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Exposures and Internal Doses of Trihalomethanes in Humans: Multi-Route Contributions from Drinking Water

National Center for Environmental Assessment
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NOTICE

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ABSTRACT

The concentrations of the four commonly-identified trihalomethanes (THM; chloroform, bromodichloromethane, chlorodibromomethane and bromoform) in U.S. drinking water systems are regulated as a group. This report develops, applies and communicates a method to estimate internal exposures to these simultaneously-exposed chemicals. Because they are present in water used for drinking, bathing and other household uses, and because they are highly volatile, this work evaluated the development of internal doses via the oral, dermal and inhalation routes following residential exposures. This was accomplished by integrating several data sets that characterize human activity patterns, water use behavior, household volumes and ventilation, and THM concentration in drinking water. Physiologically based pharmacokinetic modeling was used to translate external exposures to internal doses for the simulated adult male and female and the 6-year-old child. Results indicated that inhalation exposures predominated and that children developed higher internal doses (mg/kg body weight) than adults in the same household. This report demonstrates the technical feasibility of combining stochastic and deterministic models and modeling approaches with "real-world" concentrations of drinking water contaminants (here, THMs) to estimate internal doses for risk evaluation and for the examination of toxicokinetic interactions among mixtures of chemicals.

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LIST OF ABBREVIATIONS

ACH	Air exchange rate
AUC	Area under the curve
BDCM	Bromodichloromethane
CM_{24}	Concentration of metabolites produced in the liver over 24 hours
CMFM	Completely mixed flow model
CSFII	Continuing Survey of Food Intake by Individuals
CYP2E1	Cytochrome P450 2E1
DBCM	Dibromochloromethane
DBPs	Disinfection byproducts
gpm	Gallons per minute
ICR	Information Collection Rule
$K_{OL}A$	Overall mass transfer coefficient
Kp	Permeability coefficient of stratum corneum
MCL	Maximum contaminant level
NHAPS	National Human Activity Patters Survey
NIST	National Institute of Standards and Technology
PBPK	Physiologically based pharmacokinetic
REUWS	Residential End Use Water Survey
RECS	Residential Energy Consumption Survey
PFM	Plug flow model
PFT	Perfluorocarbon tracer
PID	Potential inhalation dose
ROH	Rest-of-House
TCE	Trichloroethylene
TEM	Total Exposure Model
THM	Trihalomethane
TTHM	Total trihalomethane
USDA	U.S. Department of Agriculture
VOCs	Volatile organic compounds

PREFACE

This report was prepared by NCEA's Cincinnati Division to support considerations undertaken by the Office of Water, and other bodies who are concerned with the transition of drinking water contaminants from finished drinking water to tissues and organs within the body. It is a research project, aimed at demonstrating the feasibility of linking several complex data sets through computer-based modeling to estimate internal doses of four concurrently-exposed trihalomethanes compounds. The outcome was successful, in that external concentrations were transformed to internal target issue doses. Health Canada bases acceptable drinking water contaminant levels, taking into account exposure by all routes based, where possible, on extrapolation from internal dose metrics. Should the U.S. EPA consider such a concept, the present report demonstrates its technical feasibility, and it identifies some research needs that would increase the confidence in predicted internal exposures for these compounds. The activities supporting this work were initiated in 2003. Internal review of draft report was completed in 2005. A formal peer panel review was conducted in June 2005. Subsequent to revisions reflecting internal and external peer review comments, a final draft was developed in May 2006.

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EXECUTIVE SUMMARY

The concentrations of the four commonly-identified trihalomethanes (THM) in U.S. drinking water systems are regulated as a group. These four compounds include chloroform, bromodichloromethane, chlorodibromomethane and bromoform and are common disinfection byproducts. Chloroform is the most well-studied of these compounds; however, this report is concerned with developing, applying and communicating a method to estimate internal exposures, rather than risk, from exposure to these compounds. Each of these compounds is metabolized by the same enzyme, and metabolism of chloroform by this route is responsible for the development of toxicologically-active metabolites. Because of this situation, and because these compounds are metabolized at different rates, it is possible that competition between them for metabolism may increase or decrease risk. The present investigation was undertaken to estimate human internal exposures to these compounds and to ascertain whether the internal concentrations attained in humans exposed to them via drinking water may be anticipated to result in metabolic interactions. Because these compounds are present in water used for drinking, bathing, and other household uses, the present investigation evaluated the development of internal doses via the oral, dermal and inhalation routes. This was accomplished by integrating several data sets.

The goal of this project is to implement comprehensive exposure and PBPK models to estimate population-based exposures and doses to the trihalomethane (THM) species originating in the drinking water. The populations of concern in this project are the following: (a) women of reproductive age (ages 15-45); (b) men of similar age (ages 15-45); and (c) children (age 6). This report presents and identifies the various model parameters needed for running the exposure and PBPK models, specifically those related to chemical volatilization, human activity patterns, ingestion, building characteristics, chemical concentrations in the water supply, tissue partition coefficients, and other physiological characteristics. In this study, information on the frequency and duration of use for the six most common household water uses (showering, bathing, using the clothes washer, dishwasher, toilet and faucet) were studied.

The initial phase of the investigation involved application of a model to estimate “contact” dose. The Total Exposure Model (TEM) was employed to integrate data sets describing (1) human water-use patterns, (2) human household activity patterns, and (3) household ventilation patterns. Drinking water THM concentrations in finished and distributed drinking water have been characterized through activities undertaken in support of the U.S. EPA’s Information Collection Rule (ICR); drinking water concentrations of these disinfection byproducts used in this report were those concentrations estimated at the 95th percentile for the distribution of their concentrations in drinking water, representing a “high-end” concentration (and resulting exposures). These concentration values were taken from an analysis of the information presented in the ICR Database. For this analysis, a computer-based evaluation developed thousands of “typical” water-use behaviors by sampling from publicly-available databases. The water-use behavior parameters needed for TEM have been

developed from the data presented in the National Human Activity Pattern Survey (NHAPS), the Residential End Use Water Study (REUWS), Residential Energy Consumption Survey (RECS), in appliance manufacturer data, and supplemented, as necessary, by best judgment. These behavior parameters were based on the characteristics defined (e.g., age, gender, etc); and water-use activities were superimposed on the sampled activity pattern in accordance with specified characteristics (e.g., frequency and duration of water uses, activities during which the water use activity can occur, etc.).

While oral ingestion relied on concentrations of the THM compounds in drinking water, estimates of contacted doses via the dermal and inhalation routes was not so straightforward. Volatilization of these compounds into indoor air was generated from water-use data employing physico-chemical characteristics obtained from the open literature or predicted according to peer-reviewed methods. Airborne concentrations were modified based on available data describing household volumes and airflow patterns (ventilation). Specified concentrations in areas (rooms or groups of rooms) were combined with data describing human household movements to develop a description of concentrations of compounds in human breathing zones. For dermal exposures, water-use behavior and exposed skin surfaces were combined via physiologically based pharmacokinetic (PBPK) modeling which incorporated measures of dermal penetrability to estimate internalized concentrations of THMs.

The exposure model (TEM) and the PBPK models were integrated such that the relevant parameters were shared on an individual simulation basis. This integration allowed the PBPK model to account for the variations in exposure as a result of individuals' behavior and environment, including accounting for the effects of variations in water-use behavior, concentrations in the water supply, physiological parameters (e.g., breathing rate), location in the home, and building parameters (e.g., ventilation rates).

To estimate internal exposures of these compounds in critical organs and tissues (i.e., liver, kidney, genital tissues), PBPK modeling approaches previously applied to chloroform were adapted. Specific human models were developed to simulate the body characteristics of the adult male and female of child-bearing age as well as the 6 year old child. Human water use and activity patterns for each of these individuals were simulated. For all simulated humans, the estimated absorbed dose from the inhalation route predominates the estimated total exposure, often surpassing the other route-specific exposures (oral, dermal) by ten-fold or more. Results in Tables 65-68 indicate that internal doses were bromoform < dibromochloromethane < bromodichloromethane < chloroform. The present analysis indicated that children absorbed a lower total amount (mg) of these compounds compared to adults, but their absorbed dose (mg/kg) was consistently higher than the absorbed doses in adults. At the 50^{th} percentile for the exposure distributions for each simulated human (exposed to THMs present at their respective 95th percentiles of their distributions) total internal doses resulting from the combined oral, dermal and inhalation exposure routes were below the respective oral Reference Dose (RfD) values for each THM.

With joint, concomitant exposure to these THM compounds, under near-extreme drinking water concentrations, metabolic interaction was not apparent under typical conditions of enzyme expression; when enzyme content was reduced by 10,000-fold, metabolism of the individual THM chemicals was only impacted 20% or less, indicating a low likelihood of metabolic interactions, given present knowledge about the enzyme responsible and its quantitative distribution among humans. These results indicate that the internal dosimetry of these compounds under the anticipated conditions of human exposures is unlikely to be changed under the conditions of a simultaneous exposure to the four-chemical mixture, versus single-chemical exposure.

This report is the second in a series that demonstrates the technical feasibility of combining stochastic and deterministic models and modeling approaches with “real-world” concentrations of drinking water contaminants (see U.S. EPA, 2003). In this report, internal doses of THMs are estimated for risk evaluation and for the examination of toxicokinetic interactions among mixtures of chemicals.

1. PROJECT OVERVIEW AND OBJECTIVES

Disinfection of drinking water is widely recognized for its significant role in reducing illness due to waterborne pathogens that are responsible for numerous diseases. Although disinfection is necessary for the elimination of these pathogenic organisms, it can also lead to the generation of a variety of chemicals, known as disinfection byproducts (DBPs), which are formed as a result of reactions of the disinfectant with organic matter in the water. In the U.S., where the primary form of disinfection is chlorination, public drinking water contains low levels of many DBPs and is a potential source of exposure to these compounds. While the potential for exposure is recognized as significant via the ingestion route, recent attention has also focused on the inhalation and dermal routes of exposure. The importance of each route varies with chemical characteristics, use patterns, physiological characteristics, and a variety of other factors (Wilkes et al., 1996; Olin, 1998). For example, exposure to a volatile drinking water contaminant occurs most significantly during large household water uses, such as showering, bathing, and clothes washing activities. These activities release volatile compounds that may persist in indoor air, prolonging exposures and resultant doses via the inhalation route. Although all three primary exposure routes can be significant, inhalation typically dominates the exposure for these volatile compounds (U.S. EPA, 2003). For the less volatile compounds, ingestion and dermal contact play more significant roles in exposure and uptake. The present work addresses exposure to a mixture of four trihalomethane (THM) compounds via each of these three routes, separately.

Exposure to DBPs originating in the drinking water is a very complex problem, influenced by a multitude of factors, including chemical properties of the contaminant, physical characteristics of the indoor environment, behavior of the individual relative to the contaminant, and behavioral and physiological characteristics of the exposed population. Previous modeling studies have demonstrated the considerable impact human behavior has on an individual's exposure to waterborne contaminants (Wilkes et al., 1996; Wilkes, 1999; U.S. EPA, 2003), demonstrating that differences in behavior can produce exposures varying across more than an order of magnitude. Mathematical

exposure and uptake models represent a realistic, cost-effective means for estimating human exposure. Mathematical models within a probabilistic framework allow a close examination of the factors that lead to exposures and provide a basis for addressing higher risk populations. However, in the case of exposure to waterborne contaminants, previous modeling studies (Wilkes et al., 1996; Wilkes, 1999) have shown that a strictly probabilistic framework would fail to capture the effect of an individual's activities on his or her exposure. The ideal model would therefore combine a probabilistic representation of human behavior related to water use and exposure with a deterministic calculation of the concentrations in the contact media leading to the exposure (i.e., in the water and air). Such modeling frameworks also offer the ability to evaluate the impacts of parameter uncertainty and variability, such that results may be incorporated into meaningful and useful sets of outcomes.

The internal doses resulting from human exposures to chemicals can be quantitated using physiologically based pharmacokinetic (PBPK) models. PBPK models provide a biologically based framework for understanding the absorption, distribution, metabolism and elimination of chemicals ingested by any route. PBPK models are based on known anatomy, physiology and biochemistry, and thus realistically reflect the flux of a chemical through an organism (Clewell and Andersen, 1994). The compartments in PBPK models represent organs or groups of organs of known volume interconnected by blood flows at known rates. Physiological parameters for human PBPK models can be obtained from the literature. Chemical-specific parameters such as tissue partition coefficients and metabolic rates can be measured experimentally or obtained from the literature. Experimental data can be obtained through whole animal or human studies *in vivo* or from experiments with *in vitro* systems. Extrapolation of laboratory animal data to humans is often problematic due to species differences in biotransformation and other pharmacokinetic processes. *In vitro* systems such as intact human cells or subcellular fractions can provide quantitative data on human metabolic rates and interindividual differences in those rates (Kedderis and Lipscomb, 2001). However, the *in vitro* data must be integrated into physiological models to understand the true impact of differences in chemical bioactivation on the target organ concentrations of toxicants.

Exposure models provide estimates of the quantity of chemical that comes into contact with an individual as a result of releases into the environment and individual product uses. Often, these estimated exposures are used to infer a risk to an individual or to a population group. However, many studies have demonstrated that external exposure is not equivalent to internal dose (Kedderis, 1997). For example, exposure to the same external concentration of furan vapors results in considerable differences between the internal dose of furan in mice, rats and humans (Kedderis and Held, 1996). The integration of exposure models with PBPK models provides a powerful method of linking chemical use in the environment to internal tissue doses, both in individuals and populations. Using the results of exposure modeling for a given environment as input to an appropriate PBPK model can provide information on the target organ concentrations of a toxicant and its metabolites in exposed humans. Variations in the exposure scenarios will produce a series of time courses of target organ exposure to toxicants that can be used to derive the relationship between external chemical exposures, human activity patterns and target organ doses of toxicants. These exposure-dose relationships can help assess the importance of various parameters in impacting the target organ dose of toxicants and enable a more rigorous, scientifically based approach to human health risk assessment.

The goal of this project is to implement comprehensive exposure and PBPK models to estimate population-based exposures and doses to the trihalomethane (THM) species originating in the drinking water. The populations of concern in this project are the following: (a) women of reproductive age (ages 15-45); (b) men of similar age (ages 15-45); and (c) children (age 6). This report presents and identifies the various model parameters needed for running the exposure and PBPK models, specifically those related to chemical volatilization, human activity patterns, ingestion, building characteristics, chemical concentrations in the water supply, tissue partition coefficients, and other physiological characteristics. The exposure model being used in this study, the Total Exposure Model (TEM), was used in the previous study (U.S. EPA, 2003) and was developed specifically to accommodate studying population-based exposure to water-borne contaminants. To assess the population doses associated with the resultant exposures, the TEM and PBPK models will be integrated such that the

relevant parameters, predicted time-varying concentrations and exposures are passed between the models.

1.1. OVERVIEW OF EXPOSURE AND PBPK MODEL APPROACH AND LINKAGE

This modeling study integrates exposure and PBPK model algorithms to construct a framework for predicting exposure, uptake and internal distribution of chemicals in humans resulting from exposure to a contaminated water supply. An overview of this approach is illustrated in Figure 1. As illustrated in the figure, the exposure model assembles the critical factors influencing exposures, implements finite difference algorithms to predict air and water concentrations, combines these predicted concentrations with location and physiological characteristics, and estimates the uptake as a result of contact with the contaminated air and water. The outputs from the exposure model, including concentrations in the contact media and uptake as a function of route of exposure, along with relevant physiological parameters are utilized by the PBPK model to predict internal concentrations and doses.

To represent the occupant behavior, TEM samples activity patterns from an activity-pattern database (e.g., National Human Activity Pattern Survey, NHAPS; Survey of Activity Pattern of California Residences, CARB) based on the characteristics defined by the user (e.g., age, gender, etc), and superimposes water-use activities on the sampled activity pattern in accordance with user-entered characteristics (e.g., frequency and duration of water uses, activities during which the water-use activity can occur, etc.).

