IV. Public Health Implications

IV.A. Introduction

This section of the public health assessment evaluates the public health implications of acute and chronic exposure to chemicals of concern for adults and children. See Figure 7 for a list of chemicals evaluated for public health implications. In these evaluations, ATSDR considered multiple factors, including bioavailability, chemical and physical properties, and the frequency and duration of the estimated exposures. For cases in which a population is affected by more than one exposure pathway, ATSDR also considered the combinations of chemicals and exposure routes. ATSDR considered characteristics of the exposed population—such as age, gender, genetics, lifestyle, nutritional status, and health status—which influence how individuals absorb, distribute, metabolize, and excrete contaminants. Where appropriate, these characteristics are included in the chemical-specific discussions.

ATSDR tries to estimate realistic, site-specific exposure scenarios to enable comparisons to actual health effect levels reported in the scientific literature. For example, 0.15 liters per day (L/day) (the amount of water ingested during a 3-hour swimming event; EPA 1999) was used as the surface water intake rate in this section of the public health assessment instead of the 0.5 L/day used in the screening evaluation. In this level of the evaluation, an average concentration is used to estimate a more probable exposure dose. Because all of the chemicals were not detected in all of the samples, it is more likely that people would be exposed to a range of concentrations over time.

For chemicals detected in at least 10 percent of the samples, averages were calculated using detected concentrations only and do not take into account nondetected values. Even though this method tends to overestimate the true average values, ATSDR chose to base its health evaluations on the more conservative averages to be more protective of public health. For chemicals detected in less than 10 percent of the samples, ATSDR calculated averages using 1/2 the detection limit for nondetected samples.

In the case of pica behavior (see the "Children's Health Considerations" section), the estimated exposure doses were calculated using the maximum concentration and then compared to acute health effect levels (acute MRLs) because this exposure pattern can be episodic and short term.

As previously discussed, health guidelines (MRLs and RfDs) are derived for chemicals using the NOAEL/LOAEL/uncertainty factor approach. Generally, the uncertainty factor (also known as the safety factor) consists of multiples of 10, each representing a specific area of uncertainty inherent in the available animal or human study data. For example, a factor of 10 could be used to account for differences between animals and humans; a second factor of 10 could then be used to account for differences among people; while an additional factor of 10 could be used to account for the use of a LOAEL, instead of a NOAEL. An additional uncertainty factor that is greater than zero and less than or equal to 10 can also be used. The magnitude of the factor depends on the professional assessment of scientific uncertainties of the study and the quality of the database. Health guidelines are generally based on the LOAELs reported in the literature, often from a single study (the "critical study"). In addition to the critical study, other studies can provide chemical-specific, dose-response data.

The following discussion focuses primarily on contaminants detected in off-site locations. Because there are limited off-site air samples, however, and people have access to on-site fish and game, on-site exposures to these media are also discussed when appropriate.

IV.B. Children's Health Considerations

ATSDR recognizes that developing fetuses, infants, and children have unique vulnerabilities. Children are not small adults; a child's exposure can differ from an adult's in many ways. A child drinks more liquid, eats more food, and breathes more air per unit of body weight than an adult, and has a larger skin surface area in proportion to body volume. A child's behavior and lifestyle also influence exposure levels. Children crawl on the floor, put things in their mouths, play closer to the ground, and spend more time outdoors. These behaviors can result in longer exposure durations and higher intake rates.

In addition, children's metabolic pathways, especially in the first few months after birth, are less developed than those of adults. In some cases, children are better able than adults to deal with chemicals, but in others, they are less able and more vulnerable. Some chemicals that are not highly toxic in adults are in children.

Children grow and develop rapidly in the first few months and years of life. Some organ systems, especially the nervous and respiratory systems, can be permanently damaged if exposed to high levels of certain chemicals during this period. Also, young children have less ability to avoid hazards, because they lack knowledge and depend on adults for decisions.

This section of the public health assessment evaluates hazards to children displaying pica behavior (a craving for non-nutritive substances like soil). Information on the incidence of soil pica behavior is limited. A study described in EPA's *Exposure Factors Handbook* (EPA 1999) showed that the incidence of soil pica behavior was approximately 16 percent among children from a rural black community in Mississippi. This behavior was described as a cultural practice among the community surveyed, however, so that community may not represent the general population. In five other studies, only one child out of more than 600 ingested an amount of soil significantly greater than the range of other children. Although these studies did not include data for all populations and represented short-term ingestion only, it can be assumed that the incidence rate of child pica behavior in the general population is low.

There is little information on the amount of soil ingested (measured in mg/day) by children with pica behavior (EPA 1999). Intake rates between 1,000 and 10,000 mg/day have been used to estimate exposure doses for pica children. In this health assessment, ATSDR assumed a soil intake rate of 5,000 mg/day for 52 days per year (once a week) to represent pica behavior in children aged 1 to 3 years old. ATSDR believes that this is a health-protective assumption and likely overestimates soil consumption. In the case of pica behavior, estimated exposure doses were calculated using the maximum surface soil concentration detected in an area of likely exposure. ATSDR then compared these doses to acute health effect levels (e.g., acute MRLs), since this exposure pattern can be episodic and short-term (see Table 4). Doses below the acute MRLs are not considered to be a health hazard because MRLs have built-in safety factors, making them considerably lower than levels at which health effects have been observed.

ATSDR evaluated pica exposures to the 22 chemicals detected above comparison values in off-site soil. As shown in Table 4, most of the chemicals were not detected at levels constituting a health hazard for children exhibiting pica behavior. Only potential pica exposure to soil containing arsenic, iron, and lead is evaluated further.

Arsenic

Arsenic occurs naturally in the environment and is usually combined with other elements such as oxygen, chlorine, and sulfur. When combined with these elements arsenic is called inorganic arsenic. When combined with carbon and hydrogen, it is called organic arsenic. The organic forms of arsenic are usually less harmful than the inorganic forms (ATSDR 2000a). To be protective of public health, ATSDR assumed that all of the arsenic was in the more harmful inorganic form.

Using the maximum detected concentration (77.3 ppm; collected from a residential property), the estimated pica child exposure dose for arsenic in soil (5.5×10^{-3} milligrams per kilogram per day [mg/kg/day]) is slightly above the acute MRL. The next highest residential concentration (12.7 ppm; collected on the same day from the same location as the maximum concentration) is not at a level constituting a health hazard (the estimated exposure dose of 9.0×10^{-4} mg/kg/day is below the acute MRL). The acute MRL is based on a study in which health effects were observed in people exposed to 5.0×10^{-2} mg/kg/day of arsenic through ingesting poisoned soy sauce (Mizuta et al. 1956). ATSDR does not expect pica child exposures to result in adverse health effects in the ORR area; however, if pica children are exposed to the maximum detected concentration, they may suffer adverse acute effects (e.g., gastrointestinal distress, vomiting, or diarrhea).

Iron

Iron is a naturally occurring element in the environment. Iron is also an important mineral, which assists in the maintenance of basic life functions. It combines with protein and copper to make hemoglobin, which transports oxygen in the blood from the lungs to other parts of the body, including the heart. It also aids in the formation of myoglobin, which supplies oxygen to muscle tissues (ANR 2003). Without sufficient iron, the body cannot produce enough hemoglobin or myoglobin to sustain life. Iron deficiency is a condition that occurs when the body does not receive enough iron. Despite iron being the fourth most abundant metal in the earth's crust, iron deficiency is the world's most common cause of anemia. The National Academy of Sciences' (NAS's) dietary reference intake (DRI) for children 1 to 3 years old is 7 mg/day (NAS 2001).

According to the FDA, doses greater than 200 mg per event could poison or kill a child (FDA 1997). Doses of this magnitude are generally the result of children accidentally ingesting iron pills, not iron in soil or water. Acute iron poisoning has been reported in children less than 6 years of age who have accidentally overdosed on iron-containing supplements for adults. Because iron is not considered to cause harmful health effects in general, toxicological and epidemiological literature is limited.

Table 4. Estimated Pica Child Exposure Doses for Chemicals Detected in Off-Site Soil Compared to Acute Screening Guidelines

Chemical	*Maximum Concentration (ppm)*	*Pica Child Exposure Dose (mg/kg/day)*	*Acute Screening Guideline (mg/kg/day)*	*Source*	*Does the Pica Dose Exceed the Screening Guideline?*
Inorganics					
Arsenic	77.3	5.5E-03	0.005	Acute MRL	Yes
Cadmium	41.3	2.9E-03	0.02	Tox profile*	No
Chromium	*Below comparison values*				
Iron	31,500	158 mg/day	7 mg/day	DRI	Yes
Lead	625	4.5E-02	0.02	Acute LOAEL	Yes
Organics					
Benzidine	4.13	2.9E-04	0.003	RfD	No
Benzo(a)anthracene	4.13	2.9E-04	0.003	RfD§	No
Benzo(a)pyrene	4.13	2.9E-04	0.003	RfD§	No
Benzo(b)fluoranthene	4.13	2.9E-04	0.003	RfD§	No
Benzo(k)fluoranthene	*Below comparison values*				
bis(2-Chloroethyl) ether	4.13	2.9E-04	0.0075	Tox profile†	No
Chrysene	*Below comparison values*				
trans-Chlordane	2.8	2.0E-04	0.001	Acute MRL (chlordane)	No
Dibenzo(a,h)anthracene	4.13	2.9E-04	0.003	RfD§	No
3,3'-Dichlorobenzidine	4.13	2.9E-04	0.003	RfD (benzidine)	No
Heptachlor epoxide	0.97	6.9E-05	0.008	Tox profile*	No
Hexachlorobenzene	4.13	2.9E-04	0.008	Acute MRL	No
HCDD	*Below comparison values*				
Indeno(1,2,3-cd)pyrene	4.13	2.9E-04	0.003	RfD§	No
n-Nitroso-di-n-butylamine	4.13	2.9E-04	0.095	Acute MRL (n-nitrosodi-n-propylamine)	No
n-Nitrosodi-n-propylamine	0.79	5.6E-05	0.095	Acute MRL	No
TCDD	*Below comparison values*				

Pica doses were calculated using the following formula:

pica dose = (maximum concentration×0.005 kg/day×52 days/year×3 years)/(10 kg×(365 days/year×3 years))

Soil samples collected from Atomic City Auto Parts were not included because this is a separate industrial site that children are unlikely to have access to and the contaminated soil was removed. These data were not removed, however, during the screening assessment or from the summary information provided in Table 16 and Table 17.

