DETERMINATION OF ACCEPTABLE RISK-BASED CONCENTRATIONS OF BTEX IN CATTLE'S DRINKING WATER

Julie A. Stickney[1], Michael M. Gates[2], Eric M. Rainey[2], and
Christopher H. Day[3], ARCADIS G&M
Portland, ME[1], Tulsa, OK[2], Houston, TX[3]

ABSTRACT

In many rural areas of the United States crude oil is produced and transported on and across land used by domestic cattle for grazing. Crude oil released to the environment can sometimes introduce dissolved petroleum hydrocarbons to surface water and groundwater. Known for their solubility, toxicity, and mobility in the environment, benzene, toluene, ethylbenzene, and xylene (BTEX) are petroleum constituents that are typically used as benchmarks for establishing risk-based cleanup criteria. While there is some technical literature available regarding the exposure of cattle to crude oil, these studies are not appropriate for the determination of health-based concentrations (HBCs) of BTEX constituents in cattle's drinking water. This paper evaluates circumstances through which cattle can become exposed to BTEX. An evaluation was performed to estimate acceptable risk-based concentrations of BTEX in cattle's drinking water. The approach used consists of two basic steps: 1) derivation of toxicological benchmarks for BTEX constituents in cattle that represent the acceptable daily intakes for each chemical, and 2) use of specific exposure assumptions for cattle to calculate acceptable drinking water concentrations. Weaning age calves were included in the evaluation to represent a potentially sensitive subpopulation.

INTRODUCTION

Crude oil releases can occur on the land surface at production or transportation facilities as a result of transfer activities and equipment failure. Crude oil may also be released directly into the subsurface from failures of pipelines and storage tanks. The crude oil or petroleum hydrocarbon constituents partitioned from the crude oil can exist in the subsurface as a separate liquid phase, as a vapor, adsorbed to the soil, or dissolved into the water environment. Examples of the more toxic and mobile of these constituents include BTEX which are present in varying amounts in crude oils.

In general, the presence of BTEX in the dissolved phase results from contact between water and the crude oil. Due to the relatively high solubility of BTEX, these constituents tend to dissolve rather easily and have a higher degree of mobility than many other petroleum hydrocarbons present in the crude oil. Contact between a crude oil release and the water environment (i.e., surface and groundwater) can occur in several ways including 1) direct contact between the oil and groundwater or surface water (i.e., ponds, streams, etc.); 2) infiltration of water through unsaturated soils containing residual oil; and 3) flow of water past residual oil present at or below the groundwater table. The resulting concentration of BTEX constituents in the water will be dependent on the concentrations occurring in the oil, contact times, attenuation activity, and other factors. Typically BTEX concentrations dissolved in groundwater will be higher near the source oil and will decrease with distance and time as available mass is attenuated through natural processes. BTEX will generally dissipate rapidly in surface water due to aeration.

Cattle may be exposed to BTEX by ingestion of surface water or groundwater in areas where a crude oil release has occurred. This study was performed in order to determine acceptable risk-based concentrations of BTEX in cattle's drinking water. HBCs were calculated as safe drinking water concentrations by combining estimates of BTEX toxicity in cattle with assumptions regarding drinking water exposure. The calculated HBCs for BTEX compounds can then be compared to groundwater and surface water concentrations at release sites to estimate potential health risks to livestock.

The approach used to develop the livestock HBCs for BTEX compounds is consistent with the U.S. Environmental Protection Agency's (USEPA's) *Ecological Risk Assessment Guidance for Superfund: Process for Designing and Conducting Ecological Risk Assessments* (USEPA, 1997) and *Risk Assessment Guidance for Superfund* (USEPA, 1989; 1991). The HBC methodology involves two basic steps; 1) derivation of toxicological benchmarks for BTEX compounds in cattle that represent the safe daily intakes for each chemical, and 2) use of specific exposure assumptions for cattle to calculate safe drinking water concentrations.