The physical properties, including the building description, air exchange and ventilation rates, and appliance characteristics are all provided as the setting in which the activities occur. Similarly, the chemical properties, source definition, and water concentrations are defined for the study. Behavior-driven water uses initiate the emissions, which are simulated using the mass-transfer models along with the defined chemical properties.

For each simulation, once the input parameters are selected, a mass-balance model is executed to predict air and water concentrations. Combining these predicted concentrations with the location of the occupant yields an estimated exposure for one representative member of the population group. These simulations are repeated to

compile a distribution of expected exposures to numerous members of the population group.

The outputs from the exposure model are a collection of files, referred to as "transfer" files, which provide time-series of concentration, exposure, and physiological information for each simulation as input to the PBPK model. Using this information along with other physiological parameters, the PBPK model predicts tissue concentrations as a function of time.

1.1.1. Modeling Theory and Numerical Methods. The modeling approach is based on representing the building and physical environment as a collection of well-mixed zones (or air parcels) interconnected by interzonal air flows, Numerous processes may affect the contaminant concentration within these zones, including emissions, transport in and out of the zone, and other removal mechanisms. This approach has been developed and used by many others (Sindent, 1978, Sandberg, 1984, Axley 1989). Setting up this modeling framework results in a set of simultaneous differential equations. For a more complete description of the mathematical basis, see Wilkes, 1994.

TEM uses the fourth-order Runga-Kutta method (Mathews, 1992) for temporal integration of the system of equations. This is an extremely accurate and stable algorithm (errors on the order of Δt^5). The PBPK model is programmed using acslXtreme software (Aegis Technologies, Huntsville, AL).

1.1.2. Simulating Water Uses. TEM simulates water uses as a two-step process: (1) all occurrences of a specified water-use type, and (2) the duration of each water-use event. Using water-use frequency information provided by the modeler, water-use occurrences are simulated as a Poisson process, consistent with the sampled activity pattern as shown schematically in Figure 2. For example, when NHAPS is used to sample activity patterns, the modeler defines specific NHAPS location and activity codes, which are then used by the model to identify time periods during the day when each water-use activity is eligible to occur. The location codes and activity codes provided in NHAPS are given in Tables 1 and 2.

Activity and location code pairs are used to identify eligible water-use periods in the sampled activity pattern. For example, the modeler may specify that periods with an

activity and location code pair of “Personal needs and care – Bathing, etc.” (activity code 40) and “Home Bathroom (location code 104) are eligible for showering; or, if the occupant is in the kitchen, the kitchen faucet water-use activity is eligible to occur. After identifying all eligible periods for a given water use, the mean duration of the water-use is subtracted from the end of each eligible time period to prevent the water use from starting to close to the end of that time period. Then the modified eligible time periods are mapped to a continuous 0 to 1 time scale, as shown in Figure 2.

Subsequently, a Poisson process is used to specify the time between starting times of successive events, by sampling a random number from an exponential distribution with the rate parameter, lambda (λ), equal to the daily frequency. The sampled number is used to place the starting time of the water-use event by adding it to the start time of the previous event. This process is repeated until the next start time falls beyond the end of the last eligible time period. This results in a simulated frequency of water-use events, on average, equaling the specified frequency.

After the water use occurrences have been specified, the water-use durations are simulated using the mean and standard deviations of event durations specified by the modeler. These durations are typically based on information gathered in surveys of water uses (e.g., EPA, 1997). The event duration is assumed to be lognormally distributed, such that

$$Y \sim Lognormal(\xi, \phi) \tag{1a}$$

where:

y = the event duration, a lognormally distributed random variable.

ξ, ϕ = the parameters of the lognormal distribution.

The mean and standard deviation, characteristics of the water-use duration, are converted to the parameters of a lognormal distribution by the following equations:

$$\phi = \left[\ln\left(\frac{\sigma^2}{\mu^2} + 1 \right) \right]^{1/2} \tag{1b}$$

$$\xi = \ln(\mu) - \frac{\phi^2}{2} \quad (1c)$$

where:

μ = the sample mean duration.

σ = the sample standard deviation of the duration.

After a random number from the above distribution is simulated, the event duration is assigned the value from Equation 1A. If the water-use event continues beyond the end of the occupant's current activity period, the water-use event will be truncated at the end of this activity period. This will happen infrequently, since the eligible time period for simulating the occurrences of the water-uses was shortened by the mean water-use duration, as described above.

2. MODEL PARAMETERS

The exposure and PBPK models rely on a variety of parameters that describe the behavioral, physical, chemical, and physiological characteristics relevant to exposure to the chemical, including rate constants, partition coefficients, volumes, and water-use behavior that affect chemical concentrations, exposures, or physiological parameters. These models (for the male, the female and the child; for chloroform, bromodichloromethane, chlorodibromomethane and bromoform) address exposures via the oral, dermal and inhalation pathways. For each model parameter, the values have either been collected from published literature or estimated. An attempt has been made to identify parameter values from multiple sources to assist in the execution of the sensitivity and uncertainty analysis. The collected values are evaluated and a judgment made, considering credibility of the source and consistency among multiple sources, to select the most appropriate value(s) for use in the model execution.

The TEM input parameters include the following:

- Parameters needed for implementation of volatilization model
- Human behavior characteristics that drive the activity model, including location and water-use behaviors
- Ingestion characteristics
- Building characteristics
- Chemical concentrations in water supply

The PBPK model input parameters include the following:

- Compartment volumes by demographic group
- Compartment blood flows by activity for each demographic group
- Alveolar ventilation rates for each demographic group
- Concentration of each chemical in inspired air
- Oral ingestion rates for each chemical
- Concentration of each chemical in drinking water
- Definition of the exposure scenarios for each exposure route for each chemical
- The compartment-to-blood partition coefficients for each chemical
- The skin permeation coefficients for each chemical

- The rate constants for the gastro-intestinal model to be used for each chemical
- The metabolism pathways for each parent chemical
- The metabolism rate constants Vmax, the maximal rate of metabolism, and K_M, the substrate concentration giving one-half Vmax, for each chemical to be modeled, and the inhibitory effect of each chemical on the metabolism of the others.

2.1. VOLATILIZATION MODEL PARAMETERS

While human exposures to drinking water contaminants immediately conjure images of an oral ingestion scenario, drinking water supplies many water use appliances in the home. The method of water use in these appliances (dishwashers, clothes washers, showers, faucets, etc.) is a major contributor to airborne concentrations of volatile contaminants, resulting in appreciable potential for an inhalation exposure pathway. This has previously been demonstrated for volatile drinking water contaminants, and previously employed methods and peer reviewed data are applied to evaluate airborne concentrations and human exposures to the THMs from drinking water, via the inhalation route.

Each of the water-using appliances or fixtures, when operated, represents an opportunity for emission of waterborne chemicals. The emission behavior during a given water use is a function of a variety of chemical and physical factors, including water temperature, surface area, concentration, chemical diffusivities, and Henry's Law constant.

To facilitate prediction of water and air concentrations, the emission behavior is idealized using two types of models: the plug flow model (PFM) and the completely mixed flow model (CMFM). The derivations of these models are presented elsewhere (Olin, 1998).

The plug flow model is derived assuming a constant uniform flow and a volume and surface area that remains essentially constant. The PFM is appropriate for use in representing emissions during continuous flowing water uses such as faucets and showers. Emissions for sources idealized as plug flow are represented by the following equation:

$$S = K_V \left(C_l - \left(\frac{C_g}{H} \right) \right) \quad (2)$$

where:

$$K_V = Q_L (1 - exp(Z)) \quad (3)$$

$$Z = - \frac{K_{OL} A}{Q_L} \quad (4)$$

$$\frac{1}{K_{OL} A} = \frac{1}{K_L A} + \frac{1}{H K_G A} \quad (5)$$

S = source emission rate (mass/time)

K_V = volatilization coefficient (volume/time)

C_l = contaminant concentration in the water supply prior to volatilization (mass/volume)

C_g = concentration in the air surrounding the water stream (mass/volume)

H = dimensionless Henry's Law constant

Q_L = volumetric flow rate of the water (volume/time)

K_{OL} = overall mass transfer coefficient (length/time)

A = interface area between water and air (length^2)

K_L = liquid phase mass transfer coefficient (length/time)

K_G = gas phase mass transfer coefficient (length/time)

The rate of volatilization is maximized if C_g/H is negligible relative to C_l. Conversely, if C_g/H approaches C_l, a state of chemical equilibrium may be achieved with a corresponding suppression of volatilization. This equilibrium condition may occur for sources that include a headspace with poor air exchange (e.g., dishwashers) or that involve chemicals with low Henry's Law constants. The concentration of a contaminant in the liquid phase may be effectively spatially uniform (e.g., in well-mixed systems such as washing machines), or may vary with space (e.g., the flowing water film or droplets associated with showers). The interfacial area, A, is typically difficult, if not impossible, to determine for residential water uses. This is particularly true when significant amounts of splashing occur (e.g., in kitchen wash basin), disintegrated films or droplets occur (e.g., showers and dishwashers), and/or when entrained air bubbles are present

(e.g., during the filling of bathtubs). Thus, interfacial area and overall mass transfer coefficients are typically combined ($K_{OL}A$).

The completely mixed flow model assumes a well-mixed volume of water with a constant surface area, and is appropriate for use in representing emissions from standing water-type water uses. An example of a CMFM type source is a filled bathtub. Emissions for sources idealized as CMFM are represented by the following equation:

$$S = K_{OL} A \left(C_l - \left(\frac{C_g}{H} \right) \right) \quad (6)$$

The volatilization coefficient represents the rate of transfer across the liquid/gas interface where the water is in contact with the air, while Henry's Law constant is used to quantify the concentration gradient relative to equilibrium.

2.1.1. Literature Review of Chemical Properties. The chemicals of interest for this study are the THMs as listed in Table 3. The properties of interest are Henry's Law constant (dimensionless), liquid phase diffusivity (length^2/time), gas phase diffusivity (length^2/time), octanol/water partition coefficient (dimensionless), and molecular weight. Boiling point and volatility are additional properties of value for the study.

2.1.1.1. Literature Search — The literature was searched to identify representative values for the desired chemical properties. Values were obtained from chemical handbooks and dictionaries or online data banks. The results of the search are summarized in Table 4. References to the relevant journal articles have been provided where available.

2.1.2. Estimating Chemical Properties. Prediction methods are used to supplement the literature review for chemical properties that were not found in the literature. Values for the liquid and gas phase diffusivity, the dimensionless Henry's Law constant, and the overall mass transfer coefficient are predicted and discussed in the following subsections.

2.1.2.1. Estimating Liquid and Gas Phase Diffusivity and Henry's Law Constant — The liquid phase diffusivity is predicted using the Hayduk and Laudie method (Lyman et al., 1990). This method is reasonably accurate for a wide range of compounds and has been validated using compiled measured data. The method uses

the molal volume as predicted by the LaBas method and the viscosity of water to predict the liquid phase diffusivity as a function of temperature. Similarly, the gas phase diffusivity is predicted using the Wilke and Lee method (Lyman et al., 1990). According to Lyman et al., this method was found to have an absolute average error of 4.3% when compared to measured values for approximately 150 compounds. This method uses the molecular weight, boiling point, the molal volume, and properties of air to predict the chemical's diffusivity in air. The liquid- and gas-phase diffusivities are estimated as a function of temperature to incorporate the effects of temperature into the estimate of the overall mass-transfer coefficient. The estimated values for liquid and gas phase diffusivities are given in Table 5.

Henry's Law constant can be found in current literature for most chemicals, but often not at the temperature of interest. Therefore, a method to adjust H to the designated temperature is necessary. The following equation is used to adjust Henry's Law constant for temperature dependence:

$$H = H^{\theta} x\, exp\left(\frac{-\Delta H}{R}\left(\frac{1}{T} - \frac{1}{T^{\theta}}\right)\right) \qquad (7)$$

where:

H = Henry's Law constant at desired temperature
H^{θ} = Henry's Law constant at standard conditions
ΔH = enthalpy of solution
R = gas constant = 0.082057 liters atm K^{-1} mol^{-1}
T = temperature (K)
θ = denotes standard condition (298.15 K)

The values for Henry's Law constant based on temperature are presented in Table 5.

2.1.2.2. Estimating Overall Mass Transfer Coefficients — Modeling emissions of drinking water contaminants during water usage requires knowledge of the overall mass transfer coefficient ($K_{OL}A$) as a function of the appliance, the water temperature, the water flowrate, and the chemical. The mass-transfer rates for the THMs have, in general, not been studied comprehensively. The possible exception, chloroform, has been investigated by other researchers. The fractional volatilization

(fraction of available chemical mass that is transferred to the air) during showering for chloroform reported in the literature generally ranges from approximately 0.5 to 0.6. For example, Giardino and Andelman (1996) reported a fractional volatilization for chloroform ranging from 43-62% for a 10-minute shower with water temperature ranging from 26-42°C and the water flowrate ranging from 5-10 L/min.

Because of the lack of measurement data for the mass-transfer parameters for the THMs under the water temperature and flowrate conditions characteristic of the general population, an estimation method is required. The volatilization coefficient, a function of the overall mass-transfer coefficient (K_{OL}), is primarily a function of the water temperature, surface area, and the chemical's diffusion coefficients in water and air. Using a power relationship between liquid-phase and gas-phase diffusivities and the liquid-phase and gas-phase mass transfer coefficients ($K_L \propto D_L^{\,p}$ and $K_G \propto D_G^{\,q}$), Little (1992) derived the following equation for predicting the overall mass-transfer coefficient for a desired chemical based on the measured coefficient for a reference chemical:

$$\frac{1}{(K_{OL}A)_i} = \frac{1}{(K_L A)_r}\left(\frac{D_{Lr}}{D_{Li}}\right)^p + \frac{1}{(K_G A)_r}\frac{1}{H_i}\left(\frac{D_{Gr}}{D_{Gi}}\right)^q \qquad (8)$$

where:

D_L = liquid-phase diffusivity (L^2/T)

D_G = gas-phase diffusivity (L^2/T)

i = chemical for which the overall mass-transfer coefficient is being estimated

r = reference chemical

p, q = power constants

Using Equation 7 and the observations of previous researchers that the ratio of K_G/K_L is approximately constant for a given mass-transfer system (Little, 1992; U.S. EPA, 2000a), U.S. EPA (2000a) presented the following equation:

$$\frac{(K_{OL}A)_i}{(K_{OL}A)_r} = \left(\frac{D_{Li}}{D_{Lr}}\right)^p \left(\frac{D_{Gi}}{D_{Gr}}\right)^q \left(\frac{H_i}{H_r}\right) \left\{ \frac{1 + \left(\frac{K_{Gr}}{K_{Lr}}\right) H_r}{\left(\frac{D_{Li}}{D_{Lr}}\right)^p + \left(\frac{D_{Gi}}{D_{Gr}}\right)^q \left(\frac{K_{Gr}}{K_{Lr}}\right) H_i} \right\} \qquad (9)$$

The above equation provides a means for estimation of $K_{OL}A$ for a chemical based on measurements for another chemical based on the diffusivities, Henry's Law constants, and the ratio of K_G/K_L for the given system. U.S. EPA (2000a) conducted a series of laboratory experiments to determine the values of $K_{OL}A$ and K_G/K_L. The experiments were conducted for five reference chemicals (acetone, ethyl acetate, toluene, ethylbenzene, and cyclohexane) and for five water-use types (sinks, showers, bathtubs, wash machines, and dishwashers) covering a significant range of Henry's Law constants and diffusivities. Using the measured values by U.S. EPA (2000a), Equation 7 can be used to estimate the product of the overall mass transfer coefficient and the interfacial surface area ($K_{OL}A$).