"Below comparison values" means that when the Atomic City Auto Parts data were removed, the remaining soil concentrations were below the conservative health-based comparison values.

* The acute screening guideline was derived from limited acute toxicological data available in ATSDR's toxicological profile. A safety factor of 100 or 1,000 was applied to account for differences between animals and humans and to account for the use of a LOAEL, instead of a NOAEL. These acute screening guidelines should be considered unofficial and are for use in this health assessment only.

§The acute screening guideline was derived from the chronic oral RfD for anthracene. A safety factor of 100 was applied for use of a chronic guideline value. These acute screening guidelines should be considered unofficial and are for use in this health assessment only.

†The acute screening guideline was derived from an acute LD50 value available in ATSDR's toxicological profile. A safety factor of 10,000 was applied for use of an LD50 value. This acute screening guideline should be considered unofficial and is for use in this health assessment only.

DRI = dietary reference intake
LOAEL = lowest-observed-adverse-effect level
mg/kg/day = milligram per kilogram per day
MRL = minimal risk level
ppm = parts per million
RfD = reference dose

For comparison, ATSDR used a modification of the dose equation (dose = concentration × intake rate) to calculate a daily consumption from exposure to iron in soil. Exposure to the maximum concentration of iron collected from a residential area (31,500 ppm) would increase a pica child's daily consumption of iron by 158 mg/day, assuming 100 percent absorption. The median daily intake of dietary iron is roughly 11 to 13 mg/day for children 1 to 8 years old and 13 to 20 mg/day for adolescents 9 to 18 years old (NAS 2001). While the estimated daily consumption of iron for a pica child exceeds the NAS DRI, the daily increase in consumption is not likely to cause a pica child's daily dose to exceed levels known to induce poisoning (greater than 200 mg/event). Further, to the ATSDR health assessors' knowledge, no case of acute iron toxicity has ever occurred as a direct result of soil consumption. The absence of such cases probably reflects the large amount of soil that would have to be ingested, combined with the much lower intestinal absorption of iron from soil than from food, and the fact that the human body regulates its own iron level. Therefore, ATSDR does not expect that children exhibiting pica behavior would experience adverse health effects from exposure to iron in soil.

Lead

Lead is a naturally occurring bluish-gray metal found in small amounts in the Earth's crust and in all environmental media. The harmful effects from lead exposure have been known for a long time. Young children and fetuses have been the main focus of health effects research because they are most sensitive to potential effects from lead exposure. Because of health concerns, lead in gasoline, paints, ceramic products, caulking materials, and pipe solder has been dramatically reduced in the past few decades.

Six surface soil lead concentrations exceeded the screening value (400 ppm). The five highest lead concentrations detected in surface soil were located on the Atomic City Auto Parts industrial property where soil removal activities have been conducted (the contaminated soil has been removed). The only remaining soil sample (625 ppm) that exceeded the soil screening value is located in a residential area.

Assuming 100 percent bioavailability of the lead, the estimated exposure dose (4.5×10^{-2} mg/kg/day) for a child exhibiting pica behavior was slightly above the noncancer screening guideline (0.02 mg/kg/day; acute LOAEL in a human study). Further, ATSDR reviewed 122 studies of human and animal exposures to various doses of lead. In general, exposure doses below 0.001 mg/kg/day do not harm humans or animals. Exposure doses from 0.001 to 0.01 mg/kg/day have been shown to produce minor changes in blood cells. Harmful effects have been observed in animals when doses reach and exceed 0.01 mg/kg/day (ATSDR 1999b). However, studies indicate that not all of the ingested lead is absorbed via the gastrointestinal tract.

As a prudent public health practice, ATSDR supports routine blood lead testing, especially for children between the ages of 6 months and 6 years at high risk for having elevated blood lead levels. For more information about CDC's Childhood Lead Poisoning Prevention Program, visit http://www.cdc.gov/nceh/lead/lead.htm.

In humans, there is a correlation between the levels of lead in blood and the harmful effects that may result. Blood lead levels can be elevated via exposure to contaminated soil, paint, dust, air, food, and/or drinking water. Neurological effects are the most important health effect. CDC considers a child to have an elevated blood lead level if the amount of lead is 10 micrograms per

deciliter (µg/dL) or higher. Epidemiologic studies have consistently found that non-pica children's blood lead levels increase by about 3.8 µg/dL for every 1,000 ppm increase in soil lead levels. The lead concentrations detected in off-site soil ranged from 5.3 to 625 ppm.

Hypothetically (worst-case scenario), if children exhibiting routine pica behavior were exposed to 625 ppm of lead in soil with 100 percent absorption, their blood lead levels could reach and exceed 10 µg/dL. However, ATSDR believes that this scenario is unlikely.

IV.C. Public Health Evaluation

Chronic exposure to specific chemicals of concern is discussed in this section. The discussion of potential health effects for each chemical of concern is based on calculated exposure doses for current and future scenarios and documented health effects from human and animal studies. It is important to remember that an exposed person would not necessarily experience adverse health effects. It is also important to note that ATSDR is *assuming* exposure to the contaminated media. The location of each detection was not individually evaluated to determine whether anyone is actually being exposed.

ATSDR evaluated pathway-specific exposure doses for populations that may be exposed to specific chemicals via multiple exposure pathways to reflect a total estimated dose. Of all the chemicals screened for current and future exposure scenarios (off-site soil, sediment, surface water, biota, and air; on-site fish, game, and air), none are expected to result in adverse effects when considered across pathways.

Table 5 summarizes the completed and potential exposure pathways evaluated in this public health assessment. This table presents the exposure pathways, exposure routes, potentially affected populations, and public health implications for each contaminant that exceeded screening guidelines (see Table 16 through Table 33). A more detailed discussion of these chemicals follows the table.

Table 5. Summary of Completed and Potential Exposure Pathways for Contaminants Above Screening Guidelines

Substance Name	*Retained Pathway(s)*	*Exposure Route(s)*	*Potentially Affected Population(s)*	*Public Health Implications*
Aldrin/dieldrin	Biota (fish)	Ingestion	Child & adult—subsistence	None expected
Antimony	Biota (on-site game)	Ingestion	Child	None expected
Arsenic	Biota (fish & vegetation) Air	Ingestion Inhalation	Child & adult Adult	None expected None expected
Benzidine	Soil	Ingestion	Adult	None expected
Cadmium	Biota (fish & game) Biota (vegetation) Air	Ingestion Ingestion Inhalation	Child & adult Child & adult Child & adult	None expected None expected (see text) None expected
Chromium	Biota (fish & vegetation) Air	Ingestion Inhalation	Child & adult Adult	None expected None expected
Dibenzo(a,h)anthracene	Biota (EFPC crayfish)	Ingestion	Adult—subsistence	None expected
2,4-Dinitrophenol	Biota (unknown game)	Ingestion	Child	None expected
4,6-Dinitro-o-cresol	Biota (unknown game)	Ingestion	Child	None expected
Dioxin	Biota (unknown fish)	Ingestion	Child & adult	Indeterminate—follow fish advisories
Heptachlor epoxide	Biota (fish)	Ingestion	Child & adult—subsistence & recreational	None expected
alpha-HCH	Biota (fish)	Ingestion	Adult—subsistence	None expected
Iron	Soil Biota (unknown game)	Ingestion Ingestion	Child Child & adult	None expected None expected
Manganese	Biota (unknown game)	Ingestion	Child	None expected
Thallium	Biota (fish & game)	Ingestion	Child & adult	None expected
Toxaphene	Biota (fish)	Ingestion	Child & adult—subsistence	None expected

This table only presents chemicals that exceeded screening guidelines during the second-tier screening process.
EFPC = East Fork Poplar Creek

Aldrin/Dieldrin

Aldrin and dieldrin are the common names of two structurally similar compounds once used as insecticides. These chemicals are made in a laboratory and do not occur naturally in the environment. The two chemicals are discussed together because aldrin readily changes into dieldrin once it enters the environment or the body.

Aldrin and dieldrin are no longer produced or used. From the 1950s until 1970, aldrin and dieldrin were used extensively as insecticides on crops such as corn and cotton. The U.S. Department of Agriculture canceled all uses of aldrin and dieldrin in 1970. In 1972, however, EPA approved the use of aldrin and dieldrin for killing termites. Use of aldrin and dieldrin to control termites continued until 1987. In 1987, the manufacturer voluntarily canceled the registration for use in controlling termites.

As shown in Table 22 through Table 29, the estimated exposure doses for children and adults under the subsistence fishing exposure scenario are above their respective noncancer and cancer screening guidelines for aldrin/dieldrin in fish (mainly sunfish). As such, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from fish ingestion. The aldrin and dieldrin levels detected in all other media are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer and cancer screening guidelines) and will not be discussed further.

Table 6 shows estimated exposure doses for fish consumption that exceeded the noncancer or cancer screening guideline for aldrin and dieldrin, respectively. For this level of the evaluation, however, ATSDR calculated the estimated exposure doses using average concentrations to more closely reflect expected exposure patterns (people are exposed to a range of concentrations over time).