Toxicological benchmarks were derived from summary sources of mammalian toxicology data, including: *Toxicological Benchmarks for Wildlife* (Sample et al., 1996), toxicological profiles published by the Agency for Toxic Substances and Disease Registry (ATSDR, 1997) and data from the USEPA's Integrated Risk Information System Database (IRIS, 1999). The specific exposure assumptions for livestock (e.g., drinking water ingestion rate, body

weight) for an adult cow and a weaning-age calf were derived from the National Research Council's (NRC's) *Nutrient Requirements of Beef Cattle* (NRC, 1996) and personal communication with cattle specialists at the Oklahoma State University's Cooperative Extension Service (Lalman, 1998). The weaning-age calf was included in the evaluation to represent a potentially sensitive subpopulation.

TOXICOLOGICAL BENCHMARKS

Literature Review and Data Evaluation

A toxicological benchmark is an estimate of the dose of a constituent at which no adverse health effects are anticipated to occur. A comprehensive literature search was performed and it was determined that no toxicity data specific to cattle were available for the individual BTEX constituents. Some information was available for cattle exposed to crude oil (Rowe et al., 1973; Alberta Environmental Centre, 1996; Ryer-Powder, et al., 1996; CCME, 2000); however these toxicity data were not appropriate for the determination of drinking water HBCs for BTEX constituents. Rowe et al. (1973) performed a study where large volumes (3 to 10 liters) of crude oil were administered to young cattle through a stomach tube as either a single dose or daily for 5 days. In addition, 1 to 2 liters of crude oil were administered via stomach tube to young cattle for 14 consecutive days. The most serious result of crude oil administration was aspiration pneumonia caused by vomiting the ingested crude oil. Rowe et al., (1973) concluded that the toxicity of a particular crude oil should be determined primarily by its aspiration hazard and the irritant activity in pulmonary tissues. This study does not contain useful information for evaluating risks to cattle exposed to concentrations of BTEX constituents dissolved in drinking water. The study demonstrated that ingestion of large volumes of free crude oil product results in vomiting and aspiration into the lung and that subsequent toxicity is related to the physical properties of oil and their interaction with pulmonary tissues (i.e., irritation of lung tissue followed by infection). Ingestion of dissolved concentrations of BTEX constituents in water would not induce vomiting in cattle and therefore pulmonary toxicity is unlikely to occur.

A report from the Alberta Environmental Centre (1996) presents a literature review pertaining to the interaction of cattle and petroleum industries. The authors of this report could not determine if there is a risk to cattle from aromatic hydrocarbons, including BTEX compounds. The Canadian Council of Ministers of the Environment also provided a more recent review of crude oil studies in cattle (CCME, 2000). The Canadian reports each propose guidelines for weathered crude oil in cattle drinking water, however calculation errors are evident in both reports. Corrected guideline values from these reports range between 370 and 850 milligrams per liter (mg/L) of total petroleum hydrocarbons (TPH) as weathered crude oil in cattle drinking water. The toxicity endpoints used in the Canadian reports relate to acute effects of crude oil ingestion in cattle, and therefore cannot be used to determine safe concentrations of BTEX compounds dissolved in water.

Ryer-Powder et al. (1996) employed an alternative approach to derive a safe level of TPH as crude oil in cattle drinking water. These authors determined that sufficient toxicity data are not available for oral crude oil exposure in cattle. Therefore, long-term studies in mice were used as the basis for calculation of safe TPH levels in cattle drinking water. A toxicological benchmark

for cattle was based on organ weight changes observed in a chronic dermal study of crude oil administration to mice. The concentration of TPH as crude oil in water considered to be protective of cattle health was 335 mg/L. This paper provides useful information for evaluating the crude oil mixture as TPH in cattle drinking water, but does not provide specific information regarding BTEX constituents.