This estimation method requires identifying an appropriate predictor chemical from the set of chemicals studied by U.S. EPA (2000a) based on physical and chemical properties. U.S. EPA (2000a) conducted laboratory experiments and estimated the overall mass transfer coefficients for common household water appliances for the following five chemicals: acetone, ethylacetate, toluene, ethylbenzene, and cyclohexane. A significant shortcoming for using any of these five predictor chemicals is that they are very different in structure and are of lower molecular weight than the THMs. In addition, important characteristics, such as Henry's Law constant, are dissimilar. Since these factors greatly influence the mobility rates and equilibrium conditions, the rate of mass-transfer between the water and air is likely to be influenced leading to lower confidence in the predictions.

An evaluation of the normalized difference between the values for the liquid-phase diffusivity, gas-phase diffusivity and Henry's Law constant for each of the five predictor chemicals and each of the four THMs was conducted. The relevant chemical properties for each chemical are given in Tables 6 and 7, with the results given in Table 8. A sample calculation for identifying the predictor chemical for chloroform is presented, as follows:

SAMPLE CALCULATION: Normalized Difference

The normalized difference between the chemical properties for each predictor chemical and chloroform is calculated as follows:

$$ND_{i,j} = Absolute\ Value\left[\frac{\left(Predictor\ Chemical\ Property_{i,i} - Chloroform\ Chemical\ Property_{i}\right)}{Chloroform\ Chemical\ Property_{i}}\right] * 100\% \quad (10)$$

where:

$ND_{i,j}$ = normalized difference between the predictor chemical property *i* and the chloroform property *i*

i = chemical property

j = predictor chemical

EXAMPLE CALCULATION (for Toluene, Liquid Diffusivity at 20°C):

$$ND_{Liquid\ Diffusivity,Toluene} = Absolute\ Value\left[\frac{Liquid\ Diffusivity_{Toluene} - Liquid\ Diffusivity_{Chloroform}}{Liquid\ Diffusivity_{Chloroform}}\right] * 100 \quad (11)$$

$$ND_{Liquid\ Diffusivity,Toluene} = Absolute\ Value\left[\frac{7.96E-06 - 9.21E-06}{9.21E-06}\right] * 100 = 13.6\% \quad (12)$$

Because the overall mass transfer coefficients for THM compounds have not been previously determined, the present analysis required a method to predict them. Mass transfer coefficients for five chemicals (acetone, ethyl acetate, toluene, ethylbenzene and cyclohexane) were previously determined (U.S. EPA, 2000a); the mass transfer coefficients for these chemicals were evaluated for use as a normalizer for the mass transfer coefficients predicted for each of the studied THM compounds. Liquid diffusivity, gas diffusivity and Henry's Law constants (at 20°C and at 40°C) were determined for each of the nine chemicals (four THM chemicals; five chemicals studied by U.S. EPA, 2000a). Differences between values for the five studied chemicals and the four unstudied (THM) chemicals were tabulated and toluene was determined to be the optimal studied chemical for use in normalizing differences in predicted values for overall mass transfer coefficient among the THM chemicals. Table 8 presents the normalized percent differences between the predictor chemicals and the four THMs based on 20°C. This evaluation considered Henry's Law constant as the most significant indicator, since Henry's Law captures the solubility and vapor pressure relationship of the compound and the diffusivities of the predictor and THM chemicals were not dissimilar. The method for estimating the overall mass-transfer coefficient was found to result in predictions that generally agree with the fractional mass of chemical reported by Giardino and Andelman (1996) for chloroform. As a comparison, the

calculation was repeated using ethylbenzene as the predictor chemical for BDCM. The difference in predicted mass-transfer coefficients between the two predictor chemicals for BDCM was less than 10% for all appliances. Therefore, since toluene as a predictor chemical provided a reasonable prediction for the chloroform mass-transfer coefficient, and because there was a relatively small difference in the predictions for BDCM, the predicted mass transfer coefficients derived from using toluene as the predictor chemical are used in this study, as presented in Table 9.

The estimated values for the overall mass transfer coefficient, presented in Table 9, are estimated based on Equation 7 using toluene as the predictor chemical and assuming a water temperature and hydrodynamic conditions similar to those under which the experiments were conducted (e.g., dropsize distribution, water flowrate, air turbulence, etc.). The predicted overall mass-transfer coefficient was the average of the predictions based on the experimental values measured for the following conditions: water temperature = 35 C (approximate), shower flowrate = 9.1 liters per minute (2.4 gallons per minute) and 6.1 liters per minute (1.6 gallons per minute); and course and fine droplet sizes, as reported by U.S. EPA (2000a). Temperature is a critical factor, affecting mass transfer and uptake kinetics. There is a great deal of uncertainty in the understanding of temperature and temperature effects, and this is an area where future research is warranted.

2.2. BEHAVIORAL CHARACTERISTICS

Activity patterns and water-use behavior have been shown to have a significant impact on predicted exposure (Wilkes et al., 1996). TEM represents the influence of behavior by using activity pattern databases and analysis of other behaviors that influence contaminant release and subsequent human exposure. The activity pattern database was queried to obtain a subset of records having the desired demographic characteristics. This subset is randomly sampled to obtain an activity pattern record, and this record is used to specify locations within the household and opportunities for conducting activities that may result in exposure. Using the activity code and location code in the sampled activity pattern, a transition matrix is used to assign a location in the modeled building as described in Section 2.2.1.2. The actual water uses are simulated based on parameters defined from analysis of other water-use studies. This

results in occupant-driven water uses, which ultimately lead to exposure to the waterborne contaminants. See Section 2.2.1.2, below, for a description of the methods for modeling activity patterns.

The chosen population for this exposure estimation modeling study is a three-person family in which both parents are within their reproductive years. The family consists of one male between the ages of 15 and 45, one female between the ages of 15 and 45, and one child approximately 6 years of age. Because there are few records in the database reflecting 6-year-olds, the child is characterized by sampling the database for children between the ages of one and nine. Although it is recognized that there is significant difference in behavior between a toddler and a 9-year-old, it was necessary to represent the child as a range of ages to allow a reasonable sample size in the database. It is not entirely clear what the impact of this assumption is on the ultimate exposure to drinking water contaminants. Younger children likely spend a greater fraction of their day at home, and for higher volatility chemicals this may increase their exposure. For less volatile chemicals, the impact of inhalation exposure is minimal, and the resultant exposure is highly dependent upon the child's water-use behavior.

2.2.1. Activity Patterns. In order to most accurately represent individuals' exposure to waterborne contaminants, it is necessary to understand the frequency of each type of water use (e.g., how often they shower), and the duration of the events (e.g., minutes occupant spends in shower). In this study, the frequency and duration are described for each of the six water-use activities most important to exposure: showering, bathing, and using the clothes washer, dishwasher, toilet, and faucet. For some of these events, the frequencies or durations are described as distributions from which individual usages will be sampled, in other cases (e.g., dishwasher duration), the parameters are specified as the best available estimate.

The water-use behavior parameters needed for TEM have been developed from the data presented in the National Human Activity Pattern Survey (NHAPS), the Residential End Use Water Study (REUWS), Residential Energy Consumption Survey (RECS), in appliance manufacturer data, and supplemented, as necessary, by best judgment, as described in Section 2.2.2. These databases are described below.

2.2.1.1. Available Activity Pattern Databases —

2.2.1.1.1. NHAPS. The NHAPS database contains the results from a 2-year nationwide activity pattern survey commissioned by the U.S. EPA National Exposure Research Laboratory. During the period from October 1992 through September 1994, 9386 persons residing in the 48 contiguous United States were chosen using a telephone random-digit dial method and interviewed over the phone (Tsang and Klepeis, 1996). The interviewees were selected and their responses weighted according to geographic, socioeconomic, time/season, and other demographic factors to ensure that they were representative of the U.S. population (Tsang and Klepeis, 1996). The weighted sample is consistent with the U.S. population for gender, age, region, and other factors.

First, respondents were asked to recall their activities and locations for the previous 24 hours. The locations and activities were recorded as codes chosen from a list of 83 possible locations and 91 possible activities. This diary section had minimal information regarding water use. The only activity choice that specifically pertained to water-use was “bathing.” All of the other activities are more generally defined such as “food clean-up”, “plant care”, “personal care”. Location codes included 12 indoor home locations such as “Home-bedroom,” and “Home-bathroom,” and a variety of other outside the home locations such as “Office,” “Grocery Store,” “Work-Transit,” and “Outdoor-Park.”

Then the respondents were asked a series of multiple-choice questions. Every respondent was asked for specific demographic information, including date of birth, gender, race, geographical region, level of education, etc., and they were asked a multitude of questions, asking for demographic information as well as information about various activities, most relating to possible exposure to contaminants in the air and water, such as “How long did you spend in the shower?” or “Was a dishwasher used yesterday when you were home?” Not everyone was asked the same questions as there were two versions of the questionnaire. NHAPS did not acquire information on toilet use, and acquired only limited information on faucet use.

2.2.1.1.2. REUWS. The REUWS database contains water-use data obtained from 1,188 volunteer households throughout North America (Mayer et al., 1998). The

REUWS study was funded by the American Water Works Association Research Foundation. During the period from May 1996 through March 1998, approximately 100 single-family detached homes in each of 12 different municipalities (located in California, Colorado, Oregon, Washington, Florida, Arizona, and Ontario) were outfitted with a data-logging device (Meter Master 100 EL, manufactured by Brainard Co., Burlington, NJ) attached to their household water meter (on only magnetic driven water meters). The data logger recorded the water flows at 10-second intervals for a total of four weeks (two in warm weather and two in cool weather) at each household. Following the study, the data were retrieved and analyzed by a flow trace analysis software program, called Trace Wizard©, developed by Aquacraft, Inc., Boulder, CO, which disaggregated the total flows into individual end uses (i.e., toilet, shower, faucet, dishwasher, clothes washer, etc.) (Mayer et al., 1998). Trace Wizard© disaggregates the household water-use signature by using a signal processing algorithm which compares segments of the signature to general characteristics of each appliance. For example, the volume of water used by a toilet falls into several small ranges, depending upon the age of the toilet, and the fill rate is relatively consistent across all toilets. The software attempts to identify all water-uses that fall into these pre-identified ranges and label them as toilet uses. After identifying the type of water use (e.g., shower, faucet, toilet), Trace Wizard© estimates the event durations, volumes, peakflows, and mode measurements for each water-using event from the resultant disaggregated water-use signature.

The REUWS database includes demographic information on each household based on a mail-in survey. This information includes employment status (unemployed, part-time, full-time), education level of the primary wage earner (less than high school, high school graduate, some college, Bachelor's, Master's, Doctoral), and household income. It also provides information on the number of adults (18 and over), children (under 13) and teenagers (13-17), as well as a variety of information about the house (type, number of floors, square footage, water-related amenities such as swimming pools, etc.), household appliances and general water-use behavior. It does not give information on age or gender.

2.2.1.1.3. RECS. The Residential Energy Consumption Survey (RECS), conducted nationwide in 1997, contains energy usage characteristics of 5900 residential housing units. The information was acquired through on-site personal interviews with residents; telephone interviews with rental agents of units where energy use is included in the rent; and mail questionnaires to energy suppliers to the units. The database contains information on physical characteristics of the housing units, demographic information of the residents, heating and cooling appliances used, fuel types, and energy consumption.

2.2.1.2. Modeling Activity Patterns — NHAPS represents the most comprehensive survey of activities of U.S. residents available. However, water-use behavior data associated with the survey data is sparse and incomplete. The 24-hour record of locations and activities contains general locations (e.g., Home-kitchen, Home-bathroom, etc.) and activities (e.g., personal care, cooking , cleaning, etc.). However, the 24-hour activity record does not specify actual water-use events such as dishwasher use, clothes washer use, and showering. To model the activity patterns, TEM samples a 24-hour record from NHAPS for each occupant and, using a transition matrix, places the occupant in the modeled house such that his/her location is consistent with the recorded activity and location in the NHAPS database. For example, if the sampled activity pattern identifies the location as “Home- Bathroom,” and the activity as “Personal needs and care – Bathing, etc.,” the model places the adults in the “Master Bathroom” or the child into the “Hall Bathroom” and assigns the specified breathing rate for that activity. Information on water-use behavior gathered from other sources is then used to simulate appropriate water-use activities for each occupant.

The water uses are incorporated into sampled activity patterns by simulating activity-appropriate water uses with appropriate frequencies and durations of use. For example, to simulate showering behavior, the portions of an activity pattern where a showering activity is appropriate are identified. This is accomplished by identifying eligible activity codes and locations codes (e.g., the combination of the NHAPS activity code of “Personal-wash, etc.,” and the NHAPS location code of “Home-Bathroom” would be eligible for showering activities). Once eligible time periods are identified, the time between the starting of successive water-use events is simulated by sampling a

Poisson distribution with the rate parameter, lambda (λ), equal to the daily frequency. The duration of the event is simulated based on a lognormal distribution with parameters appropriate for the study population. The method for sampling activity patterns and simulating appropriate water-uses is fully described in Wilkes (1999).

Water-use occurrences are simulated as a Poisson process using frequency data obtained from analyses of NHAPS, REUWS, and RECS. The water-use activity duration is also simulated based on, typically, a lognormal distribution, also resulting from analyses of NHAPS, REUWS, and RECS. For more information on how the activities are mapped to model locations and how the water-use simulation is implemented, see Wilkes (1999).

2.2.2. Water-use Behaviors for Groups of Interest. Release of airborne contaminants occurs as a result of typical household water uses. In addition, dermal contact occurs during some household water uses like showers and baths. For this reason, it is imperative to represent these water uses as accurately as is reasonable within the daily activity patterns of the model occupants. From a population exposure point of view, the water-use activities that have a significant impact are use of showers, baths, clothes washers, dishwashers, toilets, and faucets. For each of these water uses, the published literature and other data sources such as survey data have been reviewed, analyzed, and summarized in the following sections.

By comparing the data in NHAPS to other, smaller population based studies of water use, it was concluded that NHAPS provides reliable data on frequency of occasional water-use events (e.g., showering and bathing), but is believed to provide poor estimates of the event durations, because the values were based on recall (Wilkes et al., 2004). The respondents tended to estimate event durations around 5-minute intervals, and the values were not consistent with published literature (Wilkes et al., 2004). In contrast, because REUWS is derived from direct water meter measurements, REUWS provides reasonable data on the durations and volumes of some water-use events, particularly showers, clothes washers, and toilets. However, since REUWS is based on the entire household water use, personal frequencies of water-use events for individual persons cannot be reliably discerned. In regard to clothes washer frequencies, RECS provides the best data for our purposes.

2.2.2.1. Showers — The model uses shower frequency, duration, water flowrate and temperature to represent occupant showering behavior and subsequent contaminant release and occupant exposure. A Poisson process is used to simulate shower occurrence, and a lognormal distribution is sampled to simulate the duration. Analysis has shown that showering characteristics vary among demographic groups. A number of shower studies have been done throughout the United States to determine typical shower frequency, durations, and volumes. These studies include a study of 162 U.S. households by the U.S. Department of Housing and Urban Development (HUD, 1984). A study was conducted of 25 homes in Tampa, Florida (Konen and Anderson, 1993), and a study of 25 homes in Oakland, California (Aher et al., 1991). In general, these studies revealed an average frequency of around five showers per week and a duration ranging from 6.0 to 10.4 minutes. The average flowrates measured in the Tampa and Oakland studies ranged from 1.5 to 2.5 gpm.