Table 6. Estimated Exposure Doses for Aldrin and Dieldrin

Medium	*Average Concentration (ppm)*	*Subsistence-Level Exposure Dose (mg/kg/day)*		
		Child	*Adult*	*Lifetime*
Aldrin				
Clinch River sunfish	0.042	6.5E-05	3.9E-05	1.7E-05
WBR sunfish	0.035	5.4E-05	3.3E-05	1.4E-05
On-site Sunfish	0.039	6.0E-05	3.6E-05	1.6E-05
Dieldrin				
EFPC sunfish	0.040	6.2E-05	3.7E-05	1.6E-05
Clinch River sunfish	0.045	6.9E-05	4.2E-05	1.8E-05
WBR sunfish	0.041	6.3E-05	3.8E-05	1.6E-05
On-site sunfish	0.060	9.2E-05	5.6E-05	2.4E-05
Clinch River catfish	0.012	1.8E-05	1.1E-05	4.8E-06
WBR catfish	0.009	1.4E-05	8.4E-06	3.6E-06
On-site catfish	0.012	*Below screening guidelines*		4.8E-06
On-site bass	0.027	4.2E-05	2.5E-05	1.1E-05

The chronic MRL for aldrin is 3.0×10^{-5} mg/kg/day.
The chronic MRL for dieldrin is 5.0×10^{-5} mg/kg/day.
"Below screening guidelines" means that the calculated doses were below screening guidelines during the second-tier screening evaluation (see Section III.D).

Based on the reported results, sunfish contained the highest levels of aldrin and dieldrin. The estimated exposure doses for consumption of catfish, crayfish, and bass are lower than the exposure doses estimated for consumption of sunfish. As such, ATSDR will use sunfish as a surrogate for all species since the estimated exposure doses from eating sunfish are expected to be the greatest.

All estimated exposure doses for recreational fishing exposure patterns were below levels constituting a hazard for all species. Aldrin/dieldrin exposure doses from ingestion (subsistence) of sunfish are above their respective screening guidelines in multiple locations (e.g., the Clinch River, EFPC, WBR, and on-site sampling locations). In all these locations, if "sunfish" represents 25 percent of the ingested fish over a lifetime of subsistence level exposures (using the average concentrations), then the exposure doses are below screening guidelines for both cancer and noncancer effects. This means that a person could eat about 13 pounds of aldrin/dieldrin-contaminated fish per year for 30 years and not experience adverse health effects. Therefore, adverse health effects are not expected.

Further, the noncancer screening guidelines for aldrin and dieldrin are based on studies in which adverse effects were observed at doses of 2.5×10^{-2} mg of aldrin/kg/day, while no adverse effects were observed at doses of 5.0×10^{-3} mg of dieldrin/kg/day (ATSDR 2002). Cancer effects were reported at doses ranging from 0.33 to 1.5 mg/kg/day (ATSDR 2002). All of the estimated subsistence-level exposure doses (i.e., children and adults eating 16 pounds [lbs] of fish/year and 52 lbs fish/year, respectively) are at least two to three orders of magnitude below these health effect levels (see Table 6).

Antimony

Antimony is a silvery white metal that is naturally found in the environment. It can enter the body when a person eats food contaminated with it. After a few hours, a small amount enters the bloodstream and mostly distributes to the liver, lungs, intestines, and spleen. Antimony then leaves the body in urine and feces over several weeks (ATSDR 1992).

As shown in Table 30, the estimated exposure dose for a child eating on-site game is above the antimony noncancer screening guideline. As such, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential for eating game. The antimony levels detected in all other media are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer screening guidelines).

The estimated exposure dose for a child ingesting on-site game was above the noncancer screening guideline when assuming 100 percent absorption. However, antimony is only slowly absorbed from the gastrointestinal tract. Based on animal data, gastrointestinal absorption of antimony was estimated to be 2 to 7 percent (ATSDR 1992). To account for this poor absorption, ATSDR assumed that 10 percent of the antimony was absorbed. The estimated exposure dose using an absorption value of 10 percent (5.0×10^{-5} mg/kg/day) is below the noncancer screening guideline (4.0×10^{-4} mg/kg/day). Remember that the screening guideline is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects. Estimated doses that are less than this value are not considered

to be a health hazard. As such, exposure to antimony is not expected to result in adverse health effects.

Arsenic

Arsenic is naturally occurring in the environment and is usually combined with other elements such as oxygen, chlorine, and sulfur. When combined with these elements arsenic is called inorganic arsenic. When combined with carbon and hydrogen, it is called organic arsenic. The organic forms of arsenic are usually less harmful than the inorganic forms (ATSDR 2000a). To be protective of public health, ATSDR assumed that all of the arsenic was in the more harmful inorganic form.

The estimated exposure doses for children and adults ingesting fish and vegetation (Table 22 through Table 29, Table 31, and Table 32), and for people inhaling air (Table 33) are above the arsenic noncancer and cancer screening guidelines. As such, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from these pathways. The arsenic levels detected in soil, sediment, surface water, and game are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer and cancer screening guidelines) and will not be discussed further.

Table 7 shows the exposure doses for media that exceeded the arsenic noncancer or cancer screening guidelines. For this level of the evaluation, however, ATSDR recalculated the estimated exposure doses using average concentrations to represent more realistic exposure scenarios and assumed that 10 percent of the total arsenic detected in fish and crayfish was in the inorganic form.

Table 7. Estimated Exposure Doses for Arsenic

Medium	*Average Concentration (ppm)*	*Exposure Dose (mg/kg/day)*		
		Child	*Adult*	*Lifetime*
EFPC crayfish	0.38	5.8E-05	3.5E-05	1.5E-05
On-site crayfish	0.25	3.8E-05	2.3E-05	9.9E-06
Clinch River catfish	0.64	9.8E-05	5.9E-05	2.5E-05
WBR catfish	0.23	3.5E-05	2.1E-05	9.2E-06
Clinch River sunfish	0.45	6.9E-05	4.2E-05	1.8E-05
WBR sunfish	0.12	1.8E-05	1.1E-05	4.8E-06
On-site sunfish	0.19	2.9E-05	1.8E-05	7.6E-06
Clinch River bass	0.28	4.3E-05	2.6E-05	1.1E-05
WBR bass	0.18	2.8E-05	1.7E-05	7.2E-06
On-site bass	0.22	3.4E-05	2.0E-05	8.8E-06
WBR unknown fish	0.17	2.6E-05	1.6E-05	6.8E-06
On-site unknown fish	0.31	4.8E-05	2.9E-05	1.2E-05
Off-site kale	1.4	2.2E-03	2.2E-03	9.6E-04
Off-site tomato	1.5	2.4E-03	2.4E-03	1.0E-03
Air	0.00056 µg/m^3	NA		

The chronic MRL for arsenic is 3.0×10^{-4} mg/kg/day.
Exposure doses for fish represent subsistence-level fishing.
ATSDR assumed that 10 percent of the total arsenic detected in fish and crayfish was in the inorganic form.
The average kale and tomato concentrations are based on samples from both edible and inedible portions.
Air CREG = 0.0002 µg/m^3
NA = not applicable

Ingestion is the primary way arsenic enters the body. Once arsenic is in the body, the liver changes some of it into a less harmful organic form. Both inorganic and organic forms of arsenic leave the body in urine. Studies have shown that 45 to 85 percent of the arsenic is eliminated within 1 to 3 days; however, some remains for several months or longer (Buchet et al. 1981; Crecelius 1977; Mappes 1977; Tam et al. 1979).

The scientific literature indicates that some dermal health effects could result from ingesting arsenic—hyperkeratosis and hyperpigmentation were reported in humans exposed to 1.4×10^{-2} mg/kg/day of arsenic in their drinking water for more than 45 years (Tseng et al. 1968). However, because estimates of water intake and dietary arsenic are highly uncertain in this and similar studies, some scientists argue that reported effects may actually be associated with doses higher than 1.4×10^{-2} mg/kg/day. Further, these effects have never been reported in a U.S. population.

Fish

Fish and shellfish can accumulate arsenic, but more than 80 percent of the arsenic found in fish is in an organic form (arsenobetaine or fish arsenic), which is not harmful (ATSDR 2000a; FDA 1993; Francesconi and Edmonds 1997; NAS 2001). The U.S. Food and Drug Administration (FDA) proposes that 10 percent of the total arsenic be estimated as inorganic arsenic (FDA 1993). When ATSDR applied this factor, the estimated subsistence-level exposure doses for arsenic in fish were below the screening guidelines. Further, all subsistence-level exposure doses are orders of magnitude below levels shown to cause harmful health effects (1.4×10^{-2} mg/kg/day) (see Table 7). Thus, the subsistence-level exposure doses are below levels constituting a health hazard; eating fish with the detected levels of arsenic is not expected to result in adverse health effects.

Vegetation

Limited vegetable data (18 kale samples and 15 tomato samples) were used to evaluate exposure to arsenic via locally grown vegetables. Arsenic was detected in less than 60 percent of the kale and tomato samples analyzed. Plants vary in the amount of arsenic they absorb from the soil and where they store arsenic. Some plants move arsenic from the roots to the leaves, while others absorb it and store it in the roots only.

- Fruit-type vegetables, such as tomatoes, concentrate arsenic in the roots, and less arsenic is taken up in the fruit.
- Leafy vegetables also store arsenic in their roots, but some is stored in the stems and leaves. Lettuce and some members of the *Brassica* plant family (such as collards, kale, mustard, and turnip greens) store more arsenic in the leaves than other crops, but not at concentrations high enough to cause health effects.
- Root crops such as beets, turnips, carrots, and potatoes absorb most of the arsenic in the surface skin of the vegetable. Peeling the skins of root crops can help eliminate the portion of the plant that contains arsenic.