Because no toxicity information was available for BTEX constituents in cattle, toxicological benchmarks for an adult cow and a weaning-age calf were extrapolated from other mammalian species. Toxicity information presented in summary data sources (ATSDR, 1997; IRIS, 1999; Sample et al., 1996) was reviewed to determine the most appropriate no observed adverse effect level (NOAEL) in a phylogenetically related species. Scaling and uncertainty factors were then applied to calculate the toxicological benchmarks for cattle. Table 1 presents a summary of the mammalian toxicological data considered in this assessment. Oral toxicity data are available for each of the BTEX constituents for a variety of toxic endpoints. The health effects of concern include hematological effects, neurological effects, and liver and kidney toxicity. Reproductive and developmental effects are also reported, but generally occur at higher doses than those reported for other health effects.

Identification of Critical Toxicological Studies

Summary sources of mammalian toxicological data were reviewed in order to choose a critical study as the basis of the toxicological benchmark for each BTEX compound (ATSDR, 1997; IRIS, 1999; Sample et al., 1996). The choice of a critical study is based on the study duration, the dose levels and associated toxicological effects, and the quality of the study (i.e., appropriate methodology, number of animals used etc.). Chronic duration studies are those that are carried out for the majority of the test species lifespan, generally longer than 1 year for mammals. Additionally, studies in which the test organism is dosed during a critical life-stage, such as gestation or early development, are grouped with chronic duration studies (see Table 1). Acute studies typically have exposures of less than two weeks and subchronic studies are studies of intermediate exposure duration (i.e., between 2 weeks and 1 year for mammalian toxicology studies). Chronic duration studies are preferred for development of toxicological benchmarks. However, in cases where chronic exposure data are unavailable, subchronic data can be used in conjunction with a duration specific uncertainty factor (UF) to derive a benchmark value (see UF discussion below). USEPA has previously performed a comprehensive review of the literature and picked a critical study for their oral reference dose (RfD) assessments for ethylbenzene, toluene, and xylenes (IRIS, 1999). The critical studies presented in IRIS (1999) as the basis for chronic oral RfD values, were also selected as the critical studies in determining toxicological benchmarks for cattle.

The critical study selected for benzene is a chronic oral gavage study in rats that showed decreased numbers of red and white blood cells (RBCs, WBCs) after 84 weeks of benzene administration and decreased body weight measurements at 92 weeks (ATSDR, 1997; Maltoni et al., 1983). Hematotoxicity is a well-established clinical effect of benzene toxicity and is therefore an appropriate toxicological endpoint for deriving a benchmark value. This is supported by the USEPA's recent presentation of an inhalation reference concentration (RfC) for benzene that is based on hematological effects (i.e., lymphocyte count) (Jinot et al., 2001). The authors of the oral gavage study considered the hematotoxic dose employed in this study to represent a "slightly toxic" dose as compared to other data reported in the literature (Maltoni et al., 1983). Table 1

illustrates that the reproductive and developmental effects of benzene occur at higher doses than that shown to produce hematotoxicity.

The critical study for ethylbenzene was identified by USEPA as a 182-day oral gavage study that demonstrated liver and kidney toxicity in rats at high doses (IRIS, 1999). Other criteria used in judging toxic effects in study animals were growth, mortality, appearance, behavior, hematologic and clinical chemistry findings, organ and body weights, and histopathological findings.

For toluene, the USEPA presents a subchronic gavage study in rats as the critical study for toluene, where changes in liver and kidney weights were considered the toxic endpoint of concern (IRIS, 1999). The toxicological significance of these organ weight changes is supported by histopathological changes in both the liver and kidney at higher doses. Toluene has been shown to be embryolethal and teratogenic in mice, however the doses associated with these effects are much higher than the NOAEL observed for liver and kidney effects (IRIS, 1999) (see Table 1).