In addition to the above studies, NHAPS and REUWS have been analyzed for showering characteristics, as discussed above. The analysis conducted by Wilkes et al. (2004) concluded that NHAPS provided the most reasonable basis for specifying shower use frequency, and REUWS provided the most reasonable basis for specifying shower duration characteristics. The results of the frequency analyses from both NHAPS and REUWS are presented in Table 10. The results of the duration, volume and flowrate analyses from REUWS are presented in Table 11. For a more detailed discussion of these data sources and analyses, refer to Wilkes et al. (2004). The selected parameter values for showering frequency, duration and flowrate used in this modeling study are presented in Table 12. These values were selected based on the data presented in Tables 10 and 11 assuming the 15-45 age group is similar to the analyzed 18-48 age group and that a 6-year-old child is well represented by the analysis of the 5-12 age group.

2.2.2.2. Baths — The model uses bath frequency, duration and water volume and temperature to represent occupant bathing behavior and subsequent contaminant release and occupant exposure. A Poisson process is used to simulate bath occurrence, and a lognormal distribution is sampled to simulate the duration. Relatively few studies have been conducted in the United States to determine typical bath

frequencies, duration, and volumes. The HUD study in 1981-83 found that people who only bathe (do not shower) take about 2.9 baths per week. The NHAPS database is analyzed for bathing frequencies and duration. Although the bathing durations given in NHAPS tended to cluster around 5-minute intervals, and are based on recall, it is the only generalized population study of this behavior, and therefore is the best available data. The REUWS database does not provide bathing durations, only the amount of time it took to fill the tub. The results of the NHAPS bathing frequencies and durations for the three subpopulations of interest are provided in Table 13. The results of the REUWS analysis to determine bath flowrate is presented in Table 14. The bathtub emission model uses a bathtub water volume, a fill duration, and a bath duration. Although no studies have analyzed the volume of water used in bathing, HUD (1984) estimated 50 gallons (189 L) based on the physical size of a typical bathtub. The fill duration was set at 8 minutes, which is consistent with the amount of time required to fill a 50-gallon bathtub, based on a mean flowrate of 25 L/minute (6.6 gal/minute). This mean bath fill flowrate was derived by evaluating both field measurements and the REUWS data. The flowrate in two independent field measurements in household bathtubs were 8.9 and 9.3 gallons/minute (Appendix to Wilkes et al. 2004). The REUWS analysis resulted in a mean bath fill flowrate of 4.9 gallons/minute, with a standard deviation of 2.1 gallons/minute. The selected bath fill flowrate value of 6.6 gallons/minute is consistent with the REUWS study at approximately the 85th percentile. The selected parameter values used in the modeling study are presented in Table 15. These values were selected based on the data presented in Tables 13 and 14 assuming the 15-45 age group is similar to the analyzed 18-48 age group and that a 6-year-old child is well represented by the analysis of the 5-12 age group.

2.2.2.3. Clothes Washers — The model uses clothes washer frequency, the number of cycles and information about each cycle, including fill duration, agitation duration, water volume and water temperature to represent occupant use of clothes washers and subsequent contaminant release and occupant exposure. A Poisson process is used to simulate clothes washer use. Both the NHAPS and the RECS surveys asked respondents questions about their clothes washer use. The two questions asked in NHAPS were: “How often do you wash clothes in a machine?” and

"How many separate loads of laundry were done when you were home?" The answers for the first question were recorded as: Almost every day, 3-5 times a week, 1-2 times a week, Less often, or Don't know. The answers for the second question were recorded as actual number of loads under 10, or "over 10." The problem with the first question was that the frequency range in the choices is too broad, and the question is unclear whether it refers to how many actual loads or how many days per week they did laundry regardless of how many sequential loads they did in one day. The major problem with the second question is that it required the individual to be at home during the event. In the RECS survey, the question relating to clothes washer use was more specific; however, the answer choices likewise offered a range. The RECS question was: "In an average week, how many loads of laundry are washed in your clothes washer?" The answer choices were: 1 load or less each week, 2 to 4 loads, 5 to 9 loads, 10 to 15 loads, More than 15 loads, or Don't know.

RECS was analyzed for clothes washer frequency behavior (Wilkes et al., 2004) because the questionnaire was less ambiguous than the one used for NHAPS. The results for three-person families are presented in Table 16, showing the percentage of the 3-person families in the RECS database that used the clothes washer the specified number of times per week. The analysis of three-person families excluded families with individuals over the age of 65 because we were attempting to represent families with children. The REUWS and experimental data are analyzed for clothes washer volume and durations of the various wash and rinse fills, and agitation cycles. The results of the analysis are presented in Table 17. Table 18 presents selected parameters to be used in modeling clothes washer use.

2.2.2.4. Dishwashers — The model uses dishwasher frequency, the number of cycles and information about each cycle, including cycle duration, water volume and water temperature to represent occupant use of dishwashers and subsequent contaminant release and occupant exposure. A Poisson process is used to simulate dishwasher use. There are very few studies on the water-use characteristics of dishwasher use. In 1984, a HUD study reported that people generally used the dishwasher 3.7 times per household per week, or 1.2 times per person per week. A 1983 Consumer Reports study (reported in HUD, 1984) found that dishwashers at the

time were using from 8.5 to 12 gallons per load, and older dishwashers were using 14 gallons per load. Similar to the NHAPS clothes washer data, the NHAPS dishwasher data is likewise unreliable as the questions pertaining to dishwashers were ambiguous. The NHAPS questions relating to dishwashers were, “How often does (respondent) use the dishwasher?” This does not indicate how often the family used the dishwasher. However, the RECS respondents were asked, “Which category best describes how often your household actually uses the automatic dishwasher in an average week?” Their answer choices were as follows: less than 4 times a week, 4 to 6 times a week, or at least once each day. The RECS data were analyzed for three person households, excluding all families with a member over 65 years old in order to best represent families with a child. Table 19 presents the percentage of 3-person families surveyed in the RECS database that used the dishwasher either daily, 4-6 times per week, or less than 4 times per week. Since dishwasher cycle volumes and durations have not been well-characterized in any known surveys, data obtained from the manufacturers were used for these parameters. These data are presented in Table 20. Table 21 presents the values selected for use in the modeling study. The emissions during the drying portion of the cycle have not been studied, and therefore drying is not considered.

2.2.2.5. Toilets — The model uses the frequency of flushing to incorporate toilet use into the sampled activity pattern. Once a toilet flush has occurred the emission models also require the volume of water for the flush. For modeling purposes, it is assumed that a flush duration is instantaneous.

Several recent studies reported toilet flush frequency and volume. These studies focused on the performance of ultra-low flow toilets, contrasting their performance after retrofit with the performance of the low flow and older non-conserving toilets they replaced. The Tampa, Florida study (Konen and Anderson, 1993) retrofitted the showers and toilets in 25 single-family homes with ultra-low flow devices and monitored their water usage for 30 days before and 30 days after retrofit. The Oakland, California study (Aher et al., 1991) retrofitted 25 single-family homes with ultra-low flow toilets and monitored their water usage for 21 days before and 21 days after retrofit. The HUD (1984) study monitored 196 households with 545 persons found that people flushed

toilets approximately 4 times per day. The results from these studies are presented in Table 22.

REUWS also provides toilet use data. The data were derived from an analysis of household water meter monitoring. Because the water meters record total water use for the household, it is impossible to attribute each flush to any given individual. Therefore, the average frequency of toilet use in REUWS was derived by analyzing the total frequency of use for each family divided by number of persons in the household. The data contained in REUWS has been analyzed for frequency of toilet use and water volume characteristics. For a complete description of the analysis of REUWS refer to Wilkes et al. (2004).

The frequency of toilet use was modeled as a Poisson process with a mean frequency of 5.23 flushes per person per day. The volume per flush was found to be best represented as a normal distribution with a mean of 3.5 gallons and a standard deviation of 1.2 gallons. The results of the REUWS analysis are presented in Table 23. The actual toilet use frequency and volume values used in the DBP modeling study are presented in Table 24.

2.2.2.6. Faucets — Faucet use characteristics for bathrooms and kitchens were researched in a study of 25 homes in the city of Tampa (Konen and Anderson, 1993). The mean water flowrate was 2.4 gpm from the kitchen faucet and 3.4 gpm from the bathroom faucet, each with the faucets fully open. HUD (1984) estimated that faucet use in the homes they studied was 9.0 gallons/person/day. The frequency of faucet use was not given. These data are presented in Table 25.

The faucet use characteristics reported in REUWS are analyzed and reported in Table 26. The REUWS database should be used with caution in respect to faucet use, since the techniques used to acquire the data in REUWS are unreliable, and it is expected that many uses labeled as faucets are misclassified and that many of the uses labeled as “leaks” and “unknown” could be faucets. For a complete discussion of the analysis, refer to Wilkes et al. (2004). The actual faucet use parameter values selected for use in the DBP modeling study are presented in Table 27. The frequency and duration values were adjusted from those in the REUWS analysis because the room locations and activity patterns sampled from NHAPS do not typically provide adequate

opportunity for the frequency of faucet use reflected in the analysis of REUWS. Most probably resulting from the fact that people don't often report being in the locations of faucet use, they tend to under-report bathroom visits, and small water uses overall. In addition, there is no reasonable information on which household faucet is being used (e.g., bathroom, laundry, kitchen). Therefore, to compensate for the discrepancies (i.e., interface with activity patterns), the faucet frequencies were adjusted downward, while the durations were increased.

2.3. INGESTION CHARACTERISTICS

The most obvious route of human exposure to waterborne contaminants is via ingestion. Every day, people drink water directly and consume water indirectly in juices, sodas, soups, foods, coffee, tea, etc. In order to assess a person's ingestion exposure to chemicals found in the water system, it is important to appropriately represent and estimate the amount of water the person consumes, and from what sources. In order to understand the dynamics of exposure uptake and distribution in the body, we must first consider the dynamics of direct and indirect consumption from an exposure perspective. U.S. EPA (2000b) puts forth the following definitions:

Direct Water: defined by (U.S. EPA, 2000b) as plain water ingested directly as a beverage.

Indirect Water: defined by (U.S. EPA, 2000b) as water added to foods and beverages during final preparation at home, or by food service establishments such as school cafeterias and restaurants.

In this study, direct consumption is defined as "direct water" consumed by the occupant and indirect consumption is defined as "indirect water" consumed by the occupant. For direct consumption, we must develop a methodology for representing the number of drinks and volumes consumed, either assuming that the contaminant level remains constant from tap to glass to body, or consider that some contaminant volatilized during air contact. For indirect water consumption, such as via food or reconstituted drinks, we also need to consider the quantity consumed, and also evaluate whether the fraction of the contaminant remaining in the drink or food after volatilization and preparation is still significant or should the drink or food be ignored in the exposure calculation.

2.3.1. Available Data Sources. Currently, the U.S. EPA typically assumes that adults consume an upper-percentile quantity of 2 liters of tap water per day and infants (body mass of 10 kg or less) consume 1 liter per day (U.S. EPA, 1997a). These rates include the tap water consumed directly and the tap water consumed in other drinks like juices, coffee, etc. Prior to 1995, the primary survey used to estimate tap water intake in the U.S. was the U.S. Department of Agriculture's (USDA) 1977-1978 National Food Consumption Survey (Ershow and Cantor, 1989 in *Exposure Factors Handbook* (U.S. EPA, 1997a)). However, newer studies have been conducted that better reflect consumption behavior for modern times, reflecting our changed habits such as drinking more bottled or filtered water, and drinking more soda and other canned drinks. Furthermore, water intake is assumed to vary with levels of physical activity and outdoor temperatures and Americans are exercising more than ever.

There are two major recent surveys that prove useful when estimating the amount of water people ingest per day. One is NHAPS and the other is the Combined 1994-1996 Continuing Survey of Food Intake by Individuals (CSFII) (U.S. EPA, 2000b) conducted by the USDA. There are also a few other studies presented in the *Exposure Factors Handbook* (U.S. EPA, 1997a).

2.3.1.1. Ingestion: *Exposure Factors Handbook* — The *Exposure Factors Handbook*, Volume 1, Chapter 3 (U.S. EPA, 1997a) presents the key and relevant drinking water intake studies prior to 1995. These surveys and studies include the following: 1981 *Tapwater Consumption in Canada* study by the Canada Department of Health and Welfare; 1977-78 *Nationwide Food Consumption Survey* by the U.S. Department of Agriculture, analysis by Ershow and Cantor; 1978 *Drinking Water Consumption in Great Britain,* analysis by Hopkins and Ellis; 1987 *Bladder Cancer, Drinking Water Source, and Tapwater Consumption* study by the National Cancer Institute, analysis by Cantor et al.; and the 1992-1994 *National Human Activity Patterns Survey* (NHAPS) analysis by Tsang and Klepeis (1996). For a more complete discussion of these studies, see Wilkes et al. (2004). The tapwater consumption data from these studies are summarized in Table 28, specifically for the subpopulations that most closely represent the three groups of interest identified previously.

2.3.1.2. 1994-1996 USDA's Continuing Survey of Food Intake by Individuals (CSFII) — The 1994-96 USDA's CSFII is the most recent and comprehensive consumption database available. CSFII was conducted over the 3-year period between January 1994 and January 1997. More than 15,000 persons in the United States were interviewed on two non-consecutive days with questions about what drinks and foods they consumed in the previous 24 hours. The U.S. EPA report, Estimated Per Capita Water Ingestion in the United States (U.S. EPA, 2000b), presents estimates of per capita water ingestion based on the CSFII data for direct and indirect water intake. The study uses the following definitions:

- Direct water: plain water consumed directly as a beverage.
- Indirect Water: water used to prepare foods and beverages at home or in a restaurant.
- Intrinsic Water: water contained in foods and beverages at the time of market purchase before home or restaurant preparation. Intrinsic water includes both the "biological water" of raw foods and any "commercial water" added during manufacturing or processing.

In the survey, respondents were asked:

- What is the main source of water used for cooking? (Community water, private well, spring, bottled, other?)
- What is the main source of water used for preparing beverages? (same)
- What is the main source of plain drinking water? (same)
- How many fluid ounces of plain drinking water did you drink yesterday?
- How much of this plain drinking water came from your home? (All, most, some, none)
- What was the main source of plain drinking water that did not come from your home? (Tap or drinking fountain, bottled, other, don't know)
- Recall everything they ate over the past 24 hours. Where was the food obtained?

2.3.2. Ingestion Behavior for the Three Populations: Results of Analysis. Of the available references providing water consumption data on the subpopulation groups of interest for our study, the CSFII survey was chosen as the most useful because of its current relevance and its comprehensive specification of water intake in its various

forms. The intakes for the two days of the survey were averaged for each person, providing the estimated mean two-day average. Table 29 lists the distribution parameters (geometric mean and standard deviation) for direct and indirect tapwater consumption in the U.S. for women and men over 20 and children between 1 and 10 from the CSFII study. Table 30 shows a comparison of the consumption percentiles for the data set and the fitted lognormal distributions for each of the demographic groups. The actual parameters selected for use in this DBP modeling study are presented in Table 31.

2.3.2.1. Methodology for Distributing Water Consumption Throughout Day — No studies were identified that quantify the manner in which water consumption is distributed throughout the day. A reasonable, common sense approach is being adopted for implementing this distribution. The water consumption will be distributed into a specified number of consumption events represented by a Poisson process over the daytime (nonsleep) period using parameters listed in Table 31. This results in an exponential distribution with the mean frequency given in Table 31 across the modeling study for each population group. The consumption volume is sampled from the appropriate lognormal distribution as identified in Section 2.3.2 and Table 31, with the total volume randomly placed among the consumption events.

2.4. BUILDING CHARACTERISTICS

Housing characteristics, including zonal volumes, interzonal airflows, and whole house air exchange rates, also have a significant impact on the estimated exposures. The important building parameters are volumes of the whole house, volumes of the individual water-use zones, whole house air exchange rates, and interzonal airflows.