The maximum arsenic concentration (0.06 ppm) detected in an *edible* portion of the vegetables was found in kale leaves. If an adult ate 90 lbs of vegetables/year (which is equivalent to the intake rate assumption of 0.0016 kg/kg/day for a 70 kg adult) containing the maximum concentration of arsenic, the exposure dose would be 1.0×10^{-4} mg/kg/day. A child eating about 17 lbs of vegetables/year (which is equivalent to the intake rate assumption of 0.0016 kg/kg/day for a 13 kg child) with the maximum concentration would have the same estimated dose. This exposure dose is below the screening guideline (3.0×10^{-4} mg/kg/day), as well as two orders of magnitude below levels shown to cause harmful health effects (1.4×10^{-2} mg/kg/day). Further, people are not expected to consume their yearly diet of vegetables from local gardens, and a portion of arsenic in plants is in the less toxic form (organic arsenic). Therefore, ATSDR does not expect adverse health effects to result from exposure to arsenic in locally grown produce.

Air

Limited air monitoring data collected on the ORR were used to evaluate exposure to arsenic via the inhalation pathway. The average air level was 0.00056 micrograms per cubic meter ($\mu g/m^3$)—which slightly exceeds the comparison value of 0.0002 $\mu g/m^3$. Air samples were collected on the ORR, thus the surrounding off-site population would have been exposed to lower levels due to dispersion, downwash effects, and increasing distance. Therefore, ATSDR does not believe that adverse effects would result in the general population from air related arsenic exposure.

Benzidine

Benzidine is a manufactured chemical that does not occur naturally. It is a crystalline solid that may be grayish-yellow, white, or reddish-gray. In the environment, benzidine is found in either its "free" state (as an organic base) or as a salt. Benzidine was used to produce dyes for cloth, paper, and leather. It is no longer produced or used commercially in the United States.

In soil, most benzidine is likely to be strongly attached to soil particles, so it does not easily pass into underground water. Benzidine can slowly be destroyed by certain other chemicals, light, and some microorganisms (for example, bacteria). Certain fish, snails, algae, and other forms of water life may take up and store very small amounts of benzidine, but accumulation in the food chain is unlikely.

As shown in Table 17, the estimated exposure dose for adults exposed to benzidine in off-site soil is above the cancer screening guideline. As such, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from exposure to benzidine in soil. The benzidine levels detected in all other media are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer and cancer screening guidelines or benzidine was not detected).

Very little information is available on the noncancer health effects that may be caused by exposure to benzidine. Benzidine contact with your skin could possibly cause a skin allergy. Benzidine can cause cancer in humans. This has been shown in studies of workers who were exposed for many years to levels much higher than the general population would experience. It is

important to note that most of the workers did not develop cancer, even after such high exposures. When cancer does occur, however, most often it is cancer of the urinary bladder.

Benzidine was detected in two of 26 off-site surface soil samples. The two surface soil samples were from two separate residential properties, located approximately 0.5 mile apart. The reported concentrations were above ATSDR's cancer screening value for soil. The estimated exposure dose for a person exposed for 125 days per year for 30 years is below the cancer screening value. Based on the conservative exposure assumptions, the tightly bound nature of benzidine to soil and organic material, and the unlikelihood that the general population or people living near the two locations would come in routine contact with benzidine-impacted surface soil (detected in less than 8 percent of the samples), ATSDR does not expect adverse health effects from exposure to benzidine in surface soil.

Cadmium

Cadmium is an element that occurs naturally in the Earth's crust. All soils and rocks, including coal and mineral fertilizers, contain some cadmium. Pure cadmium is a soft, silver-white metal. It is often found as part of small particles in air. It does not have a distinctive flavor or smell, so it is unnoticeable in water, food, and air. Food and cigarette smoke are the largest potential sources of cadmium exposure for the general population. Average cadmium levels in U.S. foods range from 2 to 40 parts per billion (ppb) of cadmium per parts of food. Average cadmium levels in cigarettes range from 1,000 to 3,000 ppb. The current U.S. average dietary intake of cadmium in adults is about 4.0×10^{-4} mg/kg/day; smokers receive an additional amount—about 4.0×10^{-4} mg/kg/day—from cigarettes (ATSDR 1999a). Most ingested cadmium passes through the gastrointestinal tract without being absorbed (Kjellstrom et al. 1978).

The estimated exposure doses for children and adults eating EFPC fish (Table 22), on-site fish (Table 28), on-site game (Table 30), and off-site vegetation (Table 31); and people inhaling the air (Table 33) are above the ATSDR cadmium screening guidelines. As such, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from these pathways. The cadmium levels detected in soil, sediment, and surface water are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer screening guidelines) and will not be discussed further.

Table 8 shows the exposure doses for media that exceeded the cadmium screening guidelines using the second-tier screening concentrations. ATSDR does not have a specific screening value for cadmium in biota (crayfish, fish, game, or vegetables) but has derived an MRL of 0.0002 mg/kg/day for chronic oral exposure to cadmium. The chronic oral MRL is based on a lifetime accumulated threshold of 2,000 mg of cadmium from dietary sources. The threshold is associated with kidney effects (e.g., proteinuria, or protein in the urine) seen in residents of cadmium-polluted areas of Japan. The average cadmium concentration in locally grown rice was used as the measure of cadmium intake and proteinuria was used as the index of renal damage. A relevant consideration is whether the proteinuria caused by cadmium exposure should be considered an adverse effect. The increased excretion of low-molecular-weight proteins *per se* probably has no adverse effect on health. Several studies have indicated that increased calcium excretion also occurs at about the same level as proteinuria, though—and this is an adverse effect

if it leads to increased calcium wasting and osteoporosis, particularly in post-menopausal women.

EPA has calculated oral chronic RfDs for cadmium of 0.001 and 0.0005 mg/kg/day for ingestion of food and water, respectively. The critical effect is significant proteinuria in humans chronically exposed to cadmium, using a NOAEL of 200 mg of cadmium per gram wet weight in the renal cortex and a kinetic model assuming 2.5 or 5 percent cadmium absorption from food or water, respectively, and 0.01 percent cadmium excretion per day (EPA 2004b). ATSDR's chronic oral MRL (0.0002 mg/kg/day) is comparable to the EPA RfD for water (0.0005 mg/kg/day). This is probably due to the fact that the moisture content of cooked rice is about 75 percent, roughly a 3:1 ratio of water-to-rice. As such, when evaluating exposures via the consumption of rehydrated foods (such as rice, pasta, and beans), ATSDR uses the MRL/RfD for water. When considering exposures from hydrated foods (such as fish, game, and vegetables), however, ATSDR uses the RfD for food because it more closely matches the media being evaluated.

Table 8. Estimated Exposure Doses for Cadmium

Medium		*Average Concentration (ppm)*	*Exposure Dose (mg/kg/day)*	
			Child	*Adult*
EFPC crayfish	Subsistence	3.0	4.6E-03	2.8E-03
	Recreational		6.9E-04	3.4E-04
On-site crayfish	Subsistence	2.1	3.2E-03	2.0E-03
	Recreational		4.8E-04	2.4E-04
EFPC sunfish	Subsistence	1.2	1.8E-03	1.1E-03
	Recreational		2.8E-04	1.4E-04
On-site sunfish	Subsistence	0.83	1.3E-03	7.7E-04
	Recreational		1.9E-04	9.5E-05
On-site creek chub	Subsistence	0.86	1.3E-03	8.0E-04
	Recreational		2.0E-04	9.8E-05
On-site bass	Subsistence	0.24	3.7E-04	2.2E-04
	Recreational		*Below screening guidelines*	
On-site unidentified fish	Subsistence	0.80	1.2E-03	7.4E-04
	Recreational		1.8E-04	9.1E-05
On-site unknown aquatic bird		4.3	3.3E-04	1.2E-04
On-site unknown terrestrial animal		4.5	3.5E-04	1.3E-04
Off-site beets		0.69	1.1E-03	1.1E-03
Off-site kale		0.60	9.6E-04	9.6E-04
Off-site tomatoes (edible portion only)		0.17	2.7E-04	2.7E-04
Air		0.00065 µg/m³	NA	

The chronic MRL for cadmium is 2.0×10^{-4} mg/kg/day.
The EPA oral RfDs for cadmium are 1.0×10^{-3} mg/kg/day and 5.0×10^{-4} mg/kg/day from ingestion of food and water, respectively.
Air CREG = 0.0006 µg/m³
The tomato data were screened (see Section III.D) using both fruit and root samples. However, for the public health implications section we focused on the edible portion of the tomato plant (i.e., the fruit).
"Below screening guidelines" means that the calculated doses were below screening guidelines during the second-tier screening evaluation (see Section III.D).
NA = not applicable

Fish

As noted above, most ingested cadmium passes through the gastrointestinal tract without being absorbed (Kjellstrom et al. 1978). EPA has derived an oral RfD for food that reflects differences in absorption between cadmium in food and cadmium in water. The estimated exposure doses for children and adults under the recreational exposure scenario (see Table 8) are below the screening guideline for food (1.0×10^{-3} mg/kg/day) and below the NOAEL for humans (2.1×10^{-3} mg/kg/day; ATSDR 1999a).

The estimated exposure doses for subsistence behavior were above the screening guideline for sunfish and crayfish for adults and sunfish, creek chub, crayfish, and an unidentified fish species for children. The estimated exposure doses for adults and children eating locally caught crayfish at subsistence levels were also above the human NOAELs. (Subsistence levels, per the default assumption, are about 16 lbs/year for children and 52 lbs/year for adults—more than a pound per month for children and a pound per week for adults.) These doses could have health effects (e.g., proteinuria), but we believe that the recreational consumption rates (2.4 lbs/year and 6.4 lbs/year for children and adults, respectively) are more realistic regarding locally harvested crayfish. As previously mentioned, the exposure doses for adults and children via recreational activities are below levels constituting a health hazard.