USEPA has selected a chronic rat gavage study as the critical study for determiniation of the xylene RfD. Hyperactivity, decreased body weight and increased mortality were considered critical effects of xylene toxicity (IRIS, 1999). USEPA indicates that xylene is fetotoxic and teratogenic in mice at high oral doses, but the critical study chosen as the basis of the RfD is protective of these effects (IRIS, 1999). The critical studies for each of the BTEX compounds are shaded in gray on Table 1.

Application of Uncertainty Factors (UFs)

Toxicological benchmark values are based on either the NOAEL dose in the critical study or the lowest dose shown to produce an adverse effect (LOAEL). In deriving benchmark values for cattle, two types of UFs were applied. The first UF is used when a LOAEL dose forms the basis of the toxicity value (i.e., LOAEL-to-NOAEL UF). The second UF is used when the critical study is of less than chronic exposure duration (i.e., duration specific UF). An UF of 10 is generally applied to extrapolate from a LOAEL dose to derive a test species NOAEL (USEPA, 1989; Sample et al. 1996). Duration specific UFs are based on an evaluation of available data on the ratios of acute and subchronic NOAELs to chronic NOAELs (McNamara, 1976; USEPA, 1996b; Weil and McAllister, 1963). A subchronic-to-chronic UF of 3 and an acute to chronic UF of 8 are considered appropriate based on this analysis.

The test species NOAEL values presented in Tables 2 and 3 are based on experimental studies using laboratory rats. Because a NOAEL was not available for benzene, a 10-fold UF was applied to account for use of a chronic LOAEL value. In addition, an adjustment was made to derive a daily dose from the 5 day/week dosing schedule used in the critical study (dose x 5/7 days/week). The subchronic NOAEL values for ethylbenzene and toluene were divided by a UF of 3 to derive chronic NOAELs. No UFs were applied to the experimental value for xylene because the data represents a chronic NOAEL value.

Interspecies Scaling

A scaling factor was applied to account for differences in metabolism and toxicity experienced by cattle and rats. The scaling factor accounts for differences in body size between the laboratory test species and the receptor species (in this case cattle) (Travis and White, 1988; Travis et al., 1990; and USEPA, 1992). This method of interspecies scaling is common practice in both human health and ecological risk assessment (USEPA, 1996c; USEPA, 1997). In fact, the cross-species scaling method used in this analysis was proposed by USEPA, the Food and Drug Administration (FDA), and the Consumer Products Safety Commission (CPSC) as a consensus approach for risk assessment of carcinogens (USEPA, 1992). Pharmacokinetic data have revealed that larger animals exhibit slower metabolic and clearance rates, which give rise to longer biological half-lives for chemicals in the body and higher tissue concentrations per given dose. Metabolism and clearance rates vary in a predictable way from one mammal to another obeying an allometric equation with an exponent of 0.25 (Chappell, 1992). Therefore, species differences in metabolism and toxicity among different mammals can be predicted by the allometric equation based on differences in body weight. Chappell (1992) indicates that allometric scaling is appropriate for explaining differences in the toxic response of cattle and sheep to chemical toxicants.

The interspecies scaling factor is based on the body weight differences between rats and cattle. The following allometric equation was used for interspecies scaling:

$$\text{Scaling Factor} = (BW_t/BW_c)^{1/4}$$

where:

Bw_t = Body weight of test species
(0.35 kg rat, Sample, 1996)

BW_c = Body weight of target livestock
(408 kg cow, 236 kg calf, NRC, 1996; Lalman, 1998)

The scaling factors calculated for the adult cow and the weaning age calf were 0.17 and 0.2, respectively. Multiplying these scaling factors by the test species NOAEL values yields the toxicological benchmarks for BTEX compounds in the adult cow (Table 2) and the weaning age calf (Table 3).