TEM will model each subject residence as a collection of individual water-use zones in flow communication with a "Rest-of-House" (ROH) zone that aggregates the zones that are free of water-use sources. In order to execute TEM for typical conditions and building characteristics, information related to indoor volume and airflows is needed.

2.4.1. Representation of Household Volumes. The *Exposure Factors Handbook* (U.S. EPA, 1997b) recommends using 369 m^3 as the central estimate of volume for American residences, with a conservative value with respect to air concentrations of

217 m^3. These estimates are based on peer-reviewed data appraisals drawn from statistically representative surveys of American households through the Residential Energy Consumption Survey. The RECS survey was first conducted in 1978 and was updated on a biennial basis until 1984, after which the survey was conducted periodically, every 3 or 4 years. In addition to data related to energy consumption, RECS solicits information on demographics, building characteristics, and other factors that relate to the needs of TEM. The distribution of indoor residential volume contained in the *Exposure Factors Handbook* was calculated based on the estimated floor area (the estimated or measured square footage of conditioned floor space in each home) assuming 8-foot (2.44 m) ceiling height.

Estimates for total house volume contained in the *Exposure Factors Handbook* were derived primarily from RECS data collected in 1993 and published in 1995 (U.S. DOE, 1995). Results of the 1997 survey (U.S. DOE, 1999) only became available after the *Exposure Factors Handbook* was updated. Initial reviews of the 1997 RECS data indicate that total house volume estimates derived from the 1997 RECS data would be very similar to the earlier data. The RECS data was analyzed and the representativeness of several distributions was evaluated. The RECS data was further analyzed to characterize the volume of 3-person U.S. households. In Figure 3, these house-volume data are fitted to a lognormal distribution, with a geometric mean of 317 m^3 and a geometric standard deviation of 0.422. The probability density function for the chosen lognormal distribution is compared to a histogram of housing volumes in Figure 4. Based on the fit, a lognormal distribution was chosen to represent the distribution of volumes, as shown in Figure 5. Such housing corresponds to a modest (~1400 ft^2) residence occupied by 3 or 4 people. In addition to expected general appliances, all such homes are equipped with a kitchen (which usually contains an automatic dishwasher), and nearly all have two baths plus a laundry, as well as a basement. The "average" house has a central forced-air system to support heating and cooling needs.

> *Selection of Total House Volume:* Total house volume for 3-bedroom cases are selected from the statistical distribution derived from the 1997 RECS data (Table 32). The distribution of total volume for 3-bedroom homes is lognormal (Figure 3), and is characterized by a geometric mean volume of 317 m^3 (11,195 ft^3) and geometric standard deviation of 0.4218.

The RECS data does not identify volumes for individual water-use zones. Given that indoor spaces are designed to meet specific patterns of use, the *Architectural Graphics Standards* published through the American Institute of Architects (Hoke, 1988, 1994) provides a basis for assigning floor areas to specific zones. This resource summarizes the range of basic dimensions for key zones for various sized households. For example, the range of kitchen dimensions is keyed to the number of people in the household. Table 33 summarizes this range for a household composed of 3-4 people (the predominant household size for 3-bedroom U.S. homes). Bathroom dimensions, on the other hand, are largely independent of the number of people. Floor areas have been transformed to volume estimates assuming 8-foot (2.44 m) ceiling height.

This range of zonal volumes is largely unverified in the professional literature, but the values in Table 33 have the intuitive appeal of being derived from an authoritative source (Hoke, 1988, 1994) that guides residential design. Residential laundry facilities, for the most part, are installed in a host space rather than taking up a separate room. In homes featuring a heated basement, the laundry should be positioned in that zone. In homes built to slab-on-grade and crawlspace designs, the laundry is usually assigned to the kitchen, and the kitchen-laundry zone should be sized to accept both uses.

> *Selection of Indoor Volumes for Water-Use Zones*: The range for zonal sizes are defined from the *Architectural Graphics Standards*. For each type of water-use zone, each range listed in Table 33 will be used to define zone-specific uniform distributions. Values assigned to individual model cases will be randomly selected from these distributions within TEM.

2.4.2. Representation of Whole House Air Exchange Rates and Interzonal Airflows. *The Exposure Factors Handbook* (U.S. EPA, 1997b) recommends using 0.45 as the "typical" value for air exchange rate (ACH) in American residences. The national distribution of residential air exchange is described in the *Exposure Factors Handbook* and summarized in Table 34. In the absence of comprehensive measurement surveys, the distribution in Table 34 was derived from analysis of perfluorocarbon tracer (PFT) data collected for a number of research programs since the early 1980s (Koontz and Rector, 1995).

> *Selection of Air Exchange Rate*: The national distribution of residential air exchange rates are defined from the *Exposure Factors Handbook* (see Table

34). Values assigned to individual model cases will be randomly selected from the distribution representing “All Regions” within TEM.

The water-use zones are set up in this model to have airflows with the “Rest of the House (ROH),” but not with the outdoors. These zones exchange air with the ROH at rates specified in Figure 3 of the report, rates which are a function of the whole house air exchange rate (WHACH), but are somewhat lower, and subsequently, the decay rate is slowed. These relationships were developed as a result of analysis of the PFT database. Another important factor is the means of specifying the WHACH. The WHACH is sampled from a representative distribution, which is lognormal with a geometric mean of 0.46 hr-1 and a geometric standard deviation of 2.25. Sampling from this distribution will result in a wide range of WHACHs, with some values lower than 0.1 and other values greater than 10. The WHACH sampled for case 48 (the illustrative case whose results are shown in the figures) was 0.11 hr^{-1}. Table 35 summarizes the relevant parameters selected for case 48. All of the parameters are consistent with the algorithms presented in this section and represented in Figure 3.

Given the simplified scenarios envisioned for the model runs, interzonal airflows can be assigned through the air exchange rate. That is, interzonal airflows would be sized by the air exchange terms. The next level of complexity utilizes the algorithms developed by Koontz and Rector (1995) from their analysis of the PFT data cited above. Under this scheme, the normalized interzonal airflow (Q_N, h^{-1}) for any zonal pair is defined as a function of the flow from zone 1 to zone 2 (Q_{12}), flow from zone 2 to zone 1 (Q_{21}), and total (V, m^3) such that:

$$Q_N = \frac{(Q_{12} + Q_{21})}{2} \cdot \frac{1}{V} \qquad (13)$$

While the analysis showed differences in the correlation equations, the practical differences are negligible in that both estimators produce a normalized interzonal airflow term of 0.22 h^{-1} at an air exchange rate (I, h^{-1}) of 0.45:

$$\text{Bedroom: } Q_N = 0.078+0.31I \qquad (14)$$

$$\text{Kitchen: } Q_N = 0.046+0.39I \qquad (15)$$

It is expected that bathrooms are used with the door closed. Relatively little direct data exists to define airflows. Experimental work by Giardino et al. (1992) provides useful values published in a peer-reviewed journal. For a 13 m^3 bath, these determinations found exiting airflow from the bath to the adjacent hallway to be 4.2 m^3 h^{-1} with the door closed and 15.1 m^3 h^{-1} with the door open. Similarly, entering airflows from the hallway to the bath were found to be 16.3 m^3 h^{-1} with the door closed and 47.9 m^3 h^{-1} with the door open. These flows were utilized in subsequent residential exposure modeling of radon volatilized from various water-use scenarios (Rector et al., 1996). At higher levels of complexity, dynamic and engineering estimators can be applied to recognize the influences of weather and operation of the heating/cooling system.

A modeling study conducted by researchers at the National Institute of Standards and Technology (NIST) developed simplified approaches to modeling interzonal dispersal of indoor contaminants in homes served by central air-conditioning/heating systems (Persily, 1998). Under the NIST study, patterns of fan operation were defined by the following rules:

- Airflows were assumed to be 50 L s^{-1} (180 m^3 h^{-1}) at major supply registers and 25 L s^{-1} (90 m^3 h^{-1}) at minor supply registers when the central air handler was running. (These values are consistent with standard guidance in ASHRAE 1992.)
- System on-time was assumed to be 60% (of the total timeframe) at design conditions. (i.e., the highest outdoor temperature reached 98-99% of the time during the cooling months, or the lowest outdoor temperature reached 98-99% of the time during the heating months).

The NIST study also addressed local exhaust fans operating in the kitchen and bathrooms under user control. Based on analysis of commercially-available equipment and engineering judgment, kitchen exhaust flows were assigned to be 170 m^3 h^{-1} (100 cfm), and bath exhaust flows in the NIST study were assigned to be 80 m^3 h^{-1} (47 cfm).

> *Selection of Interzonal and Exhaust Airflows*: Interzonal airflows are scaled by the air exchange rate using the algorithm developed by Koontz and Rector (1995). Exhaust flows for the kitchen and bathrooms will be assigned in conformance with the NIST study (170 m^3 h^{-1} in the kitchen, 80 m^3 h^{-1} in each bath, under user control). These flows will be superimposed on the airflows that prevail when the fans are not operating.

2.4.3. Model Representation of Building. As described in Section 1.4.1, the house is idealized as a collection of compartments where water-use zones are explicitly represented and the remaining indoor zones are lumped into a common zone called "Rest of House" (ROH). The volume parameters and the air exchange rate parameters are specified in accordance with Sections 1.4.1 and 1.4.2. The idealized representation of the house is presented in Figure 5.

2.5. CONCENTRATIONS IN WATER SUPPLY

The concentrations of DBPs in U.S. drinking water supplies vary significantly across utilities largely influenced by the source water characteristics and the treatment processes. The results of three national surveys and a limited 35-city survey of total trihalomethane (TTHM) concentrations in finished U.S. drinking water both at the plant and in the distribution systems found mean concentrations between 42 and 68 µg/L and maximum concentrations ranging from 185 to 482 µg/L (McGuire et al., 2002). However, these studies varied in methods of sample collection and laboratory analysis, and they showed considerable variation in THM concentrations. Another recent case study in two U.S. municipal water systems showed wide variation across individual distribution systems (Lynberg et al., 2001).

Data on water concentrations of a variety of contaminants, including THMs, has been collected as the result of requirements mandated by the Information Collection Rule (ICR). These data encompass the period of July 1997 through December 1998 for more than 330 water treatment facilities, which has been assembled as a database, referred to herein as the ICR database (U.S. EPA, 2000c). A recent analysis of this data by the U.S. EPA (McGuire et al., 2002) found significant variations as a function of a variety of factors, including source of the water supply (e.g., surface water, groundwater, etc.), season, EPA region, and plant disinfectant type (e.g., ozonation, chlorine dioxide, chloramines, etc.).

A specific objective of this project is to examine the relationship between the THM concentrations in the water supply and the blood and tissue concentrations in the human body. The blood and tissue concentrations are affected by a variety of factors, including exposures, uptake characteristics, metabolic and other removal processes. The oxidative metabolism of the four THMs is catalyzed by the cytochrome P450 2E1

(CYP2E1) isoform (Guengerich et al., 1991; Raucy et al., 1993). Metabolism of the THMs by CYP2E1 forms phosgene or its brominated analogs, which can react with tissue macromolecules to produce toxicity. Since the THMs are all substrates for CYP2E1, mutual competitive inhibition of metabolism is expected to occur. During mixed exposures to the THMs in water, each THM would inhibit the bioactivation of the other THMs that are alternative substrates for CYP2E1. This inhibition would decrease the formation of phosgene and its analogs from the THMs, leading to higher circulating concentrations of the parent THMs in the body. The relative extent of these inhibitory effects would depend upon the concentrations of the four THMs in the water supply and their kinetic characteristics. The brominated THMs may also be metabolized by a glutathione conjugation pathway (Ross and Pegram, 2003), but this study will focus on the oxidative bioactivation pathways of the THMs.

Considering that the four THMs may not act independently with respect to metabolic removal, it is important to appropriately represent the concentration of all THMs when modeling metabolic processes. For this reason, we investigated the data in the ICR database to evaluate the correlation among THMs at the upper ends of their respective distributions (in the vicinity of the 90^{th} percentile). In our analysis of the ICR data, we addressed values reported as below the "Minimum Reporting Level (MRL)" by assigning a concentration of half the MRL. The MRL reported by the ICR is 1 µg/L for all four THMs, so the concentration 0.5 µg/L is used for reported values below the MRL.

To evaluate the correlation for a given compound, all samples in the $85^{th}$to 95^{th} percentile were selected, and then the Pearson correlation coefficient was calculated for that compound with each of the other three THMs. This approach was applied separately to chloroform, BDCM, DBCM, and bromoform. The results of these analyses are presented in Tables 36-39.

The results, given in Tables 36-39, exhibit a significant correlation between each individual THM compound and its closest neighbors in terms of the number of chlorine or bromine atoms. For example as can be seen in Table 36, the chloroform concentrations are significantly correlated with the BDCM concentrations, with minimal correlation with the DBCM and bromoform concentrations. Similarly in Table 37, BDCM

concentrations exhibit correlations with the chloroform and DBCM concentrations, but minimal correlation with bromoform concentrations.

Based on the results of the correlations analysis, we considered using a specific percentile (e.g., the 95th percentile) for the concentration of compound of interest, and assigning the concentration of the remaining three THMs based on a regression analysis, but that approach is somewhat artificial because of the inconsistent degree of correlation in the concentrations of the individual chemicals. So we chose the alternative of using concentrations from the actual sample corresponding to the desired percentile. For example, for chloroform, we analyzed the data set to determine the chloroform concentration at the desired percentile, identified the actual records (drinking water samples) for which that chemical was present at the concentration representing the 95th percentile for its overall distribution. The correspondingly measured concentrations for all four THMs taken from that record are reported in Tables 40-43 to demonstrate the fluctuation of the "other three" chemicals, versus the consistency of the concentration of the "target" THM. For simplicity sake, only records from treatment systems relying on surface water are reported in that series of tables. Table 44 demonstrates concentration results from all systems, those relying on surface water, as well as those relying on ground water as source water. For each analysis, because of the size of the dataset, a number of records were found to have the same 95th percentile value (i.e., the same concentration which corresponded to the 95th percentile). For example, Tables 40-43 present the ICR database records for the 95th percentile concentration for chloroform, BDCM, DBCM, and bromoform, respectively. In selecting an actual record to be used to represent the 95th percentile, we opted for the record where the sum of the concentrations of the brominated compounds (i.e., bromoform DBCM, and BDCM) is maximized. We chose this condition to examine exposure scenarios where the maximum inhibition of the oxidative metabolism of the THMs (i.e., their bioactivation) is expected to occur. Using these criteria, the ICR database was analyzed for the 95th percentile record for each THM as presented in Table 44.

A number of water treatment factors were found to influence the THM concentrations. We chose to evaluate the effect of the subset of these factors, listed in

Table 45. The factors were chosen to investigate the effects of the raw water source, the disinfection methods and seasonal factors. A number of other factors that are expected to be important include retention time in the distribution system, the organic content, and the effects of the hot water heater that were not considered in these analyses because they were outside the scope of this project. The ICR database was analyzed for each variable in Table 45 to identify the 95th percentile record for each THM, using the maximized sum of the brominated compounds to identify the worst-case record, as discussed above. The results of the analysis are presented in Table 46. The concentrations presented in Tables 44 and 46 were used as inputs.

2.5.1. Water Concentrations Selected as Model Inputs. The concentrations of THMs presented in Tables 44 and 46 represent the available water concentration inputs for the exposure and dose analysis. From this dataset, the exposure and dose analysis will be conducted using concentrations presented in Table 44 and 46 for the following variable subgroups:

- The entire dataset,
- The “Surface Water Intake” treatment facilities,
- Treatment plants that include “all chlorine based disinfection,”
- And, “systems sampled between July and September (1997 and 1998).