The estimated exposure doses for subsistence behavior were slightly above the EPA RfD for children consuming sunfish, creek chub, and an unidentified fish species and only for adults consuming EFPC sunfish. However, these estimated doses were below the human NOAEL under the default assumptions of eating approximately 16 lbs/year and 52 lbs/year for children and adults, respectively. The estimated exposure doses were calculated using limited species/area-specific fish data. For on-site fish there were a total of 69 fish samples (38/69 had cadmium) and for EFPC fish there were 7 samples (7/7 sunfish had cadmium). None of the 122 fish samples from the Clinch River had detectable levels of cadmium; only 2 of 88 fish samples from WBR had cadmium. Given that subsistence fishing behavior would likely occur at multiple locations (e.g., the Clinch River, EFPC, and WBR) to provide roughly 16 lbs of fish/year and 52 lbs of fish/year for children and adults, respectively, and that cadmium was infrequently detected (in less than 8 percent of the fish samples), exposure to cadmium in fish is not expected to result in adverse health effects.

Game

Adult and child exposure doses for an unknown on-site aquatic bird and terrestrial animal exceeded the ATSDR screening guideline for cadmium but were below the EPA RfD for cadmium in food (see Table 8). All other game (Canada goose and wood duck) were below the ATSDR screening guideline for cadmium. Thus, exposure to cadmium via ingestion of game is not expected to result in adverse health effects.

Vegetables

The exposure doses from eating kale and tomatoes are below EPA's RfD for ingestion of food (1.0×10^{-3} mg/kg/day). With an exposure dose of 1.1×10^{-3} mg/kg/day, eating beets only slightly exceeds the RfD, but is below the human NOAEL assuming a consumption rate of 90 lbs of

vegetables/year (which is equivalent to the intake rate assumption of 0.0016 kg/kg/day for a 70 kg adult).

Air

Limited air monitoring data were used to evaluate exposure to cadmium via the inhalation pathway. Air samples were collected on the ORR, and the average air level was 0.00065 $\mu g/m^3$—which slightly exceeds the screening guideline of 0.0006 $\mu g/m^3$. The surrounding population would have been exposed to lower levels due to dispersion, downwash effects, and increasing distance; as such, the ambient levels off site would have been below the screening level. Therefore, ATSDR does not believe that the general population would suffer adverse effects from air-related cadmium exposure.

Chromium

Chromium is a naturally occurring element found in rocks, animals, plants, soil, and volcanic gases. Chromium occurs in the environment in several chemical forms depending on the valance state of the chromium metal (e.g., trivalent [III] chromium or hexavalent [VI] chromium). Trivalent chromium—an essential nutrient—is more likely to be found in the environment and the body than hexavalent chromium. Trivalent chromium helps regulate how the body uses insulin. Hexavalent chromium is considerably more toxic to humans than trivalent chromium. The absorption of orally ingested chromium is relatively poor, with less than 10 percent absorption for the trivalent and hexavalent forms (ATSDR 2000b).

The estimated exposure doses for children and adults eating EFPC crayfish (Table 22), eating WBR fish (Table 26), eating off-site vegetation (Table 31), and inhaling the air (Table 33) are above the hexavalent chromium screening guidelines. As such, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from these pathways. The chromium levels detected in soil, surface water, sediment, and game are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer screening guideline) and will not be discussed further.

Table 9 shows the exposure doses for media that exceeded the hexavalent chromium screening guidelines. For this level of the evaluation, however, ATSDR recalculated the estimated exposure doses using average concentrations to represent more realistic exposure scenarios. Further, because the environmental data are not specific as to valence, ATSDR estimated exposure doses assuming that 50 percent of the measured concentrations are present as the more toxic hexavalent form. To account for chromium's poor absorption, ATSDR assumed that 10 percent of the chromium was absorbed.

Table 9. Estimated Exposure Doses for Chromium

Medium	*Average Concentration (ppm)*	*Exposure Dose (mg/kg/day)*	
		Child	*Adult*
EFPC crayfish	1.5	1.2E-04	*Below*
WBR unknown fish	5.6	4.3E-04	2.6E-04
Off-site kale	7.6	6.1E-04	6.1E-04
Off-site tomato	9.9	7.9E-04	7.9E-04
Air	0.0013 µg/m^3	NA	

The chronic RfD for hexavalent chromium is 3.0×10^{-3} mg/kg/day.
Air CREG = 0.00008 µg/m^3
Exposure doses for fish represent subsistence-level fishing.
ATSDR assumed 50 percent of the chromium detected was in the more harmful hexavalent form. Therefore, doses are calculated using one half the average concentration.
To account for the poor absorption of chromium, ATSDR assumed that 10 percent of the chromium was absorbed.
"Below" means that the calculated doses were below screening guidelines during the second-tier screening evaluation (see Section III.D).
NA = not applicable

ATSDR has not established a screening guideline for ingestion of chromium because the available data are insufficient or too contradictory to establish minimum effect levels. Because chromium is an essential nutrient, the National Research Council has established a range of "estimated safe and adequate daily dietary intakes" for it. This range is 50 to 200 micrograms per day (µg/day) (NAS 1989, 1994). The value at the upper end of the range, 200 µg/day, has been adopted by ATSDR as an interim guideline for oral exposure to hexavalent and trivalent chromium compounds (ATSDR 2000b). This interim guideline is equivalent to an exposure dose of 3.0×10^{-3} mg/kg/day for a 70-kilogram adult, and 2.0×10^{-2} mg/kg/day for a 13-kilogram child. EPA's RfD for chronic oral exposure, based on animal studies, is 3.0×10^{-3} mg/kg/day (EPA 2004c).

Biota

The estimated exposure doses related to chromium in biota were above screening guidelines for EFPC crayfish, WBR unknown species of fish, and off-site vegetation when assuming 100 percent absorption. When considering the poor absorption of chromium from the gastrointestinal tract (less than 10 percent), however, the resulting exposure doses were below the screening guideline (see Table 9). Estimated doses that are less than the screening guideline are not considered to be a health hazard. Therefore, ATSDR does not expect adverse health effects to result from exposure to chromium in biota.

Air

Limited air monitoring data collected on the ORR were used to evaluate exposure to chromium via the inhalation pathway. The average concentration of chromium in measured air was 0.0013 µg/m^3, which exceeds the ATSDR cancer comparison value but is within the acceptable cancer risk level of one in 10,000. Furthermore, the average air level does not exceed EPA's established noncancer inhalation guideline value of 0.008 µg/m^3 for hexavalent chromium. Therefore, ATSDR does not expect adverse effects to result from chromium exposure in air.

Dibenzo(a,h)anthracene

Dibenzo(a,h)anthracene is one of more than 100 different polycyclic aromatic hydrocarbons (PAHs). PAHs are formed during incomplete burning and generally occur as complex mixtures, rather than single compounds. All other PAHs were below screening values individually and/or in combination for all pathways considered. Because screening values do not exist for all PAHs, ATSDR used the "toxicity equivalency factors" (TEFs) available in the scientific literature. The TEF approach can be applied to individual congeners to generate a single concentration for the compound class. (Note that the highest reported concentrations of PAHs in surface soil were located on an industrial property—Atomic City Auto Parts—where the contaminated soil has been removed. This has eliminated exposure to impacted soil on that property, so these highest soil concentrations were deleted from consideration for current and future soil exposures. As such, ATSDR does not expect adverse effects to result from exposure to PAHs in surface soil.)

As shown in Table 23, the estimated exposure dose for adults eating EFPC crayfish at a subsistence level is above the dibenzo(a,h)anthracene cancer screening guideline. Accordingly, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from eating EFPC crayfish. (None of the dibenzo(a,h)anthracene levels detected in other media are high enough to constitute a health hazard: either the estimated doses are below the noncancer and cancer screening guidelines or dibenzo(a,h)anthracene was not detected.) When the lifetime exposure dose is recalculated using the average concentration (0.15 parts per million, or ppm), the resulting dose (6.0×10^{-6} mg/kg/day) is below levels constituting a health hazard (i.e., below the screening guideline, which uses safety factors that make it considerably lower than levels at which health effects have been observed). Additionally, it is unlikely that people would be able to maintain a subsistence diet on crayfish alone. As such, ATSDR does not expect adverse health effects to result from exposure to dibenzo(a,h)anthracene in crayfish.

2,4-Dinitrophenol

Dinitrophenols are a class of manufactured chemicals that do not occur naturally in the environment. There are six different dinitrophenols. The most commercially important dinitrophenol, 2,4-dinitrophenol, is a yellow, odorless solid. It is used in making dyes, wood preservatives, explosives, and insect control substances, and as a photographic developer.

As shown in Table 30, the estimated exposure doses for children and adults eating on-site game are above the 2,4-dinitrophenol noncancer screening guideline. Accordingly, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from eating on-site game. The 2,4-dinitrophenol levels detected in soil, sediment, surface water, and on-site fish are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer screening guideline or 2,4-dinitrophenol was not detected).[17]

To further evaluate exposures from eating game, ATSDR recalculated the exposure doses using the average concentration (55 ppm) to represent a more realistic exposure scenario. The estimated exposure doses for children and adults eating on-site game (unknown terrestrial

[17] 2,4-Dinitrophenol was not sampled in off-site fish, off-site game, or vegetation.

animals) are 4.2×10^{-3} mg/kg/day and 1.6×10^{-3} mg/kg/day, respectively. Only the child dose slightly exceeds EPA's chronic RfD for 2,4-dinitrophenol (2.0×10^{-3} mg/kg/day). The LOAEL (2.0 mg/kg/day) used to derive the chronic RfD is from a human study and incorporates an uncertainty factor of 1,000. The highest estimated exposure dose was about 475 times less than the LOAEL. Based on the low number of samples, the margin of safety relative to the LOAEL, and the conservative assumptions used for the estimation of exposure doses, adverse effects are not expected from eating on-site game.

4,6-Dinitro-o-Cresol

Dinitrocresols are a class of manufactured chemicals that do not occur naturally in the environment. There are 18 different dinitrocresols. The most commercially important dinitrocresol, 4,6-dinitro-o-cresol, is a yellow, odorless solid. It is used primarily for insect control and crop protection.