HBCs FOR CATTLE

HBCs for cattle were calculated to represent BTEX concentrations in drinking water that would present no risk. HBCs were calculated using exposure parameters for cattle and the estimated toxicological benchmarks. The following equation was used to calculate drinking water HBCs for cattle:

$$HBC_{water} = \frac{TB \times BW}{IR_{water}}$$

where:

HBC_{water}	=	Health-based concentration for drinking water (mg/L);
TB	=	Toxicological benchmark (mg/kg/day);
BW	=	Body weight (kg); and
IR_{water}	=	Ingestion rate of water (L/day).

The representative body weights and water ingestion rates for an adult lactating cow and weaning-age calf were obtained from the document entitled *Nutrient Requirements of Beef Cattle* (NRC, 1996) and from an Extension Beef Cattle Specialist at Oklahoma State University (Lalman, 1998). The average weight of a lactating cow and a weaning age calf in Oklahoma is 408 kg (900 lbs) and 236 kg (521 lbs), respectively (NRC, 1996; Lalman, 1998). The average water ingestion rate (at 80° F) of a lactating cow and weaning-age calf in Oklahoma is 68 L/day (18 gal/day) and 38 L/day (10 gal/day), respectively (NRC, 1996; Lalman, 1998). It is important to note that alternative exposure assumptions may be necessary in some cases; for example, when dairy cattle are considered the receptor of greatest concern.

The calculated HBCs for an adult cow are presented in Table 4, and range from 33 mg/L for ethylbenzene to 183 mg/L for xylenes. The calculated HBCs for a weaning-age calf are presented in Table 5, and range from 40 mg/L for ethylbenzene to 222 mg/L for xylenes. These values can be compared to maximum BTEX concentrations measured in groundwater and surface water at a release site. If site BTEX levels do not exceed calculated HBCs, the BTEX concentrations detected in the groundwater and surface water are not expected to pose a risk to adult or weaning-age livestock. It is most appropriate to compare HBCs to long-term average concentrations in drinking water. This would avoid the overly conservative assumption that a single animal would be exposed to the maximum possible concentration on a daily basis**.**

REFERENCES

Alberta Environmental Centre. 1996. *Cattle and the Oil and Gas Industry in Alberta: A Literature Review with Recommendations for Environmental Management.* Alberta Cattle Commission, Calgary, Alberta. July.

ATSDR. 1997. *Toxicological Profiles for Benzene, Ethylbenzene, Toluene, and Xylenes*. Agency for Toxic Substances and Disease Registry, Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA.

CCME. 2000. *Canada-Wide Standards for Petroleum Hydrocarbons (PHCs) in Soil: Scientific Rationale, Supporting Technical Document*. Canadian Council of Ministers of the Environment. December 2000.

Chappell, W.R. 1992. Scaling toxicity data across species. *Environ. Geochem. Health.* 14(3):71-80.

IRIS. 1999. Integrated Risk Information System. U.S. Environmental Protection Agency, Substance files for benzene, toluene, ethylbenzene, and xylene.

Jinot et al., 2001. Benchmark dose modeling of hematological effects associated with exposure to benzene. *Toxicol. Sci. Suppl.The Toxicologist.* 60(1):2089.

Lalman, D. 1998. Personal communication via telephone between Dr. David Lalman (Extension Beef Cattle Specialist, Oklahoma State University, Stillwater, Oklahoma) and Cynthia Murray (ARCADIS Geraghty & Miller, Houston, Texas), August 25, 1998.

Maltoni, C., B. Conti and G. Cotti. 1983. Benzene: A multipotential carcinogen: Results of long-term bioassays performed at the Bologna Institute of Oncology. *Am. J. Ind. Med.* 4:589-630.

McNamara, B.P. 1976. Concepts in Health Evaluation of Commercial and Industrial Chemicals. In: M.A. Mehlman et al., eds., *Advances in Modern Toxicology, Volume 1, Part 1: New Concepts in Safety Evaluation.* John Wiley & Sons, New York, NY.

NRC. 1996. *Nutrient Requirements of Beef Cattle, Seventh Revised Edition*. National Research Council.