Within each data set, the concentrations for each THM were selected so that maximum exposure might occur. Under that condition, the “worst case” 95th percentile concentration for each distribution was selected. Given their chemical nature, and because of differences in treatment options, source water characteristics, etc., these compounds are formed at different rates in different systems. Within each category of treatment (i.e., All Systems Using Surface Water Intake), the 95th percentile values for each THM were different, and were somewhat related. In Table 46, the first row indicates that when chloroform is present at the 95th percentile of its distribution, the BDCM is present at the 98th percentile of its distribution, DBCM is present at the 90th percentile of its distribution, and bromoform is present at the 0th percentile of its distribution – treatments that favor the formation of chloroform disfavor the formation of bromoform. When bromoform is present at the 95th percentile for its distribution, then

chloroform is present at the 34th percentile of its distribution, BDCM is present at the 96th percentile of its distribution and DBCM is present at the 98th percentile of its distribution. To simulate a potential worst-case exposure, the exposure model incorporated drinking water THM concentrations at the 95th percentile of their distributions (e.g., chloroform @ 66 ppb, BDCM @ 23.8 ppb, DBCM @ 17.0 ppb and bromoform @ 5.6 ppb).

Each paired set of data will be used and the resulting exposures and doses will be estimated.

2.5.2. Estimated Concentrations in Consumed Tap Water. This section presents the development of reasonable representations of the chemical concentrations in consumed tap water for the four THMs. The volatilization of contaminant occurs during the filling activity, from the water surface while sitting in a glass or storage and as a result of any processing action. Each of these is analyzed below, and a combined volatilization is calculated for a number of scenarios. The results of this calculation are used to recommend estimated fractional volatilization and first order removal rate constants for each chemical.

2.5.2.1. Volatilization During Filling — Volatilization during a filling activity occurs in much the same way as during any other faucet use. There are differences in the volatilization occurring in the pool of water in a partially filled glass of water and the film of water in the bottom of a sink.

The experiments from Howard and Corsi (1996) as well as those performed by Batterman et al. (2000) attempt to quantify this volatilization. Batterman et al. implement an experiment meant to represent an "experimental procedure portray(ing) the filling of a pitcher from the tap and then the filling of a glass from the pitcher." The authors describe the procedure as follows:

> The THM stock solution (2 mg/mL of each THM) was diluted in a filled 4 L black bottle to obtain the test mixture containing 100 µg/L of each THM compound and then transferred to a typical covered water pitcher (Rubbermaid, capacity = 2.34 L, filled to 1.96 L, height = 21.7 cm, dia = 12.2 cm, material = resin) and used to fill glasses and mugs.

According to the authors, the "water transfers were done quickly (3-5 seconds) and at a minimal (2 cm) pouring height."

Unfortunately, neither the quick filling nor the filling height is typical of filling a glass of water for consumption. Filling 1.96 L in 3-5 seconds yields a flowrate in the range of 23.5-39.2 L/min. A typical faucet has a possible flowrate ranging from 0 (user controlled) to approximately 11 L/min, with a typical faucet use being in the range of about 2-8 L/min (Wilkes et al., 2004). The large flowrate used by Batterman et al. would significantly lower the opportunity for volatilization. Although no behavioral studies have been identified that quantify the distance the water must travel, it seems likely from personal experience that 2 cm would represent a reasonable minimum, and a reasonable maximum is probably on the order of 12-15 cm. The combination of the large flowrate and low height of the filling in the Batterman et al. experiment has the effect of significantly lowering volatilization, and therefore this research is not useful in estimating the volatilization during filling.

Howard and Corsi (1996) conducted experiments measuring the volatilization resulting from using the kitchen faucet. The most consequential differences between the Howard and Corsi experiments and the filling of a glass or pitcher for consumption are the larger height of the drop and the potential splashing that could occur when the water lands in the sink. Both of these differences lead to a higher volatilization rate. Howard and Corsi measured the stripping efficiency (percent of the chemical moving from the water to the air during the process of filling the glass or pitcher with tap water) for three compounds: cyclohexane, toluene, and acetone. The chemical properties impacting the volatilization rate for the three compounds measured by Howard and Corsi are given in Table 47. The chemical properties impacting volatilization for the compounds being modeled are given in Table 48. Table 49 summarizes the stripping efficiency measured by Howard and Corsi for the three compounds. These measured values are used as a basis for estimating the stripping efficiency for each THM during filling.

2.5.2.2. Volatilization During Storage — After preparation and prior to consumption, the water may sit in a pitcher in the refrigerator or in a glass or cup on the table. During this period, volatilization occurs at the liquid/air interface. Batterman et al. studied the rate at which this occurred for the four trihalomethanes at a variety of temperatures (4, 25, 30, and 100°C) and in two containers (tall glass, wide mouth glass)

for a 2-hour period. Batterman et al. fit the resulting measurements to an exponential decay model with good results (R^2 values for chloroform ranged from 0.59 to 0.86). Table 50 summarizes these results. The recommended fractions volatilized as a function of time are summarized in Table 51 for three conditions (cold water, room temperature water, and hot water). These data will be used in conjunction with the estimated volatilization during filling to estimate the amount of each THM remaining in the water at the time of consumption.

2.5.2.3. Volatilization During Processing — A wide variety of activities influence the removal of compounds from tap water. These activities include primarily heating and mixing activities that occur when using the water to make coffee, tea, other water based beverages, and in the process of preparing food. Beverages made from tap water fall into two primary categories: heated and non-heated beverages. The non-heated beverages undoubtedly have some volatilization due to the process of mixing the water with any additives, such as orange juice from concentrate. These losses have not been quantified in the literature sources identified above. The heating of water greatly reduces the concentration of volatile constituents. Batterman et al. report an average chloroform loss of 81% resulting from bringing water to 100^{o}C (presumably from room temperature, although this is not stated) in a kettle. After pouring the water into a mug, the measured fraction volatilized is an average of 85%.

2.5.2.4. Recommendations — Similar to volatilization from other water uses, the volatilization during filling is correlated with the chemicals' Henry's Law constant, the liquid phase diffusivity, and the gas phase diffusivity. Table 52 presents a variety of consumption scenarios and estimated volatilization fraction as a result of each scenario for each of the THMs. Table 53 presents recommended values for model inputs for the THMs. The model uses an initial fraction volatilized and a rate constant to estimate the amount of contaminant remaining at the time of consumption. The values presented in Table 53 for the fraction of the compound remaining prior to consumption or storage accounts for an estimate of the average amount volatilized as a result of filling a container with tap water. The rate constant is used by the model to estimate the volatilization during storage or while a glass of water is consumed over an extended period (e.g., used to represent the volatilization from a glass of water over a period like

30 minutes when someone slowly sips the water). The effects of expected heating, stirring and other factors often encountered during food processing activities results in a larger fraction of the original mass being released into the air a for indirect consumption, as reflected in Table 53.

2.6. UPTAKE AND SOLUBILITY PARAMETERS

The PK model requires sets of input parameters by chemical, by exposure, by compartment, by demographic group, and by activity.

2.6.1. Breathing Rates by Activity and Demographic Group. The breathing rates (alveolar ventilation rates, QA) based on the *Exposure Factors Handbook*, Table 5.6 (U.S. EPA, 1997b) are presented in Table 54 for an adult male and female (15-45 years old) and a child of approximately age 6 for two activity levels: resting and sedentary.

2.6.2. Skin Permeability Coefficients for Each Chemical. The skin permeation coefficient, called the Permeability Coefficient of Stratum Corneum, Kp, is required for each chemical to be modeled. For each of the four chemicals of interest, the Kp is given in Table 55. Some of these values remain to be determined and are not available at this time.

2.6.3. Partition Coefficients for Each Chemical. The partition coefficients between the skin and blood and between the blood and air are required for the fundamental uptake modeling in TEM. Partition coefficients for each physiological compartment are given in Table 56 for the four DBPs of interest.

2.7. UPTAKE CALCULATIONS

The dermal uptake calculation implemented in TEM is based on membrane equations developed by Cleek and Bunge (Olin, 1998). This representation uses two simple functions, representing the non-steady-state and steady-state periods. The dermal uptake does not account for issues such as skin hydration and skin temperature.

The ingestion uptake calculation implemented in TEM is based on the estimated water concentrations at the time the water is consumed, and assumes that the entire mass of the chemical in the consumed water is absorbed into the bloodstream.

The inhalation uptake calculation implemented in TEM is based on the predicted air concentrations in the breathing zone. TEM implements an equilibrium calculation

between the inhaled air and the bloodstream. This calculation is described below. The inhalation uptake used for the PBPK model is described in Section 3.2.

2.7.1. Dermal Uptake Calculations. The dermal uptake is dependent upon a number of factors, including the concentration in the water in contact with the skin, the duration of the contact, the temperature of the water, and chemical properties. The water concentration, which is dependent upon the amount of the chemical that has volatilized prior to contact, is assumed to be the concentration in the incoming water for flowing water type exposures (e.g., showers, facuets) and is calculated for the amount volatilized for standing water type exposures (e.g., baths).

Dermal contact with the household water supply occurs primarily during two types of water-using activities: (1) showering and bathing; and (2) faucet use. This study assumes that for any bathing activity, 90 % of the skin is in contact with the contaminated water, and for any faucet use, 5.2% of the skin (hands) is in contact. The body surface areas corresponding to these assumptions are estimated to be 16,920 cm^2 (adult female), 19,400 cm^2 (adult male), and 7930 cm^2 (child) for the entire body (U.S. EPA, 1997a). The contact is assumed to occur for the time period that the water-use is active at the initial water concentration. Water temperature is likely to impact the rate of uptake (Gordon et al., 1997), but is not accounted for in the dermal uptake calculation.

This case study implements the technique presented by Cleek and Bunge (1993), as given by the following equations:

$$M_{in} = AC_w^o \sqrt{\frac{4R_{sc/w}L_{sc}P_{sc}t_{exp}}{\pi}} \qquad \text{when } t_{exp} \geq 2.4t_{lag} \tag{16}$$

and

$$M_{in} = AC_w^o(P_{sc}t_{exp} + R_{sc/w}L_{sc}) \qquad \text{when } t_{exp} \geq 2.4t_{lag} \tag{17}$$

where: M_{in} = mass entering the skin

A = area of skin in contact with water

C_w^0 = concentration of solute in the aqueous solution

t_{exp} = duration of exposure

$R_{sc/w}$ = equilibrium partition coefficient stratum corneum (*sc*) and water (*w*)

L_{sc} = diffusion path length through the stratum corneum (*sc*)

P_{sc} = permeability coefficient of the stratum corneum (*sc*)

$t_{lag} = \frac{R_{sc/w} L_{sc}}{6 P_{sc}}$ = estimated time to reach steady state

2.7.2. Inhalation Uptake Calculations. The inhalation uptake calculated by TEM is based on the assumption that the lung-alveolar and lung blood achieve instantaneous equilibrium at each breath, and that at equilibrium, the partition coefficient given in Table 56 describes the partitioning of the chemicals between the vapor and liquid (blood) phases. The following steps are used to approximate chemical uptake into the blood:

The equilibrium concentrations in the alveolar blood and the alveolar air are as follows:

$$C_{bl,eq} = C_{alv,eq} * P \quad (18)$$

where:

$C_{bl,\ eq}$ = concentration in the lung blood after equilibrium is reached with alveolar air

$C_{alv,eq}$ = concentration in the alveolar air after equilibrium is reached with lung blood

P = Blood/Air partition coefficient.

The equilibrium concentration in the lung blood and alveolar air is calculated by the following equations:

$$C_{bl,eq} = (C_{bi}\, V_{bl} + C_{air}\, V_{alv})/(V_{bl} + V_{alv}/P) \quad (19)$$

and

$$C_{alv,eq} = C_{bl,eq} / P \quad (20)$$

where:

V_{alv} = alveolar volume for a time step = breathing rate multiplied by time step

V_{bl} = lung blood volume for a time step = cardiac output multiplied by time step

C_{bi} = bulk blood concentration at the start of the time step

C_{air} = air concentration entering lungs.

The mass accumulated in the lung blood is assumed to accumulate in the body, and the lung blood concentration is reset to zero between time steps. The cumulative mass accumulated in the body is calculated as follows:

$$\text{Mass absorbed} = \sum \Delta C * V \quad \text{over all time steps} \qquad (21)$$

The air concentration outside the body is assumed to be unaffected by the mass transferred into the blood.

3. PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODEL

PBPK modeling has proven useful in a number of different types of risk assessment applications. Here, it is used to translate external concentrations and exposure doses to internal doses, when the human exposure to four THM compounds is simulated. The modeling approach makes use of the physicochemical properties of the four THMs studies, physiological and anatomic characteristics of the demographic groups evaluated, as well as the chemical-specific biochemical characteristics of interest (e.g., metabolic rate constants). Some definitions of PBPK terms are provided in Table 57.

3.1. MODEL STRUCTURE

The PBPK model for human exposure to THMs consists of seven compartments representing organs or groups of organs: liver, kidney, rapidly perfused tissues, slowly perfused tissues, genitalia, fat, and a gas-exchange lung (Figure 6). Skin is considered to be a barrier in the PBPK model rather than a physiological compartment. The compartments are interconnected by blood flows (Q). All biotransformation is assumed to take place in the liver and follow Michaelis-Menten saturation kinetics. The PBPK model is based on a 5-compartment PBPK model used to analyze the pharmacokinetics of over 30 volatile organic compounds (VOCs) (Gargas et al., 1986, 1990), including the THM chloroform. The PBPK model of Gargas et al. (1986, 1990) has been used as the basis for more detailed PBPK models for chloroform (Corley et al., 1990) and bromodichloromethane (Lilly et al., 1998). In the present study, separate PBPK models for a human adult male, adult female, and 6-year-old male child will be used to analyze tissue concentrations following exposure to THMs through water usage. The physiological parameters are shown in Table 58. Because of concern for the potential for developmental toxicity and reproductive toxicity of these compounds, the PBPK model has been developed to include specific compartments for testes and ovary tissues. In addition, it focuses on adults of reproductive age, broadly defined as ages 15-45. A single set pf parameter values for physiologic parameters (i.e., testes, as percent of body weight) can be developed, inasmuch as these values do not change appreciably with age – between ages 15 and 45. However, because of the rapid growth

during childhood, with its accompanying changes in organ size and relative blood flow, a single set of parameter values cannot be developed that would be descriptive of the child at various ages. Thus, the present endeavor was limited to the hypothetical 6-year old male child. The chemical-specific parameters for each of the four THMs are shown in Table 59. Simulations of the PBPK model will be done using acslXtreme software (Aegis Technologies, Huntsville, AL).

The most information about the solubility of the THMs in human tissues is available for chloroform, where partition coefficients have been directly measured in several human tissues (U.S. EPA, 2003). The human blood:air partition coefficients for the other three THMs have been measured (Batterman et al., 2002), but solubility measurements have not been made in other human tissues. Therefore, the human blood:air partition coefficients for the three THMs have been divided by rat tissue:air partition coefficients (da Silva et al., 1999) to obtain estimated human blood:tissue partition coefficients (Table 59). Information regarding the solubility of the THMs in human reproductive tissues was not available, so the solubilities of the THMs in these tissues (testes, ovaries) were calculated based on tissue lipid and water content using the algorithms of Krishnan (2002). These calculated tissue:air partition coefficients were divided by the appropriate measured blood:air partition coefficients to yield estimates of the testes:blood and ovaries:blood partition coefficients (Table 59).

