen

A substance that causes cancer.

Case study

A medical or epidemiologic evaluation of one person or a small group of people to gather information about specific health conditions and past exposures.

Case-control study

A study that compares exposures of people who have a disease or condition (cases) with people who do not have the disease or condition (controls). Exposures that are more common among the cases may be considered as possible risk factors for the disease.

CAS registry number

A unique number assigned to a substance or mixture by the American Chemical Society Abstracts Service.

Central nervous system

The part of the nervous system that consists of the brain and the spinal cord.

CERCLA [see Comprehensive Environmental Response, Compensation, and Liability Act of 1980]

Chronic

Occurring over a long time (more than 1 year) [compare with acute].

Chronic exposure

Contact with a substance that occurs over a long time (more than 1 year) [compare with acute exposure and intermediate duration exposure].

Cluster investigation

A review of an unusual number, real or perceived, of health events (for example, reports of cancer) grouped together in time and location. Cluster investigations are designed to confirm case reports; determine whether they represent an unusual disease occurrence; and, if possible, explore possible causes and contributing environmental factors.

Community Assistance Panel (CAP)

A group of people, from a community and from health and environmental agencies, who work with ATSDR to resolve issues and problems related to hazardous substances in the community. CAP members work with ATSDR to gather and review community health concerns, provide information on how people might have been or might now be exposed to hazardous substances, and inform ATSDR on ways to involve the community in its activities.

Comparison value (CV)

Calculated concentration of a substance in air, water, food, or soil that is unlikely to cause harmful (adverse) health effects in exposed people. The CV is used as a screening level during the public health assessment process. Substances found in amounts greater than their CVs might be selected for further evaluation in the public health assessment process.

Completed exposure pathway [see exposure pathway].

Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA)

CERCLA, also known as Superfund, is the federal law that concerns the removal or cleanup of hazardous substances in the environment and at hazardous waste sites. ATSDR, which was created by CERCLA, is responsible for assessing health issues and supporting public health activities related to hazardous waste sites or other environmental releases of hazardous substances.

Concentration

The amount of a substance present in a certain amount of soil, water, air, food, blood, hair, urine, breath, or any other media.

Contaminant

A substance that is either present in an environment where it does not belong or is present at levels that might cause harmful (adverse) health effects.

Delayed health effect

A disease or injury that happens as a result of exposures that might have occurred in the past.

Dermal

Referring to the skin. For example, dermal absorption means passing through the skin.

Dermal contact

Contact with (touching) the skin [see route of exposure].

Descriptive epidemiology

The study of the amount and distribution of a disease in a specified population by person, place, and time.

Detection limit

The lowest concentration of a chemical that can reliably be distinguished from a zero concentration.

Disease prevention

Measures used to prevent a disease or reduce its severity.

Disease registry

A system of ongoing registration of all cases of a particular disease or health condition in a defined population.

DOD

United States Department of Defense.

DOE

United States Department of Energy.

Dose (for chemicals that are not radioactive)

The amount of a substance to which a person is exposed over some time period. Dose is a measurement of exposure. Dose is often expressed as milligram (amount) per kilogram (a measure of body weight) per day (a measure of time) when people eat or drink contaminated water, food, or soil. In general, the greater the dose, the greater the likelihood of an effect. An "exposure dose" is how much of a substance is encountered in the environment. An "absorbed dose" is the amount of a substance that actually got into the body through the eyes, skin, stomach, intestines, or lungs.

Dose (for radioactive chemicals)

The radiation dose is the amount of energy from radiation that is actually absorbed by the body. This is not the same as measurements of the amount of radiation in the environment.

Dose-response relationship

The relationship between the amount of exposure [dose] to a substance and the resulting changes in body function or health (response).

Environmental media

Soil, water, air, biota (plants and animals), or any other parts of the environment that can contain contaminants.

Environmental media and transport mechanism

Environmental media include water, air, soil, and biota (plants and animals). Transport mechanisms move contaminants from the source to points where human exposure can occur. The environmental media and transport mechanism is the second part of an exposure pathway.

EPA

United States Environmental Protection Agency.

Epidemiologic surveillance

The ongoing, systematic collection, analysis, and interpretation of health data. This activity also involves timely dissemination of the data and use for public health programs.

Epidemiology

The study of the distribution and determinants of disease or health status in a population; the study of the occurrence and causes of health effects in humans.

Exposure

Contact with a substance by swallowing, breathing, or touching the skin or eyes. Exposure may be short-term [acute exposure], of intermediate duration, or long-term [chronic exposure].

Exposure assessment

The process of finding out how people come into contact with a hazardous substance, how often and for how long they are in contact with the substance, and how much of the substance they are in contact with.

Exposure-dose reconstruction

A method of estimating the amount of people’s past exposure to hazardous substances. Computer and approximation methods are used when past information is limited, not available, or missing.