Rowe, L.D., J.W. Dollahite and B.J. Camp. 1973. Toxicity of two crude oils and of kerosene to cattle. *J. Amer. Vet. Med. Assoc.* 162(1):61-66.

Ryer-Powder, J., R. Scofield, A. Lapierre, and C.E. Lambert. 1996. Determination of safe levels of total petroleum hydrocarbons as crude oil in cattle's drinking water and in meat from cattle. *Petroleum Hydrocarbons and Organic Chemicals in Ground Water: Prevention, Detection, and Restoration.* Conference Proceedings, Houston, TX.

Sample, B.E., D.M. Opresko and G.W. Suter, II. 1996. Toxicological Benchmarks for Wildlife: 1996 Revision. Health Sciences Research Division, Oak Ridge National Laboratory, Oak Ridge, TN. ES/ER/TM-86/R3.

Travis, C.C. and R.K. White. 1988. Interspecific Scaling of Toxicity Data. *Risk Anal.* 8:119-125.

Travis, C.C., R.K. White and R.C. Wards. 1990. Interspecies Extrapolation of Pharmacokinetics. *J. Theor. Biol.* 142:285-304.

USEPA. 1989. Risk Assessment Guidance for Superfund, Volume 1, Human Health Evaluation Manual (Part A), Interim Final. U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. EPA/540/1-89/002, December.

USEPA. 1991. Risk Assessment Guidance for Superfund, Volume 1, Human Health Evaluation Manual (Part B, Development of Risk-based Preliminary Remediation Goals), Interim. U.S. Environmental Protection Agency, Office of Research and Development. EPA/540/R-92/003, December.

USEPA. 1992. Draft Report: A Cross-Species Scaling Factor for Carcinogen Risk Assessment Based on Equivalence of $mg/kg^{3/4}$/day. U.S. Environmental Protection Agency. *Federal Register*, 57(109):24152-24173.

USEPA. 1996a. Soil Screening Guidance: Technical Background Document. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. EPA/540/R-95/128.

USEPA. 1996b. *Review and Analysis of Toxicity Data to Support the Development of Uncertainty Factors for Use in Estimating Risks of Contaminant Stressors to Wildlife.* U.S. Environmental Protection Agency, Office of Water, Washington, D.C.

USEPA. 1996c. *Proposed Guidelines for Carcinogen Risk Assessment*. U.S. Environmental Protection Agency, Office of Research and Development. EPA/600/P-92/003C. April.

USEPA. 1997. Ecological Risk Assessment Guidance for Superfund: Process for Designing and Conducting Ecological Risk Assessments, Interim Final. U.S. Environmental Protection Agency, Office of Solid Waste and Emergency Response. EPA 540-R-97-006, June.

Weil, C.S. and D.D. McAllister. 1963. Relationship between short- and long-term feeding studies in designing an effective toxicity test. *Agricul. Food Chem.* 11;486-491.

Table 1. Summary of Oral Toxicity Data for Benzene, Ethylbenzene, Toluene and Xylene