3.2. MASS BALANCE EQUATIONS

For each of the 4 THMs, the rate of change of the concentration in arterial blood (*d*CA/*dt*; Equation 22) is described by accounting for the influx of the THM in arterial blood from the lung (CI), the venous concentration of the THM (CV) and dermal exposure (DD):

$$dCA/dt = (QC * CV + QP * CI)/(QC + (QP/PB)) + DD \quad (22)$$

where QC is cardiac output, QP is the alveolar ventilation rate, PB is the blood:air partition coefficient for each THM, and DD is the dermal dose. The DD was calculated by TEM as described in Section 2.7 using the membrane equations developed by Cleek and Bunge and the skin permeability coefficients given in Table 55. When dermal exposures occurred in the activity scenarios, the dermal dose was calculated for each

5-minute exposure interval. The results of the TEM dermal exposure calculations were then inputted to the PBPK model at each 5-minute interval for the duration of the dermal exposure episode.

The rate of change of the amount of each THM in non-metabolizing tissues (*d*AT/*dt*; Equation 23) (kidney, fat, genitalia, rapidly perfused, and slowly perfused) is described by:

$$dAT/dt = QT(CA - CVT) \quad (23)$$

where QT is the blood flow to tissue T and CVT is the venous blood concentration of the THM leaving tissue T. The concentration of each THM in the venous blood leaving tissue T (CVT; Equation 24) is given by:

$$CVT = AT/(VT * PT) \quad (24)$$

where AT is the amount of each THM in tissue T, VT is the volume of tissue T, and PT is the partition coefficient of each THM in tissue T.

The rate of change of the amount of each THM in the metabolizing tissue liver (*d*AL/*dt*; Equation 25) is described by:

$$dAL/dt = QL(CA - CVL) - RAM + RAO \quad (25)$$

where QL is blood flow to the liver, CVL is the venous blood concentration of the THM leaving the liver (described by Equation 24), RAM is the rate of metabolism (discussed in Section 3.3) and RAO is the rate of oral absorption. RAO is a first-order process described by Equation 26:

$$RAO = KA * DOSE * e^{(-KA * t)} \quad (26)$$

where KA is the oral absorption rate constant for each THM, DOSE is the amount of THM administered orally, and t is time.

The concentration of each THM in venous blood (CV; Equation 27) is described by:

$$CV = (QF * CVF + QL * CVL + QK * CVK + QG * CVG + QR * CVR + QS * CVS)/QC \quad (27)$$

where Q is blood flow and CV is the venous blood concentration leaving each tissue F (fat), L (liver), K (kidneys), G (genitalia), R (rapidly perfused) and S (slowly perfused).

The overall mass balance for each THM in the PBPK model is given by the sum of the amount of the THM in each tissue or tissue group.

3.3. RELATIONSHIP BETWEEN THM METABOLISM AND TOXICITY

The target organ toxicity produced by chloroform requires metabolic activation by cytochromes P450, specifically CYP2E1 (Constan et al., 1999). The oxidative bioactivation of chloroform proceeds via CYP2E1 oxidation to trichloromethanol, which eliminates HCl to form phosgene (Pohl et al., 1980). Phosgene is likely to be the reactive metabolite that acylates proteins (Potts et al., 1949) to produce hepatic centrilobular necrosis and renal proximal tubular necrosis (Ilett et al., 1973). An analogous oxidative bioactivation occurs with the brominated THMs involving elimination of HBr and formation of brominated analogues of phosgene or phosgene itself in the case of bromodichloromethane (Lilly et al., 1997). Oxidation of the lower energy C-Br bond would occur more readily than oxidation of the C-Cl bond (March, 1968). The most appropriate dosimeter for the metabolite-mediated hepatic toxicity of the THMs is CM_{24}, the concentration of metabolites produced in the liver over 24 hours. CM_{24} represents the integrated exposure of the liver to the reactive metabolites of THM oxidation by CYP2E1 over 24 hours. The reactive metabolites formed from THM oxidation (phosgene and its brominated analogs) are transient and do not accumulate in the liver. Thus, CM_{24} represents exposure of the liver to the metabolites, not the concentration of metabolites in the liver at any given time.

Local metabolic activation of the THMs in the extrahepatic target organs kidney and genitals may occur. Renal metabolism has been observed with chloroform (Corley et al., 1990; Constan et al., 1999) and BDCM (Lily et al., 1997, 1998). Extrahepatic metabolism was not described in the present PBPK model for the THMs because the enzymes involved and the kinetics of these potential metabolic pathways have not been characterized. Therefore, the area under the curve (AUC) for the parent THMs provides the most appropriate dosimeter for the exposure of the extrahepatic target tissues kidneys and genitals to each THM. The AUC represents the integrated exposure of the organ to the parent THM over 24 hours.

3.4. METABOLIC INTERACTIONS

The cytochrome P450 2E1 isoform (CYP2E1) is the principal catalyst of the oxidative metabolism of the THMs (Guengerich et al., 1991; Raucy et al., 1993). This has been unequivocally demonstrated for chloroform (Constan et al., 1999) and bromodichloromethane (Allis and Zhao, 2002; Zhao and Allis, 2002) and inferred for dibromochloromethane and bromoform (da Silva et al., 1999). The oxidative bioactivation of chloroform proceeds via CYP2E1 oxidation to trichloromethanol, which eliminates HCl to form phosgene (Pohl et al., 1980). Phosgene is likely to be the reactive metabolite that acylates proteins (Potts et al., 1949) to produce hepatic centrilobular necrosis and renal proximal tubular necrosis (Ilett et al., 1973). An analogous oxidative bioactivation occurs with the brominated THMs involving elimination of HBr and formation of brominated analogues of phosgene or phosgene itself in the case of bromodichloromethane (Lilly et al., 1997). Oxidation of the lower energy C-Br bond would occur more readily than oxidation of the C-Cl bond (March, 1968). While the lower energy of the C-Br bond would also be expected to allow nucleophilic displacement of Br by glutathione S-transferases (Ross and Pegram, 2003), this study will focus on the oxidative bioactivation pathways of the THMs. In addition, because the GST-mediated pathway is not active for each of these compounds, because it is expected that the oxidative pathway accounts for a substantially higher fraction of a metabolized dose of compounds that are also metabolized by this pathway, and because this study focuses on estimating internal dose without estimating toxicity or risk, this approach seems valid.

Corley et al. (1990) postulated that high concentrations of chloroform produced inactivation of cytochrome P450 via metabolic activation. They inferred this suicide inactivation pathway from gas uptake studies with mice where metabolic uptake was observed to decrease after several hours exposure to 10,000 ppm chloroform. The suicide inactivation pathway was not invoked for rats or humans (Corley et al., 1990). However, there is no direct evidence for inactivation of cytochrome P450 by chloroform. Experiments at CIIT with isolated mouse hepatocytes *in vitro* were not consistent with cytochrome P450 inactivation by chloroform (Kedderis and Held, unpublished observations; Kedderis et al., 1993; Held et al., 1994). The freshly isolated cells were

incubated with high but sublethal (Ammann et al., 1998) concentrations of chloroform (~1 mM) for 2 hours, washed in fresh medium by centrifugation, resuspended in fresh medium, and assessed for viability by microscopy and metabolic capability toward chloroform by gas chromatography. Treatment with chloroform under these conditions did not affect cell viability or the metabolic capacity of the cells toward chloroform (Kedderis and Held, unpublished observations). These results suggest that the suicide inactivation pathway for cytochrome P450 postulated by Corley et al. (1990) is not operative in mice. Necropsy of mice following gas uptake studies at 10,000 ppm chloroform revealed macroscopic and microscopic evidence of liver toxicity (Kedderis and Held, unpublished observations), suggesting that acute liver injury rather than inactivation of cytochrome P450 was responsible for the decreased metabolism of chloroform observed by Corley et al. (1990) in their gas uptake studies. Therefore, the postulated suicide inactivation of cytochrome P450 by chloroform was not included in the PBPK model used in this study to describe THM metabolism.

Since the THMs are all substrates for CYP2E1, mutual competitive inhibition of metabolism is expected to occur. During mixed exposures to the THMs, each THM would inhibit the bioactivation of the other THMs that are alternative substrates for CYP2E1. For competitive alternative substrate inhibition, the inhibition constant for each substance would be the same as the K_M, the substrate concentration giving one-half the maximal velocity (V_{max}) (Segel, 1975). For each THM, the general rate equation describing metabolism in the presence of 3 competitive inhibitors (Segel, 1975) is given in Equation 28:

$$RAM1 = (Vmax1 * CVL1)/(KM1 * (1 + CVL2/KM2 + CVL3/KM3 + CVL4/KM4) + CVL1) \quad (28)$$

where RAM1 is the rate of metabolism of THM1, Vmax1 is the maximal rate of metabolism of THM1, KM*i* is the Michaelis constant for each THM*i* (*i* = 1-4), and CVL*i* is the venous blood concentration of THM*i* leaving the liver (*i* = 1-4). CVL represents the concentration of the substrates presented to the liver for metabolism via hepatic blood flow, and thus is equivalent to the substrate concentration in the Michaelis-Menten equation. The rate of metabolism of each THM would be given by a separate equation

analogous to Equation 28 for RAM2, RAM3, and RAM4. The values of Vmax and KM used in the PBPK model are given in Table 60.

Michaelis-Menten kinetic parameters (Vmax, K_M) are obtained from experiments where the concentration of the substrate is varied under conditions where the initial rate of the enzyme-catalyzed reaction is linear with time and added source of enzyme (Kedderis, 1997). This experimental approach can be used *in vitro* with a variety of systems including isolated cells, tissue homogenates or subcellular fractions, or purified enzymes. The *in vitro* data can be extrapolated to the intact organism based on hepatocellularity or enzyme content, since the initial rates of enzyme-catalyzed reactions are directly proportional to the enzyme content (Kedderis, 1997). Michaelis-Menten kinetic parameters can also be estimated from *in vivo* pharmacokinetic studies but in general it is difficult to obtain accurate estimates of the kinetic parameters from *in vivo* data, particularly for rapidly metabolized compounds like the THMs. The difficulties arise from the inhomogeneous distribution of substrates in tissues, incomplete absorption of substrates from the gastrointestinal tract and other barriers, excretion pathways that compete with metabolism such as exhalation of the substrate, and the limitation of metabolism by blood flow delivery to the liver. The hepatic blood flow limitation of metabolism essentially prevents accurate measurement of the initial rate of metabolism of rapidly metabolized compounds such as the THMs (Kedderis, 1997). *In vivo* pharmacokinetic studies with rapidly metabolized chemicals can yield reasonable estimates of Vmax but generally the estimates of K_M values are upper limits. This is because other processes such as blood flow limit the overall rate of metabolism of the chemical and essentially mask the more rapid initial rate of metabolism (Kedderis, 1997). The chloroform kinetic parameters in Table 60 were obtained from *in vitro* experiments with human liver microsomes from adults and children (U.S. EPA, 2006). Other PBPK models for chloroform report much higher values for K_M. This is explained by PBPK model optimization routines which communicate only the highest value that provides an adequate fit to the data. The present work incorporated biochemically-derived values for K_M, extrapolated from *in vitro* studies conducted with samples of rat and human liver microsomal preparations (Lipscomb et al., 2005; U.S. EPA, 2006). Both the previously available (optimized) values and the presently-developed lower

(biochemically-derived) values provide adequate fit to the observed data (not shown). The parameters for the other THMs were estimated from *in vivo* gas uptake studies in rats (da Silva et al., 1999) and assumed to be the same for humans. The K_M values for the brominated THMs in Table 60 are likely to be upper limits. Lower values of K_M (i.e., more rapid initial rates) are likely to fit the gas uptake data just as well as the upper limits. Human metabolic data for the brominated THMs were not available.

4. TRANSFER FILE DEFINITIONS

The exposure model (TEM) and the PBPK model communicate by passing parameters, media concentrations, physiological, and other necessary data in "transfer files." These transfer files are text files (ASCII) formatted such that the data are passed in fixed column format. Each model run, which encompasses the model predictions for a single household simulation, in this case a family of three, generates a group of files with related filenames. A description of the file naming convention is given in Table 61. Each of the files listed in Table 61 contains data in a fixed column format. For each of the file types listed in Table 61, a description of the file format is presented below:

4.1. BREATHING RATE FILES

The breathing rate files contain a definition of the time-varying breathing rate of the subject. The file format is a comma separated ASCII file with the following characteristics:

- Each line contains a record of the subject's breathing rate for a time interval. The first number is the time that the breathing rate interval started in hours, the is the breathing rate in L/hour. These numbers are separated by commas.
- A breathing rate defined by a given line is in effect until the start time of the subsequent line in the file.
- Any line that contains a semi-colon (;) in the first column is ignored (indicates a comment).

Example: The data for a scenario where the breathing rate is modeled as 540 L/hour from midnight to 7:05 am, 600 L/hour from 7:05 am to 10:40 pm, and 540 L/hour from 10:40 pm to midnight. The resulting breathing rate data file contained the following data:

```
; THIS IS THE Breathing Rate FILE IN THE FOLLOWING FORMAT
; TIME(hours),Breathing Rate (L/hour)
0.000000,540.000000
7.08333,600.000000
22.6667,540.000000
```

4.2. DERMAL DATA FILES

The dermal data files contain a definition of the time-varying doses due to water contact with portions of the subject's skin along with the time and duration of the event. The file format is a comma separated ASCII file with the following characteristics:

- Each line contains a record of an exposure event with the first number being the time that the dermal exposure event started in hours, the second number is the dose in µg, and the third number is the duration of the event in hours. These numbers are separated by commas.
- Any line that contains a semi-colon (;) in the first column is ignored (indicates a comment).

Example: The data for a scenario where three dermal exposure events occur: (1) from 6:00 to 6:04:21 am, the dose is 0.0000125 µg corresponding to a handwashing activity; (2) from 6:09:00 to 6:16:30 am, the dose is 0.000085 µg, corresponding to a showering activity; and (3) 7:22:30 to 7:23:41 am, the dose is 0.00000164 µg, corresponding to a handwashing activity. The resulting breathing rate data file contained the following data:

```
; THIS IS THE Dermal Contact FILE IN THE FOLLOWING FORMAT
; TIME(hours),Dose(µg),Duration(hours)
6.000000,1.24726e-005,0.0725
6.15,8.5e-005,0.125
7.375,1.64623e-006,0.019722
```

4.3. INGESTION DATA FILES

The ingestion data files contain a definition of the ingestion doses due to water consumption. The file format is a comma separated ASCII file with the following characteristics:

- Each line contains a record of an consumption event with the first number being the time that the event started in hours, followed by an "I" or a "D" indicating either direct or indirect consumption, followed by the dose due to the consumption event in µg, and then followed by the duration of the event in hours. These numbers are separated by commas.
- Any line that contains a semi-colon (;) in the first column is ignored (indicates a comment).

Example: The data for a scenario where three ingestion exposure events occur: (1) from 5:39:50 to 5:40:20 am, ingestion route is direct, and the dose is 0.00009663 µg; (2) from 6:47:50 to 6:50:10 am, ingestion route is indirect, and the dose is 0.000007059 µg; and (3) 7:41:50 to 7:43:23 am, ingestion route is indirect, and the dose is 0.0000585795 µg. The ingestion data file contained the following data:

```
; THIS IS THE Consumption Rate FILE IN THE FOLLOWING FORMAT
; TIME(hrs),I or D for Indirect or Direct, Consumption Mass (µg), Duration (hrs)
5.6639,D,9.6663e-005,0.00333
6.7972,I,7.05986e-006,0.03888
7.6972,I,5.85795e-005,0.02583
```

4.4. INHALATION DATA FILES

The inhalation data files contain a definition of the time-varying inhalation concentrations. The file format is a comma separated ASCII file with the following characteristics:

- Each line contains a time-varying record of an inhalation concentrations with the first number being the time that the event started in hours, the second number is the current inhaled concentration in µg/m^3. These numbers are separated by commas.
- Any line that contains a semi-colon (;) in the first column is ignored (indicates a comment).