As shown in Table 30, the estimated exposure doses for children eating game caught on site are above the 4,6-dinitro-o-cresol noncancer screening guideline. As such, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from eating on-site game. The 4,6-dinitro-o-cresol levels detected in soil, sediment, surface water, and on-site fish are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer screening guideline or 4,6-dinitro-o-cresol was not detected).[18]

The frequency of detection was low for the data set (17 percent, or one in six samples). Therefore, only this one detected sample (3.5 ppm) was used to estimate the exposure dose. The estimated exposure dose for children eating on-site game (unknown terrestrial animals) is 2.7×10^{-4} mg/kg/day. This dose only slightly exceeds EPA's provisional RfD for 4,6-dinitro-o-cresol (1.0×10^{-4} mg/kg/day). Based on the low frequency of detection and conservative assumptions used for the estimation of exposure doses, adverse effects are not expected.

Dioxin (Chlorinated Dibenzo-p-Dioxins)

Chlorinated dibenzo-p-dioxins (CDDs) are a family of 75 chemically related compounds commonly known as chlorinated dioxins. One of these compounds is called 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). It is one of the most toxic of the CDDs and one of the most studied.

In their pure forms, CDDs are crystals or colorless solids. CDDs enter the environment as mixtures containing a number of individual components. CDDs are not intentionally manufactured by industry except for research purposes. They (mainly 2,3,7,8-TCDD) can be formed during the chlorine bleaching process at pulp and paper mills. CDDs are also formed during chlorination by waste and drinking water treatment plants. They can occur as contaminants in the manufacture of certain organic chemicals. CDDs are also released into the air as emissions from municipal solid waste and industrial incinerators.

The estimated exposure doses for people eating unknown species of fish from WBR (Table 26 and Table 27) were above the dioxin noncancer and cancer screening guidelines. Therefore,

[18] 4,6-Dinitro-o-cresol was not sampled in off-site fish, off-site game, or off-site vegetation.

ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from fish ingestion. The dioxin levels detected in soil, sediment, and surface water are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer and cancer screening guidelines).[19]

The estimated exposure doses for children and adults eating fish (unknown species) from WBR are above the screening guidelines (see Table 10). The data set used to estimate the exposure dose consisted of three fish samples (unknown fish species) collected from a pond near the K-25 site. Due to the lack of "dioxin" fish data, ATSDR classifies the potential for public health effects to result from exposure to dioxin in fish as an indeterminate public health hazard. In the absence of additional data, ATSDR recommends following the State of Tennessee fish advisories. If community members are concerned and wish to reduce their exposures, they can follow the cleaning and cooking methods presented in *A Guide to Healthy Eating of the Fish You Catch*, provided in Appendix C.

Table 10. Exposure Doses for Dioxin

Medium		*Average Total Relative Concentration (ppm)*	*Exposure Dose (mg/kg/day)*		
			Child	*Adult*	*Lifetime*
Unknown fish	Subsistence Recreational	0.000028	4.3E-08 6.5E-09	2.6E-08 3.2E-09	1.1E-08 1.4E-09

The chronic MRL for TCDD is 1.0×10^{-9} mg/kg/day.

Total relative concentrations were calculated using the toxic equivalency factor (TEF) approach for dioxins. This approach to evaluating health hazards has been developed and used to some extent to guide public health decisions (see EPA 1996b and ATSDR 2000c for more details). In short, the TEF approach compares the relative potency of individual congeners with that of TCDD, the best-studied member of this chemical class. The concentration or dose of each dioxin-like congener is multiplied by its TEF to arrive at a toxic equivalent (TEQ), and the TEQs are added to give the total toxic equivalency. The total toxic equivalency is then compared to reference exposure levels for TCDD expected to be without significant risk for producing health hazards.

[19] Dioxins and furans were not sampled in EFPC fish, Clinch River fish, on-site fish, off-site game, or vegetation.

Fish Advisories for Waterways Near the ORR

Tennessee River
Catfish, striped bass, and hybrid (striped bass-white bass) bass should not be eaten. Children, pregnant women, and nursing mothers should not consume white bass, sauger, carp, smallmouth buffalo, and largemouth bass, but other people can safely consume one meal per month of these species.

Clinch River
Striped bass should not be eaten. Children, pregnant women, and nursing mothers should not consume catfish and sauger, but other people can safely consume one meal per month of these species.

East Fork Poplar Creek
No fish should be eaten.

For the advisory, go to http://www.state.tn.us/environment/wpc/publications/advisories.pdf.

Heptachlor Epoxide

Heptachlor epoxide is a breakdown product of heptachlor, a synthetic chemical used before 1988 to kill insects in homes, in buildings, and on food crops. Heptachlor epoxide was not manufactured—bacteria in the environment form heptachlor epoxide from heptachlor. Ingestion of soil containing heptachlor epoxide is one way the chemical can enter the body. The toxicokinetics (i.e., absorption, distribution, metabolism, and excretion) of heptachlor epoxide is not well studied in humans. Animal studies suggest that heptachlor epoxide is primarily stored in adipose tissue (i.e., fat). One animal study reported that the levels of heptachlor epoxide decreased to below detection limits 6 to 8 weeks after exposure (ATSDR 1993a).

As shown in Table 22 through Table 29, the estimated exposure doses for children and adults under the subsistence fishing exposure scenarios are above the chronic oral screening guidelines for heptachlor epoxide. The only recreational exposure scenario above the heptachlor epoxide noncancer screening guideline is for a child eating sunfish from EFPC. Accordingly, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from fish ingestion. The heptachlor epoxide levels detected in soil, sediment, surface water, and on-site game are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer and cancer screening guidelines) and will not be discussed further.[20]

Table 11 shows the exposure doses for media that exceeded the heptachlor epoxide noncancer and cancer screening guidelines. For this level of the evaluation, however, ATSDR recalculated the estimated exposure doses using average concentrations to represent more realistic exposure scenarios.

[20] Heptachlor epoxide was not sampled in off-site game or off-site vegetation.

Table 11. Estimated Exposure Doses for Heptachlor Epoxide

Medium		Average Concentration (ppm)	Exposure Dose (mg/kg/day)		
			Child	Adult	Lifetime
EFPC sunfish	Subsistence	0.038	5.8E-05	3.5E-05	1.5E-05
	Recreational		8.8E-06	*Below screening guidelines*	
Clinch River sunfish	Subsistence	0.039	6.2E-05	3.7E-05	1.6E-05
	Recreational		*Below screening guidelines*		
WBR sunfish	Subsistence	0.031	4.8E-05	2.9E-05	1.2E-05
	Recreational		*Below screening guidelines*		
On-site sunfish	Subsistence	0.031	4.8E-05	2.9E-05	1.2E-05
	Recreational		*Below screening guidelines*		
Clinch River catfish	Subsistence	0.005	7.7E-06	4.6E-06	2.0E-06
	Recreational		*Below screening guidelines*		
WBR catfish	Subsistence	0.005	7.7E-06	4.6E-06	2.0E-06
	Recreational		*Below screening guidelines*		
On-site catfish	Subsistence	0.009	1.4E-05	8.4E-06	3.6E-06
	Recreational		*Below screening guidelines*		

The chronic RfD for heptachlor epoxide is 1.3×10^{-5} mg/kg/day.
"Below screening guidelines" means that the calculated doses were below screening guidelines during the second-tier screening evaluation (see Section III.D).

The estimated exposure doses for adults and children eating fish are above their respective guidelines for noncancer and cancer effects (see Table 22 through Table 29). The highest exposure doses were for subsistence children and adults eating sunfish from the Clinch River. The Clinch River data set used to estimate exposure doses for sunfish had 13 percent detects (13/100 sunfish samples). The oral screening guideline for heptachlor epoxide is based on a study in which liver-to-body weight ratios were significantly increased in dogs fed heptachlor epoxide at doses of 1.25×10^{-2} mg/kg/day for 60 weeks (Dow Chemical Company 1958). Supporting animal studies report no adverse health effects for doses ranging from 2.5×10^{-2} to 2.5×10^{-1} mg/kg/day (EPA 2004a). The estimated exposure doses are at least 400 times below these health effect levels. As such, adverse effects are not expected.

EPA classifies heptachlor epoxide as a probable human carcinogen based on rodent studies in which liver carcinomas were induced in two strains of mice and female rats (EPA 2004a). There are three epidemiologic studies of workers exposed to chlordane and/or heptachlor. One retrospective cohort study of pesticide applicators was considered inadequate in sample size and duration of follow up. This study showed marginal statistically significant increased mortality from bladder cancer. Two other retrospective cohort studies were based on pesticide manufacturing workers. Neither of these studies showed any statistically significant increased cancer mortality. Both of these populations also had confounding exposures to other chemicals (EPA 2004a).

The estimated exposure doses for cancer effects are slightly above the cancer screening guidelines. Based on the low probability that a person would be exposed to significant levels over 30 years, the conservative exposure assumptions, and the lack of statistically significant cancer mortality in three human studies, ATSDR does not expect cancer effects from exposure to heptachlor epoxide in fish.

Alpha-Hexachlorocyclohexane (Alpha-HCH)

Hexachlorocyclohexanes are synthetic chemicals that were once used as insecticides. They exist in eight chemical forms called isomers, each of which is named according to the position of the hydrogen atoms (ATSDR 2003). Alpha-HCH is one of these isomers.

The estimated exposure dose for subsistence behavior was slightly above the cancer screening guideline for people ingesting sunfish from the Clinch River (see Table 25), WBR (see Table 27), and on site (see Table 29). The alpha-HCH levels detected in all other media are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer and cancer screening guidelines). Table 12 shows the exposure doses for sunfish that exceeded the alpha-HCH cancer screening guideline. For this level of the evaluation, however, ATSDR recalculated the estimated exposure doses using average concentrations to represent more realistic exposure scenarios.