Exposure investigation

The collection and analysis of site-specific information and biologic tests (when appropriate) to determine whether people have been exposed to hazardous substances.

Exposure pathway

The route a substance takes from its source (where it began) to its end point (where it ends), and how people can come into contact with (or get exposed to) it. An exposure pathway has five parts: a source of contamination (such as an abandoned business); an environmental media and transport mechanism (such as movement through groundwater); a point of exposure (such as a private well); a route of exposure (eating, drinking, breathing, or touching), and a receptor population (people potentially or actually exposed). When all five parts are present, the exposure pathway is termed a completed exposure pathway.

Exposure registry

A system of ongoing followup of people who have had documented environmental exposures.

Feasibility study

A study by EPA to determine the best way to clean up environmental contamination. A number of factors are considered, including health risk, costs, and what methods will work well.

Geographic information system (GIS)

A mapping system that uses computers to collect, store, manipulate, analyze, and display data. For example, GIS can show the concentration of a contaminant within a community in relation to points of reference such as streets and homes.

Grand rounds

Training sessions for physicians and other health care providers about health topics.

Groundwater

Water beneath the earth's surface in the spaces between soil particles and between rock surfaces [compare with surface water].

Half-life ($t_{½}$)

The time it takes for half the original amount of a substance to disappear. In the environment, the half-life is the time it takes for half the original amount of a substance to disappear when it is changed to another chemical by bacteria, fungi, sunlight, or other chemical processes. In the human body, the half-life is the time it takes for half the original amount of the substance to disappear, either by being changed to another substance or by leaving the body. In the case of radioactive material, the half life is the amount of time necessary for one half the initial number

of radioactive atoms to change or transform into another atom (that is normally not radioactive). After two half lives, 25% of the original number of radioactive atoms remain.

Hazard

A source of potential harm from past, current, or future exposures.

Hazardous Substance Release and Health Effects Database (HazDat)

The scientific and administrative database system developed by ATSDR to manage data collection, retrieval, and analysis of site-specific information on hazardous substances, community health concerns, and public health activities.

Hazardous waste

Potentially harmful substances that have been released or discarded into the environment.

Health consultation

A review of available information or collection of new data to respond to a specific health question or request for information about a potential environmental hazard. Health consultations are focused on a specific exposure issue. Health consultations are therefore more limited than a public health assessment, which reviews the exposure potential of each pathway and chemical [compare with public health assessment].

Health education

Programs designed with a community to help it know about health risks and how to reduce these risks.

Health investigation

The collection and evaluation of information about the health of community residents. This information is used to describe or count the occurrence of a disease, symptom, or clinical measure and to estimate the possible association between the occurrence and exposure to hazardous substances.

Health promotion

The process of enabling people to increase control over, and to improve, their health.

Health statistics review

The analysis of existing health information (i.e., from death certificates, birth defects registries, and cancer registries) to determine if there is excess disease in a specific population, geographic area, and time period. A health statistics review is a descriptive epidemiologic study.

Indeterminate public health hazard

The category used in ATSDR's public health assessment documents when a professional judgment about the level of health hazard cannot be made because information critical to such a decision is lacking.

Incidence

The number of new cases of disease in a defined population over a specific time period [contrast with prevalence].

Ingestion

The act of swallowing something through eating, drinking, or mouthing objects. A hazardous substance can enter the body this way [see route of exposure].

Inhalation

The act of breathing. A hazardous substance can enter the body this way [see route of exposure].

Intermediate duration exposure

Contact with a substance that occurs for more than 14 days and less than a year [compare with acute exposure and chronic exposure].

In vitro

In an artificial environment outside a living organism or body. For example, some toxicity testing is done on cell cultures or slices of tissue grown in the laboratory, rather than on a living animal [compare with in vivo].

In vivo

Within a living organism or body. For example, some toxicity testing is done on whole animals, such as rats or mice [compare with in vitro].

Lowest-observed-adverse-effect level (LOAEL)

The lowest tested dose of a substance that has been reported to cause harmful (adverse) health effects in people or animals.

Medical monitoring

A set of medical tests and physical exams specifically designed to evaluate whether an individual's exposure could negatively affect that person's health.

Metabolism

The conversion or breakdown of a substance from one form to another by a living organism.

Metabolite

Any product of metabolism.

mg/kg

Milligram per kilogram.

mg/cm^2

Milligram per square centimeter (of a surface).

mg/m^3

Milligram per cubic meter; a measure of the concentration of a chemical in a known volume (a cubic meter) of air, soil, or water.

Migration

Moving from one location to another.

Minimal risk level (MRL)

An ATSDR estimate of daily human exposure to a hazardous substance at or below which that substance is unlikely to pose a measurable risk of harmful (adverse), noncancerous effects. MRLs are calculated for a route of exposure (inhalation or oral) over a specified time period (acute, intermediate, or chronic). MRLs should not be used as predictors of harmful (adverse) health effects [see reference dose].