Study Duration	Endpoint	Compound	Species	Duration	Result	Summary Data Source
Acute	Neurological	Benzene	Rat	1 day	LOAEL 88 mg/kg/day (neuro); LOAEL 1870 mg/kg/day (neuro)	ATSDR, 1997
Chronic	Reproductive	Benzene	Rat	gd 6-15	NOAEL 1000 mg/kg/day	ATSDR, 1997
Chronic	Developmental	Benzene	Rat	gd 6-15	NOAEL 1000 mg/kg/day	ATSDR, 1997
Chronic	Developmental	Benzene	Mouse	gd 8-12	LOAEL 1300 mg/kg/day (decreased fetal weight)	ATSDR, 1997
Chronic	Reproductive	Benzene	Mouse	gd 6-12	LOAEL 780 mg/kg/day	IRIS, 1999
Chronic	Systemic	Benzene	Rat	92wks; 4-5d/wk	LOAEL 500 mg/kg/day (hemato 84 weeks); (bd wt 92 wks)	ATSDR, 1997
Subchronic	Systemic	Ethylbenzene	Rat	6mo; 5d/wk	NOAEL 97.1 mg/kg/day (hepatic/renal)	IRIS, 1999
Subchronic	Systemic	Toluene	Rat	13wk; 5d/wk	NOAEL 223 mg/kg/day (hepatic/renal)	IRIS, 1999
Subchronic	Systemic	Toluene	Rat	6mo; 5d/wk	NOAEL 590 mg/kg/day (hemato); NOAEL 590 mg/kg/day (hepatic); NOAEL 590 mg/kg/day (renal)	ATSDR, 1997
Subchronic	Systemic	Toluene	Mouse	13wk; 5d/wk	NOAEL 2500 mg/kg/day (cardio); NOAEL 2500 mg/kg/day (hemato); LOAEL 312 mg/kg/day (hepatic); NOAEL 2500 mg/kg/day (renal)	ATSDR, 1997
Subchronic	Neurological	Toluene	Rat	13wk; 5d/wk	NOAEL 625 mg/kg/day	ATSDR, 1997
Subchronic	Neurological	Toluene	Mouse	13wk; 5d/wk	NOAEL 625 mg/kg/day	ATSDR, 1997
Chronic	Reproductive	Toluene	Mouse	gd 6-12	LOAEL 780 mg/kg/day	IRIS, 1999

Table 1. Summary of Oral Toxicity Data for Benzene, Ethylbenzene, Toluene and Xylene

Study Duration	Endpoint	Compound	Species	Duration	Result	Summary Data Source
Chronic	Developmental	Xylene	Mouse	gd 6-15	NOAEL 1,030 mg/kg/day	ATSDR, 1997
Chronic	Systemic	Xylene (mix)	Rat	103wk; 5d/wk	NOAEL 179 mg/kg/day (neuro, bd wt, mortality)	IRIS, 1999
Chronic	Systemic	Xylene (mix)	Mouse	103wk; 5d/wk	NOAEL 1000 mg/kg/day (cardio, gastro, hemato, mus/skel, hepatic, renal, dermal, ocular, bd wt)	ATSDR, 1997
Chronic	Neurological	Xylene (mix)	Rat	103wk; 5d/wk	NOAEL 500 mg/kg/day	ATSDR, 1997
Chronic	Reproductive	Xylene (mix)	Rat	103wk; 5d/wk	NOAEL 500 mg/kg/day	ATSDR, 1997
Chronic	Reproductive	Xylene (mix)	Mouse	103wk; 5d/wk	NOAEL 1000 mg/kg/day	ATSDR, 1997

Notes:

gd	gestation days
wk(s)	week(s)
mo	months
d/wk	days per week
NOAEL	no observed adverse effects level
LOAEL	lowest observed adverse effects level
mg/kg/day	milligrams per kilograms per day.
cardio	cardiovascular effects
gastro	gastrointestinal effects
hemato	hematological effects
mus/skel	musculoskeletal effects
neuro	neurological effects
bd wt	body weight changes

Table 2. Toxicological Benchmark Values for an Adult Lactating Cow.

Constituent	Test Species	Experimental Value (mg/kg/day)		Test Species NOAEL (mg/kg/day)		Toxicological Endpoint	Summary Data Source	Scaling Factor [f]	Toxicological Benchmark for Cow (mg/kg/day) [g]
Benzene	Rat	500	[a]	35.7	[d]	Hematological	ATSDR, 1997	0.17	6.1
Ethylbenzene	Rat	97.1	[b]	32.4	[e]	Hepatic/Renal	IRIS, 1999	0.17	5.5
Toluene	Rat	223	[b]	74.3	[e]	Hepatic/Renal	IRIS, 1999	0.17	12.6
Xylene	Rat	179	[c]	179		Neurological	IRIS, 1999	0.17	30.4