Table 12. Estimated Exposure Doses for alpha-HCH

Medium	*Average Concentration (ppm)*	*Subsistence-Level Exposure Dose (mg/kg/day)*		
		Child	*Adult*	*Lifetime*
Clinch River sunfish	0.042	*Below screening guidelines*		1.7E-05
WBR sunfish	0.035	*Below screening guidelines*		1.4E-05
On-site sunfish	0.034	*Below screening guidelines*		1.4E-05

"Below screening guidelines" means that the calculated doses were below screening guidelines during the second-tier screening evaluation (see Section III.D).

The estimated lifetime exposure doses (see Table 12) are well below the cancer effect levels (CELs) reported in the literature (CELs range from 2 to 90 mg/kg/day; ATSDR 2003). Based on the conservative assumptions used to estimate exposure and the unlikelihood that subsistence behavior would occur with sunfish only, ATSDR does not expect adverse health effects from exposure to alpha-HCH in fish.

Iron

Iron is a naturally occurring element in the environment. In fact, it is the fourth most abundant element in the Earth's crust by weight (LANL 2001). The most common iron ore is hematite, which frequently can be seen as black sand along beaches and stream banks. It is hard and brittle, and is usually combined with other metals to form alloys, including steel.

Iron is an important mineral that assists in the maintenance of basic life functions. It combines with protein and copper to make hemoglobin, which transports oxygen in the blood from the lungs to other parts of the body, including the heart. It also aids in the formation of myoglobin, which supplies oxygen to muscle tissues (ANR 2003). Without sufficient iron, the body cannot produce enough hemoglobin or myoglobin to sustain life. Despite the fact that iron is the fourth most abundant metal in the earth's crust, iron deficiency is the world's most common cause of anemia. The NAS DRI for children 4- to 8- years-old is 10 mg/day (NAS 2001).

Too much iron, however, can be dangerous to children. According to the FDA, doses greater than 200 mg per event could poison or kill a child (FDA 1997). Doses of this magnitude are

generally the result of children accidentally ingesting iron pills, not ingesting iron in soil or in water. Acute iron poisoning has been reported in children less than 6 years of age who have accidentally overdosed on iron-containing supplements for adults. Because iron is not considered to cause harmful health effects in general, toxicological and epidemiological literature is limited.

The average adult stores about 1 to 3 grams of iron in his or her body. A balance between dietary uptake and loss maintains this equilibrium. There is no physiologic mechanism of iron excretion. Consequently, absorption alone regulates body iron stores.

The estimated exposure doses for children ingesting off-site soil (Table 16) and people eating on-site game (Table 30) are above the iron noncancer screening guideline. Accordingly, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from these pathways. The iron levels detected in sediment, surface water, and fish are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer screening guideline) and will not be discussed further.[21]

Table 13 shows the exposure doses for media that exceeded the iron noncancer screening guideline. For this level of the evaluation, however, ATSDR recalculated the estimated exposure doses using average concentrations to represent more realistic exposure scenarios. ATSDR also calculated daily intake rates.

Table 13. Estimated Exposure Doses and Daily Intake Rates for Iron

Medium	*Average Concentration (ppm)*	*Exposure Dose (mg/kg/day)*		*Daily Intake Rates (mg/day)*	
		Child	*Adult*	*Child*	*Adult*
Off-site soil	23,000	2.8E-01	*Below*	5	*Below*
On-site unknown terrestrial animal	7,600	5.8E-01	2.2E-01	8	15

The chronic RfD for iron is 3.0×10^{-1} mg/kg/day.
"Below" means that the calculated doses were below screening guidelines during the second-tier screening evaluation (see Section III.D).

Soil

Based on the child soil intake rate, the soil iron concentration at which the DRI of 10 mg/day would be reached was calculated to be 50,000 ppm (assuming 200 mg soil/day for 365 days/year at 100 percent absorption). Concentrations of iron in soil ranged from 5,790 to 61,600 ppm, with an average concentration of about 23,000 ppm. The body normally reduces absorption of iron from the gastrointestinal tract in response to higher concentrations. As a result, the levels of iron found in the soil are not likely to pose a health hazard to children.

For comparison, ATSDR calculated a daily consumption from exposure to the iron in soil using a modification of the dose equation (dose = concentration × intake rate). Exposure to the average level of iron in the soil would increase a non-pica child's daily consumption of iron by 5 mg/day, assuming 100 percent absorption. The median daily intake of dietary iron is roughly 11 to 13 mg/day for children 1 to 8 years old and 13 to 20 mg/day for adolescents 9 to 18 years old (NAS 2001). The daily consumption of iron for a child does not exceed the NAS DRI for children 4 to

[21] Iron was not sampled in off-site vegetation.

8 years old (10 mg/day; NAS 2001), and the daily increase in consumption is not likely to cause a child's daily dose to exceed levels known to induce poisoning (greater than 200 mg/event). Therefore, ATSDR does not expect that non-pica children would experience adverse health effects from exposure to iron in soil.

Game

ATSDR estimated a daily exposure dose for eating game (unknown terrestrial animal) by multiplying the average concentration of iron detected (7,600 ppm or mg/kg) by the daily intake rate (0.002 kg of game/day for an adult and 0.001 kg/day for a child). Based on this estimate, eating game could have increased an adult's daily consumption of iron by 15 mg/day and a child's daily consumption of iron by 8 mg/day. These estimated daily increases in game consumption are not expected to cause a person's daily dose to exceed levels known to induce poisoning (e.g., greater than 200 mg/event). Further, the body uses a homeostatic mechanism to keep iron burdens at a constant level despite variations in the diet (Eisenstein and Blemings 1998). Therefore, ingesting game containing this level of iron is not expected to result in adverse noncancer health effects.

Manganese

Manganese is naturally found in many types of rocks and comprises about 0.1 percent of the Earth's crust (ATSDR 2000d). It is an essential trace element and is required by the body to break down amino acids and produce energy. Manganese can enter the body via ingestion, but most manganese is excreted in feces—only 3 to 5 percent of manganese is absorbed by the body when ingested (Davidsson et al. 1988; Mena et al. 1969). Typically, people have small amounts of manganese in their bodies. Under normal circumstances, the amount is regulated so the body has neither too much nor too little (EPA 1984). For example, if large amounts of manganese are consumed, large amounts will be excreted.

As shown in Table 30, the estimated exposure dose for a child eating on-site game is above the manganese noncancer screening guideline. As such, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential for this pathway. The manganese levels detected in all other media are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer screening guideline).

The Food and Nutrition Board of the National Research Council determined that 2 to 5 mg of manganese/day is an "estimated safe and adequate daily dietary intake" (NRC 1989). The World Health Organization (WHO) concluded that 2 to 3 mg/day is "adequate" and 8 to 9 mg/day is "perfectly safe" (WHO 1973). Based on these studies, EPA has determined that an appropriate RfD for manganese in food is 10 mg/day, which EPA calculated to a NOAEL of 0.14 mg/kg/day. The estimated exposure dose for a child ingesting on-site game (9.8×10^{-2} mg/kg/day) is below this NOAEL. Further, only a small amount of manganese is absorbed, and a homeostatic mechanism regulates the amount in the body. Therefore, ATSDR does not expect adverse health effects from exposure to manganese in game.

Thallium

Pure thallium is a bluish-white metal that is found in trace amounts in the Earth's crust. In the past, thallium was obtained as a byproduct from smelting other metals. In its pure form, thallium is odorless and tasteless. It can also be found combined with other substances such as bromine, chlorine, fluorine, and iodine to form a colorless-to-white or yellow substance. Thallium is used mostly in manufacturing electronic devices, switches, and closures, primarily for the semiconductor industry. It also has limited use in the manufacture of special glass, and for certain medical procedures. Thallium has not been produced in the United States, however, since 1984.

As shown in Table 28 and Table 30, the estimated exposure doses for children and adults eating on-site fish (specifically, bass and sunfish) and game (unknown terrestrial animal) are above the thallium noncancer screening guideline. Accordingly, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from eating fish and game. The thallium levels detected in soil, sediment, surface water, and off-site fish are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer screening guideline) and will not be discussed further.[22]

Table 14 shows the estimated exposure doses for media that exceeded the thallium noncancer screening guideline. For this level of the evaluation, however, ATSDR recalculated the estimated exposure doses using average concentrations to represent more realistic exposure scenarios.

Table 14. Estimated Exposure Doses for Thallium

Medium		*Average Concentration (ppm)*	*Exposure Dose (mg/kg/day)*	
			Child	*Adult*
On-site bass	Subsistence	0.027	4.2E-05	*Below*
	Recreational		*Below screening guidelines*	
On-site sunfish	Subsistence	1.0	1.5E-03	9.3E-04
	Recreational		2.3E-04	1.1E-04
On-site unknown terrestrial animal		1.8	1.4E-04	5.1E-05

The chronic RfD for thallium is 7.0×10^{-5} mg/kg/day.
"Below" and "Below screening guidelines" mean that the calculated doses were below screening guidelines during the second-tier screening evaluation (see Section III.D).

EPA has RfDs for several thallium compounds. Each RfD covers a particular compound and is based on animal studies for that compound. For example, the RfD for thallium sulfate is based on a failure to observe harmful effects in rats that were administered as much as 0.25 mg/kg/day of thallium by gavage (stomach tube). EPA divided this dose by an uncertainty factor of 3,000 to account for humans being more sensitive than rats to thallium, for some humans being more sensitive than others, and for a lack of reproductive and chronic toxicity data to derive the RfD (EPA 2004d).

On average, a person takes in about 2 micrograms of thallium per gram of food daily. The thallium dose that did not cause toxic effects in rats (2.3×10^{-1} mg/kg/day) was about 150 times

[22] Thallium was not sampled in off-site vegetation.

higher than the estimated exposure dose for a child and 250 times higher than an adult with subsistence exposure patterns for on-site fish. The exposure doses for the recreational fishing scenario and eating on-site game are thousands of times lower than the level at which no health effects were seen in rats. Based on this margin of safety, adverse effects are not expected.