Morbidity

State of being ill or diseased. Morbidity is the occurrence of a disease or condition that alters health and quality of life.

Mortality

Death. Usually the cause (a specific disease, condition, or injury) is stated.

Mutagen

A substance that causes mutations (genetic damage).

Mutation

A change (damage) to the DNA, genes, or chromosomes of living organisms.

National Priorities List for Uncontrolled Hazardous Waste Sites (National Priorities List or NPL)

EPA's list of the most serious uncontrolled or abandoned hazardous waste sites in the United States. The NPL is updated on a regular basis.

No apparent public health hazard

A category used in ATSDR's public health assessments for sites where human exposure to contaminated media might be occurring, might have occurred in the past, or might occur in the future, but where the exposure is not expected to cause any harmful health effects.

No-observed-adverse-effect level (NOAEL)

The highest tested dose of a substance that has been reported to have no harmful (adverse) health effects on people or animals.

No public health hazard

A category used in ATSDR's public health assessment documents for sites where people have never and will never come into contact with harmful amounts of site-related substances.

NPL [see National Priorities List for Uncontrolled Hazardous Waste Sites]

Physiologically based pharmacokinetic model (PBPK model)

A computer model that describes what happens to a chemical in the body. This model describes how the chemical gets into the body, where it goes in the body, how it is changed by the body, and how it leaves the body.

Pica

A craving to eat nonfood items, such as dirt, paint chips, and clay. Some children exhibit pica-related behavior.

Plume

A volume of a substance that moves from its source to places farther away from the source. Plumes can be described by the volume of air or water they occupy and the direction they move. For example, a plume can be a column of smoke from a chimney or a substance moving with groundwater.

Point of exposure

The place where someone can come into contact with a substance present in the environment [see exposure pathway].

Population

A group or number of people living within a specified area or sharing similar characteristics (such as occupation or age).

Potentially responsible party (PRP)

A company, government, or person legally responsible for cleaning up the pollution at a hazardous waste site under Superfund. There may be more than one PRP for a particular site.

ppb

Parts per billion.

ppm

Parts per million.

Prevalence

The number of existing disease cases in a defined population during a specific time period [contrast with incidence].

Prevalence survey

The measure of the current level of disease(s) or symptoms and exposures through a questionnaire that collects self-reported information from a defined population.

Prevention

Actions that reduce exposure or other risks, keep people from getting sick, or keep disease from getting worse.

Public comment period

An opportunity for the public to comment on agency findings or proposed activities contained in draft reports or documents. The public comment period is a limited time period during which comments will be accepted.

Public availability session

An informal, drop-by meeting at which community members can meet one-on-one with ATSDR staff members to discuss health and site-related concerns.

Public health action

A list of steps to protect public health.

Public health advisory

A statement made by ATSDR to EPA or a state regulatory agency that a release of hazardous substances poses an immediate threat to human health. The advisory includes recommended measures to reduce exposure and reduce the threat to human health.

Public health assessment (PHA)

An ATSDR document that examines hazardous substances, health outcomes, and community concerns at a hazardous waste site to determine whether people could be harmed from coming into contact with those substances. The PHA also lists actions that need to be taken to protect public health [compare with health consultation].

Public health hazard

A category used in ATSDR's public health assessments for sites that pose a public health hazard because of long-term exposures (greater than 1 year) to sufficiently high levels of hazardous substances or radionuclides that could result in harmful health effects.

Public health hazard categories

Public health hazard categories are statements about whether people could be harmed by conditions present at the site in the past, present, or future. One or more hazard categories might be appropriate for each site. The five public health hazard categories are no public health hazard, no apparent public health hazard, indeterminate public health hazard, public health hazard, and urgent public health hazard.

Public health statement

The first chapter of an ATSDR toxicological profile. The public health statement is a summary written in words that are easy to understand. The public health statement explains how people might be exposed to a specific substance and describes the known health effects of that substance.

Public meeting

A public forum with community members for communication about a site.

Radioisotope

An unstable or radioactive isotope (form) of an element that can change into another element by giving off radiation.

Radionuclide

Any radioactive isotope (form) of any element.

RCRA [See Resource Conservation and Recovery Act (1976, 1984)]

Receptor population

People who could come into contact with hazardous substances [see exposure pathway].

Reference dose (RfD)

An EPA estimate, with uncertainty or safety factors built in, of the daily lifetime dose of a substance that is unlikely to cause harm in humans.

Registry

A systematic collection of information on persons exposed to a specific substance or having specific diseases [see exposure registry and disease registry].

Remedial Investigation

The CERCLA process of determining the type and extent of hazardous material contamination at a site.