Notes:

[a]	chronic LOAEL
[b]	subchronic NOAEL
[c]	chronic NOAEL
[d]	chronic NOAEL = (chronic LOAEL/LOAEL-to-NOAEL UF of 10) x 5/7 days/wk (see text)
[e]	chronic NOAEL = subchronic NOAEL/duration specific UF of 3 (see text)
[f]	see text for derivation of scaling factor
[g]	toxicological benchmark value = test Species NOAEL x scaling factor (see text)
mg/kg/day	milligrams per kilogram per day
LOAEL	lowest observed adverse effect level
NOAEL	no observed adverse effect level

Table 3. Toxicological Benchmark Values for Weaning-Age Calf.

Constituent	Test Species	Experimental Value (mg/kg/day)		Test Species NOAEL (mg/kg/day)		Measurement Endpoint	Summary Data Source	Scaling Factor [f]	Toxicological Benchmark for Cow (mg/kg/day) [g]
Benzene	Rat	500	[a]	35.7	[d]	Hematological	ATSDR, 1997	0.20	7.1
Ethylbenzene	Rat	97.1	[b]	32.4	[e]	Hepatic/Renal	IRIS, 1999	0.20	6.5
Toluene	Rat	223	[b]	74.3	[e]	Hepatic/Renal	IRIS, 1999	0.20	14.9
Xylene	Rat	179	[c]	179		Neurological	IRIS, 1999	0.20	35.8

Notes:

[a]	chronic LOAEL
[b]	subchronic NOAEL
[c]	chronic NOAEL
[d]	chronic NOAEL = (chronic LOAEL/LOAEL-to-NOAEL UF of 10) x 5/7 days/wk (see text)
[e]	chronic NOAEL = subchronic NOAEL/duration specific UF of 3 (see text)
[f]	see text for derivation of scaling factor
[g]	toxicological benchmark value = test Species NOAEL x scaling factor (see text)
mg/kg/day	milligrams per kilogram per day
LOAEL	lowest observed adverse effect level
NOAEL	no observed adverse effect level

Table 4. Health-Based Concentrations (HBCs) for Ingestion of Water, Adult Cow.

Constituent	Toxicological Benchmark[a] (mg/kg/day)	Body Weight[b] (kg)	Water Ingestion Rate[c] (L/day)	HBC[d] (mg/L)
Benzene	6.1	408	68	36
Ethylbenzene	5.5	408	68	33
Toluene	12.6	408	68	76
Xylene	30.4	408	68	183

Notes:

[a]	
[b]	average weight of an adult lactating cow (NRC, 1996)
[c]	average ingestion rate of water for a lactating cow at 80 F (NRC, 1996)
[d]	HBC (mg/L) = (toxicological benchmark x body weight)/water ingestion rate
mg/kg/day	milligrams per kilogram per day
L/day	liters per day
kg	kilograms
mg/L	milligrams per liter

Table 5. Health-Based Concentrations (HBCs) for Ingestion of Water, Weaning-Age Calf.

Constituent	Toxicological Benchmark[a] (mg/kg/day)	Body Weight[b] (kg)	Water Ingestion Rate[c] (L/day)	HBC[d] (mg/L)
Benzene	7.1	236	38	44
Ethylbenzene	6.5	236	38	40
Toluene	14.9	236	38	92
Xylene	35.8	236	38	222

Notes:

[a]	toxicological benchmark for weaning-age calf (from Table E3)
[b]	average weight of a weaning-age calf (NRC, 1996)
[c]	average ingestion rate of water for a weaning-age calf at 80 F (NRC, 1996)
[d]	HBC (mg/L) = (toxicological benchmark x body weight)/water ingestion rate
mg/kg/day	milligrams per kilogram per day
L/day	liters per day
kg	kilograms
mg/L	milligrams per liter