Toxaphene

Toxaphene is an insecticide containing more than 670 chemicals. It is usually found as a solid or a gas, and in its original form it is a yellow to amber waxy solid that smells like turpentine. It does not burn and it evaporates when in solid form or when mixed with liquids. Toxaphene is also known as camphechlor, chlorocamphene, polychlorocamphene, and chlorinated camphene. It was used primarily in the southern United States to control insects on cotton and other crops. It was also used to control insects on livestock and to kill unwanted fish in lakes. Toxaphene was one of the most heavily used insecticides in the United States until 1982, when it was canceled for most uses. All uses were banned in 1990.

As shown in Table 22 through Table 29, the estimated exposure doses for children and adults ingesting fish are above the toxaphene noncancer and cancer screening guidelines. Accordingly, ATSDR further examined the effect levels reported in the scientific literature and more fully reviewed exposure potential from fish ingestion. The toxaphene levels detected in all other media are not at levels constituting a health hazard (i.e., the estimated doses are below the noncancer and cancer screening guidelines) and will not be discussed further.[23]

Table 15 shows the exposure doses for media that exceeded the toxaphene noncancer or cancer screening guidelines. For this level of the evaluation, however, ATSDR recalculated the estimated exposure doses using average concentrations to represent more realistic exposure scenarios.

Table 15. Estimated Exposure Doses for Toxaphene

Medium		*Average Concentration (ppm)*	*Subsistence-Level Exposure Dose (mg/kg/day)*		
			Child	*Adult*	*Lifetime*
Clinch River sunfish	Subsistence	0.84	1.3E-03	7.8E-04	3.3E-04
	Recreational		*Below screening guidelines*		
WBR sunfish	Subsistence	0.70	1.1E-03	6.5E-04	2.8E-04
	Recreational		*Below screening guidelines*		
On-site sunfish	Subsistence	0.78	1.2E-03	7.2E-04	3.1E-04
	Recreational		*Below screening guidelines*		
WBR bass	Subsistence	0.24	3.7E-04	2.2E-04	9.6E-05
	Recreational		*Below screening guidelines*		
On-site bass	Subsistence	1.9	2.9E-03	1.8E-03	7.6E-04
	Recreational		*Below screening guidelines*		9.3E-05
WBR catfish	Subsistence	0.20	3.1E-04	1.9E-04	8.0E-05
	Recreational		*Below screening guidelines*		

The intermediate MRL for toxaphene is 1.0×10^{-3} mg/kg/day.
"Below screening guidelines" means that the calculated doses were below screening guidelines during the second-tier screening evaluation (see Section III.D).

[23] Toxaphene was not sampled in off-site vegetation.

The frequency of detection was low for all data sets (ranging from 2 to 17 percent). The NOAEL (0.35 mg/kg/day) used to derive the intermediate-duration MRL is from an animal study and incorporates an uncertainty factor of 300 (ATSDR 1996). The highest estimated exposure dose was about 120 times less than the NOAEL. The estimated exposure doses for subsistence behavior are also well below (almost 17,000 times less than) the cancer effects levels reported in the scientific literature (CELs range from 12.9 to 55.6 mg/kg/day; ATSDR 1996). Based on the low frequency of detection and conservative assumptions used for the estimation of exposure doses, adverse effects are not expected.

Multiple Chemical Exposures

ATSDR has reviewed the scientific literature on chemical interactions and noted that if the estimated exposure doses for individual contaminants are well below doses shown to cause adverse effects, then the combined effects of multiple chemicals are not expected to result in adverse health effects. Therefore, ATSDR does not expect interactive health effects because, for each chemical evaluated, the conservatively estimated exposure doses are below health effect levels reported in the scientific literature.

ATSDR does not expect interactive health effects from exposure to multiple chemicals because, for each chemical evaluated, the conservatively estimated exposure doses are below health effect levels reported in the scientific literature.

Several animal and human studies (Berman et al. 1992; Caprino et al. 1983; Drott et al. 1993; Harris et al. 1984) have reported thresholds for interactions. Studies have shown that exposure to a mixture of chemicals is unlikely to produce adverse health effects as long as components of that mixture are detected at levels below the NOAEL for individual compounds (Feron et al. 1995; Seed et al. 1995). Additionally, Jonker et al. (1990) and Groten et al. (1991) demonstrated the absence of interactions at doses tenfold or more below effect thresholds. In two separate subacute toxicity studies in rats (Groten et al. 1997; Jonker et al. 1993), adverse effects disappeared altogether as the dose was decreased to below the threshold level. Other studies have provided evidence that exposure to chemical mixtures, in which the chemicals were administered at doses near their individual thresholds, can produce additive toxic effects. For example, rats exposed to a mixture of sub-threshold doses of 1,1,1-trichloroethane, trichloroethylene, and tetrachloroethylene experienced signs of liver toxicity (Stacey 1989). The dose given to the rats in this study was greater than 2,000 mg/kg, while the estimated exposure doses in the United States and Canada are below 0.003 mg/kg/day (ATSDR 2004).

The interactions of carcinogens are more difficult to quantify at environmental doses because a large study group (humans or animals) is needed for statistical significance at the lower doses observed from environmental exposure. In the mid-1970s, under contract to the National Cancer Institute, 12 chemicals were tested in 918 pair-wise tests in over 14,500 rats (Gough 2002). Dose levels were expected to produce tumors in 20 to 80 percent of the exposed animals. The results of that study produced no convincing evidence for synergistic carcinogen interactions while 20 possible cases of antagonism were observed (Gough 2002). In an animal study, Takayama et al. (1989) reported that 40 substances tested in combination at 1/50 of their CELs resulted in an increase in cancer. However, Hasegawa et al. (1994) reported no increase in cancer when dosing animals at 1/100 of the CELs for 10 compounds. It should be noted that typical environmental

exposures to chemicals (noncarcinogens and carcinogens) are more than 1,000 times below laboratory-induced health effect thresholds.

IV.D. Pregnant and Breast-Feeding Women's Health Considerations

Woman and infants can sometimes be affected differently from the general population by chemicals in the environment. The effect of hormonal variations, pregnancy, and lactation can change the way a woman's body responds to some chemicals. Past exposures experienced by the mother, as well as exposure during pregnancy and breast-feeding, can expose a fetus or infant to chemicals through the placenta or breast milk. Depending on the stage of pregnancy, the nature of the chemical involved, and the dose of that chemical, fetal exposure can result in a variety of problems, including miscarriage, still birth, and birth defects.

Based on the evaluation in Section IV.C., ATSDR does not expect pregnant and breast-feeding women to experience adverse effects from exposures to site-related chemicals in soil, sediment, surface water, biota (other than fish), and air.

Due to limited sampling data, dioxins in fish pose an indeterminate health hazard. Therefore, it would be prudent public health practice for pregnant and breast-feeding women to limit their consumption of locally caught fish. Although fish are a healthy food that provide many nutritional benefits, it is unknown whether the potential risks of exposure to dioxin contamination outweigh the benefits of eating fish.

Due to the levels of PCBs, the State of Tennessee advises pregnant women and nursing mothers to not eat catfish, striped bass, hybrid bass (striped bass–white bass), white bass, sauger, carp, smallmouth buffalo, and largemouth bass from the Tennessee River or striped bass, catfish, and sauger from the Clinch River.

V. Health Outcome Data Evaluation

Health outcome data are measures of disease occurrence in a population. Common sources of health outcome data are existing databases (cancer registries, birth defects registries, and death certificates) that measure morbidity (disease) or mortality (death). Health outcome data can provide information on the general health status of a community—where, when, and what types of diseases occur and to whom they occur. Public health officials use health outcome data to look for unusual patterns or trends in disease occurrence by comparing disease occurrences in different populations over periods of years. These health outcome data evaluations are descriptive epidemiologic analyses. They are exploratory in that they provide additional information about human health effects and they are useful in that they help identify the need for public health intervention activities (for example, community health education). That said, however, health outcome data cannot—and are not meant to—establish cause and effect between environmental exposures to hazardous materials and adverse health effects in a community.

ATSDR scientists generally consider health outcome data evaluation when a plausible, reasonable expectation emerges of adverse health effects associated with the observed levels of exposure to contaminants. In this PHA, ATSDR scientists determined that current and future exposures to ORR site-related chemicals (individually or in combination) in soil, sediment, surface water, biota (other than fish), and air do not pose a public health hazard. Very limited "dioxin" data exist for fish; therefore, exposure to dioxins in fish poses an indeterminate public health hazard.

Criteria for Conducting a Health Outcome Data Evaluation

To determine how to use or analyze health outcome data in the public health assessment process, or even whether to use the data at all, ATSDR scientists receive input from epidemiologists, toxicologists, environmental scientists, and community involvement specialists. These scientists consider the following criteria, based only on site-specific exposure considerations, to determine whether a health outcome data evaluation should be included in the PHA.

1. Is there at least one current (or past) potential or completed exposure pathway at the site?
2. Can the time period of exposure be determined?
3. Can the population that was or is being exposed be quantified?
4. Are the estimated exposure doses(s) and the duration(s) of exposure sufficient for a plausible, reasonable expectation of health effects?
5. Are health outcome data available at a geographic level or with enough specificity to be correlated to the exposed population?
6. Do the validated data sources or databases have information on the specific health outcome(s) or disease(s) of interest—for example, are the outcome(s) or disease(s) likely to occur from exposure to the site contaminants—and are those data accessible?

Using the findings of the exposure evaluation in this PHA, ATSDR sufficiently documented completed exposure pathways. However, current and future exposures to ORR site-related

chemicals in soil, sediment, surface water, biota, and air do not pose a public health hazard. Because the estimated doses are not expected to cause health effects, no further analysis of health outcome data is appropriate. Analysis of site-related health outcome data is not scientifically reasonable unless the level of estimated exposure is likely to result in an observable number of health effects. And because such an estimate of exposure is not feasible, the requirement to consider analysis of site-related health outcome data on the basis of exposure is fulfilled.