Resource Conservation and Recovery Act (1976, 1984) (RCRA)

This Act regulates management and disposal of hazardous wastes currently generated, treated, stored, disposed of, or distributed.

RFA

RCRA Facility Assessment. An assessment required by RCRA to identify potential and actual releases of hazardous chemicals.

RfD

See reference dose.

Risk

The probability that something will cause injury or harm.

Risk reduction

Actions that can decrease the likelihood that individuals, groups, or communities will experience disease or other health conditions.

Risk communication

The exchange of information to increase understanding of health risks.

Route of exposure

The way people come into contact with a hazardous substance. Three routes of exposure are breathing [inhalation], eating or drinking [ingestion], or contact with the skin [dermal contact].

Safety factor [see uncertainty factor]

SARA [see Superfund Amendments and Reauthorization Act]

Sample

A portion or piece of a whole. A selected subset of a population or subset of whatever is being studied. For example, in a study of people the sample is a number of people chosen from a larger population [see population]. An environmental sample (for example, a small amount of soil or water) might be collected to measure contamination in the environment at a specific location.

Sample size

The number of units chosen from a population or environment.

Solvent

A liquid capable of dissolving or dispersing another substance (for example, acetone or mineral spirits).

Source of contamination

The place where a hazardous substance comes from, such as a landfill, waste pond, incinerator, storage tank, or drum. A source of contamination is the first part of an exposure pathway.

Special populations

People who might be more sensitive or susceptible to exposure to hazardous substances because of factors such as age, occupation, sex, or behaviors (for example, cigarette smoking). Children, pregnant women, and older people are often considered special populations.

Stakeholder

A person, group, or community who has an interest in activities at a hazardous waste site.

Statistics

A branch of mathematics that deals with collecting, reviewing, summarizing, and interpreting data or information. Statistics are used to determine whether differences between study groups are meaningful.

Substance

A chemical.

Substance-specific applied research

A program of research designed to fill important data needs for specific hazardous substances identified in ATSDR's toxicological profiles. Filling these data needs would allow more accurate assessment of human risks from specific substances contaminating the environment. This

research might include human studies or laboratory experiments to determine health effects resulting from exposure to a given hazardous substance.

Superfund Amendments and Reauthorization Act (SARA)

In 1986, SARA amended CERCLA and expanded the health-related responsibilities of ATSDR. CERCLA and SARA direct ATSDR to look into the health effects from substance exposures at hazardous waste sites and to perform activities including health education, health studies, surveillance, health consultations, and toxicological profiles.

Surface water

Water on the surface of the earth, such as in lakes, rivers, streams, ponds, and springs [compare with groundwater].

Surveillance [see epidemiologic surveillance]

Survey

A systematic collection of information or data. A survey can be conducted to collect information from a group of people or from the environment. Surveys of a group of people can be conducted by telephone, by mail, or in person. Some surveys are done by interviewing a group of people [see prevalence survey].

Synergistic effect

A biologic response to multiple substances where one substance worsens the effect of another substance. The combined effect of the substances acting together is greater than the sum of the effects of the substances acting by themselves [see additive effect and antagonistic effect].

Teratogen

A substance that causes defects in development between conception and birth. A teratogen is a substance that causes a structural or functional birth defect.

Toxic agent

Chemical or physical (for example, radiation, heat, cold, microwaves) agents which, under certain circumstances of exposure, can cause harmful effects to living organisms.

Toxicological profile

An ATSDR document that examines, summarizes, and interprets information about a hazardous substance to determine harmful levels of exposure and associated health effects. A toxicological profile also identifies significant gaps in knowledge on the substance and describes areas where further research is needed.

Toxicology

The study of the harmful effects of substances on humans or animals.

Tumor

An abnormal mass of tissue that results from excessive cell division that is uncontrolled and progressive. Tumors perform no useful body function. Tumors can be either benign (not cancer) or malignant (cancer).

Uncertainty factor

Mathematical adjustments for reasons of safety when knowledge is incomplete. For example, factors used in the calculation of doses that are not harmful (adverse) to people. These factors are applied to the lowest-observed-adverse-effect-level (LOAEL) or the no-observed-adverse-effect-level (NOAEL) to derive a minimal risk level (MRL). Uncertainty factors are used to account for variations in people's sensitivity, for differences between animals and humans, and for differences between a LOAEL and a NOAEL. Scientists use uncertainty factors when they have some, but not all, the information from animal or human studies to decide whether an exposure will cause harm to people [also sometimes called a safety factor].

Urgent public health hazard

A category used in ATSDR's public health assessments for sites where short-term exposures (less than 1 year) to hazardous substances or conditions could result in harmful health effects that require rapid intervention.

Volatile organic compounds (VOCs)

Organic compounds that evaporate readily into the air. VOCs include substances such as benzene, toluene, methylene chloride, and methyl chloroform.