Example: The data for an example 24-hour period are presented as follows:

```
; THIS IS THE Chloroform Concentration FILE IN THE FOLLWING FORMAT
; TIME(hours),Chloroform Concentration(µg/m3)
0.0000,1.8506283E-04
3.2500,1.6588291E-04
4.3375,1.9244952E-04
4.8375,2.1207979E-04
5.8375,2.3687192E-04
7.8375,2.5063853E-04
8.0833,3.3065418E-04
8.1250,3.9391501E-04
8.1708,7.4332117E-04
8.2167,9.3008879E-04
8.4667,2.5130055E-04
9.1708,2.9071942E-04
9.9208,3.2748350E-04
12.9208,3.4774606E-04
13.1708,0
15.8417,8.9983922E-03
15.9208,9.4782892E-03
15.9500,1.1975224E-02
15.9708,1.3346261E-02
16.1333,1.5013896E-02
16.2250,1.6454347E-02
16.3167,8.0999167E-04
16.4167,9.6454433E-04
16.5125,1.0124308E-03
16.5875,1.2882611E-03
16.7500,1.7599108E-03
17.0000,3.0958622E-04
21.9792,2.7701297E-04
24.0000,2.5127959E-04
```

Note: The concentration reported at 13.1708 as 0 reflects the subject location of outdoors. The outdoor concentration is assumed to be zero.

5. RESULTS

5.1. EXPOSURE TO THE THMs THROUGH WATER USAGE

5.1.1. Water Concentrations. The analyses presented in Section 2.5, Table 46, provided the basis for selecting representative water concentrations for the THMs. Considering a variety of factors, including the effect of chlorination, the impact of organics found at higher levels in surface water systems, and the impact of the warmer summer period on the formation of DBPs in the drinking water distribution system, we chose to limit our set of data to investigate these factors. The pertinent concentrations from our analyses are presented in Table 62.

To maximize the likelihood of identifying chemical interactions, we biased our investigation to rely on the highest from among several possible measures of an upper bound for THM concentration data. The ICR database was analyzed to determine which factors resulted in higher values for the 95th percentile for the distribution of resulting individual THM compounds. The ICR database evaluated drinking water treatment and can be characterized in several ways. Table 62 presents some of the more conventional categorization of the systems. Systems were initially divided into either systems relying on groundwater or surface water as source water. Systems relying on groundwater demonstrated lower values for concentrations at the 95th percentile of the distribution (data not shown). Reliance on chlorine, rather than ozone as primary disinfectant resulted in appreciably higher levels of THM compounds formed (ozonation results not shown). With respect to timing of the sampling period, samples taken between July and September (summer months) demonstrated higher concentrations of THM compounds than samples taken at other times during the year (data from other seasons not shown). Further subdivision of systems into categories (i.e., systems employing ozonation and relying on groundwater as source water) was not undertaken, in part due to a reluctance to further reduce the number of samples available for distributional analysis. Finally, the complete database was analyzed.

After a closer inspection of the concentration data, it was clear that there is very little difference between three of the four subgroups (Surface Water Intake, Systems using Chlorine, and All Samples). Furthermore, the concentrations reported in the

"Systems Sampled between July and September" exhibit the largest concentrations at the 95th percentile of these subgroups. Since we are examining the effect of these contaminants, we are limiting our analysis to the July to September subgroup.

5.2. INTERNAL DOSES OF THE THMS FROM WATER USAGE: AN ILLUSTRATIVE CASE RESULTS

As a method of demonstrating the predicted water-use behavior, the result from one of the cases will be presented. We chose a case that demonstrated a variety of water uses to show how the water-use behavior and occupant activities leads to air concentrations and exposure by each of the three routes (inhalation, ingestion, and dermal). For this purpose, simulation case 48 was chosen. The demographic characteristics of the sampled and modeled individuals are presented in Table 63. The water uses modeled for this simulation are given in Table 64.

Table 64 is broken down by location. The first line indicates that the kitchen dishwasher was started by the female. The dishwasher was turned on at approximately 10:17 a.m. (10.29 hours past midnight), and ended 74.9 minutes later at approximately 11:31 a.m. (11.527 hours past midnight). This dishwasher event is indicated in the upper panel of Figures 7-13 which demonstrate room air concentrations and personal air concentrations of the four THMs. Personal air concentration profiles differ from room air profiles due to the influence of the human activity pattern – humans move from room to room during the course of the day. A series of three master bathroom events for the female occurred in series beginning at approximately 9:30 a.m. These events may have been "brushing teeth", "washing hands" and "drying hands" for example.

The water uses and the resultant air concentrations predicted in each of the modeled compartments are displayed in Figures 7 through 10 for chloroform, BDCM, DBCM and bromoform, respectively. In addition, the personal concentration in the breathing zone of each occupant, determined by the model by considering the predicted air concentrations along with the location of the occupant throughout the day, are given in Figures 11 through 13 for the adult male, the adult female and the child, respectively. The personal air concentrations provided in Figures 11, 12, and 13 are a union between the predicted air concentrations given in Figures 7, 8, 9 and 10 and the location of each occupant in the home. In addition, the personal air concentration is assumed to be zero if the occupant is outside of the home. The movement from one location in the house

with a lower air concentration to another location with a higher air concentration leads to the sharp rise in personal air concentration shown in Figures 11, 12, and 13.

The resultant concentrations internal doses for this case are shown to demonstrate the predictions. As discussed below, the concentration of metabolites produced in the liver over 24 hours (CM_{24}) was used as the internal dosimeter for THM bioactivation. The CM_{24} is given in Figures 14-16 for the male, female, and child, respectively. Also, as discussed below, the AUC for the parent THMs provides the most appropriate dosimeter for the exposure of the non-metabolizing target tissues kidneys and genitals to each THM. Figures 17-19 show the predicted AUC for the kidneys for each of the three subjects, and Figures 20-22 show the predicted AUC for the genitals for each of the three subjects.

5.3. INTERNAL DOSES OF THE THMS FROM WATER USAGE: POPULATION-BASED RESULTS

The simulation predictions (results) for absorbed dose are analyzed for each chemical as a function of route (dermal, ingestion, and inhalation) and presented in the following sections. For each chemical, a table containing the absorbed dose is presented as a function of route, population group, and percentile of the population. In addition, the cumulative distribution function is plotted along with histograms.

Tables 65-68 present the predicted distribution of total absorbed dose (mg) for the four THM compounds, as well as the predicted dose via route. In order to compare doses per kg body mass, the total absorbed dose at the 50th percentile for each THM was divided by body weight used for PBPK modeling (given in Table 58). For chloroform, the doses at the 50th percentile were 0.0044, 0.0052 and 0.0078 mg/kg for the adult female, adult male and child, respectively. For BDCM, the doses at the 50th percentile were 0.0014, 0.0017 and 0.0026 mg/kg, respectively. For DBCM, the doses at the 50th percentile were 0.00094, 0.0012 and 0.0016 mg/kg, respectively. For bromoform, the doses at the 50th percentile were 0.00029, 0.00035 and 0.00049 mg/kg, respectively.

5.3.1. Population Results for Chloroform. Table 65 presents the predicted absorbed dose of chloroform from the analysis of the dermal, ingestion and inhalation exposure routes for each of the population groups: female age 15-45, male age 15-45, and child age 6. Figures 23, 24 and 25 present the histograms for absorbed dermal dose,

inhalation dose, and ingestion dose, respectively, for the female, male and child populations. Figure 26 presents the total absorbed chloroform dose.

5.3.2. Population Results for BDCM. Table 66 presents the predicted absorbed dose of BDCM from the analysis of the dermal, ingestion and inhalation exposure routes for each of the population groups: female age 15-45, male age 15-45, and child age 6. Figures 27, 28 and 29 present the histograms for absorbed dermal dose, inhalation dose, and ingestion dose, respectively, for the female, male and child populations. Figure 30 presents the total absorbed BDCM dose.

5.3.3. Population Results for DBCM. Table 67 presents the predicted absorbed dose of DBCM from the analysis of the dermal, ingestion and inhalation exposure routes for each of the population groups: female age 15-45, male age 15-45, and child age 6. Figures 31, 32 and 33 present the histograms for absorbed dermal dose and inhalation dose, respectively, for the female, male and child populations. Figure 34 presents the total absorbed DBCM dose.

5.3.4. Population Results for Bromoform. Table 68 presents the predicted absorbed dose of bromoform from the analysis of the dermal, ingestion and inhalation exposure routes for each of the population groups: female age 15-45, male age 15-45, and child age 6. Figures 35, 36 and 37 present the histograms for absorbed dermal dose, inhalation dose, and ingestion dose, respectively, for the female, male and child populations. Figure 38 presents the total absorbed bromoform dose.

5.4. METABOLIC INTERACTIONS BETWEEN THE THMs

Since the THMs are all substrates for the same isoform of cytochrome P450, CYP2E1 (Guengerich et al., 1991; Raucy et al., 1993), the THMs are expected to be alternative substrate competitive inhibitors upon coexposure. The inhibition constants for each THM are the same as their K_M values (Segel, 1975). The extent of inhibition observed during an exposure event will depend upon the exposure concentrations of the THMs and the capacity of the metabolizing enzyme CYP2E1.

The metabolic interactions between the THMs were investigated using NHAPS water-use activity pattern 728 for the male subject, which was the 86th percentile for both chloroform and DBCM exposures. Data sets of the four THM concentrations corresponding to the 95th percentile for each THM were determined from the complete

data set for water systems sampled from July to September 1997-1998 and used to investigate the interactions between the THMs. Use of near-maximally expected concentrations was accomplished to maximize the likelihood of detecting metabolic interactions. Interactions observed under these circumstances would indicate a need to closely examine the possibility of interactions at lower concentrations/doses. Lack of interaction at these (high) exposures would indicate that interactions at lower concentrations/doses would not be anticipated. The concentration data sets are shown in Table 69. Concentrations corresponding to the 95th percentile for each THM were chosen to represent those concentrations having the maximum potential for interactions of all the THM concentration data.

The present report surpasses the level of detail previously developed (U.S. EPA, 2003), in that metabolic interactions have been examined. Metabolic interactions between the THMs were investigated by simulating the exposure to each THM individually and comparing the results to simulations of exposure to all the THMs together (Table 69) for each water concentration scenario sampled July-September 1997 and 1998 (see Table 46). Since metabolism represents bioactivation for each of the THMs, the concentration of metabolites produced in the liver over 24 hours (CM_{24}) was used as the internal dosimeter for THM bioactivation. Under these exposure conditions, inhibition of the metabolic activation of the THMs was not observed with the 95th percentile water concentration scenarios for chloroform, BDCM, or bromoform. A very slight inhibition of DBCM bioactivation (0.0001%) was observed with the DBCM 95th percentile water concentration scenario (Table 70). The inhibition of DBCM bioactivation was due to the combination of chloroform and BDCM (Table 70), as each THM alone did not produce any inhibition of metabolism under these exposure conditions.

One reason that metabolic interactions were not evident between the four THMs may be that the metabolic capacity of CYP2E1 was large enough to metabolize all of the THMs the subject was exposed to from the water-use scenarios. This hypothesis was tested by lowering the capacity of CYP2E1 in the PBPK model by decreasing Vmaxc, since the maximal velocity of an enzyme-catalyzed reaction is directly proportional to the amount of enzyme present and is an indication of the amount of

active enzyme (Segel, 1975). Table 71 shows that as CYP2E1 capacity (Vmaxc) decreased, more inhibition of THM metabolism became evident. These results are consistent with the interpretation that the lack of metabolic interactions between the THMs following exposure from water usage was due to the large capacity of the metabolizing enzyme, CYP2E1. However, the extent of inhibition of THM metabolism was only approximately 0.2% at most after lowering Vmaxc by a factor of one million (Table 71). At such a low enzyme capacity, the exposure of the liver to THM metabolites (indicated by CM_{24}) became vanishingly small. Taken together, these results indicate that inhibitory interactions between the four CYP2E1 substrate THMs would not be expected to be significant under the low level, intermittent exposures encountered through water use in the home setting.

5.5. INFLUENCE OF WATER-USE PATTERNS ON INTERNAL DOSIMETRY FOR THE THMs

Just as external exposure to the THMs was dependent upon water use patterns, the internal dosimetry of the THMs was also dependent upon water use patterns. In the present PBPK model for the THMs, metabolism was assumed to only take place in the liver and not in the extrahepatic target organs. While the vast majority of THM metabolism does take place in the liver such that the overall pharmacokinetics of the THMs can be accurately described assuming that metabolism only takes place in the liver (da Silva et al., 1999), local metabolism of the THMs in the extrahepatic target organs kidney and genitals may occur. Renal metabolism has been observed with chloroform (Corley et al., 1990; Constan et al., 1999) and BDCM (Lily et al., 1997, 1998). Extrahepatic metabolism was not described in the present PBPK model for the THMs because the enzymes involved and the kinetics of these potential metabolic pathways in these organs have not been quantified. Because of this limitation, the AUC for the parent THMs provides the next most reliable dosimeter for the exposure of the extrahepatic target tissues kidneys and genitals to each THM. The AUC (mg-hr) represents the integrated exposure of the organ to the parent THM over 24 hours. The distributions of the AUCs for each of the four THMs in the male, female and child subjects are shown in Figures 39-42 for the kidney and in Figures 43-46 for the genitals.

The most appropriate dosimeter for exposure of the metabolizing target organ liver is CM_{24}, the concentration of metabolites produced in the liver over 24 hours. CM_{24}

represents the integrated exposure of the liver to the reactive metabolites of THM oxidation by CYP2E1 over 24 hours. The reactive metabolites formed from THM oxidation (phosgene and its brominated analogs) are transient and do not accumulate in the liver. Thus, CM_{24} represents exposure of the liver to the metabolites, not the concentration of metabolites in the liver at any given time. The distributions of the CM_{24} values for each of the four THMs in the livers of the male, female and child subjects are shown in Figures 47-50. The distributions of CM_{24} in the liver for the THMs were similar to the distributions of the AUCs for the parent THMs in extrahepatic tissues.

5.6. LIMITED SENSITIVITY ANALYSIS OF THE PBPK MODEL

The sensitivity of the PBPK model to changes in selected parameter values was determined from simulations of exposure of an adult male to the THMs from water usage described by activity scenario 2, which involves household activities leading to inhalation, dermal and oral ingestion exposures to the THMs. Sensitivity was estimated by varying the values of QCC (cardiac output, L/hr/kg) and QLC (liver blood flow, fraction of cardiac output) on the concentration of metabolites in the liver (CAM, mg/L) and the area under the curve for the liver concentration of the parent THM (AUCL, mg-hr). Since TEM specifies the values of QPC (alveolar ventilation, L/hr/kg) used in the PBPK model, the effects of systematically varying QPC could not be readily determined at this time, but those effects are anticipated to be similar to the effects of varying QCC since these two physiological parameters are linked. Additionally, sensitivity to changes in the metabolic parameters VmaxC (mg/hr/kg) and KM (mg/L) for chloroform and bromoform were determined.

The CAM for both chloroform and bromoform was not sensitive to changes in VmaxC in the range of 2 to 20 mg/hr/kg (Figures 51 and 52). Similar results are expected for bromodichloromethane and dibromochloromethane. These results are consistent with the interpretation that the rate of THM metabolism in the liver is limited by the rate of hepatic blood flow (Figures 53-56). Figures 51 and 52 clearly demonstrate that VmaxC values greater than 2 mg/hr/kg do not significantly increase CAM. Thus, interindividual variability in VmaxC (a reflection of variability in enzyme content) at values greater than approximately 2 mg/hr/kg would not translate to interindividual variability in THM metabolism or CAM (a risk-related endpoint), as has

been previously been demonstrated in PBPK simulations for chloroform (U.S. EPA, 2004). In contrast, the AUCL for parent chloroform (Figure 57) and bromoform (Figure 58) decreased with increasing VmaxC. Similar results are expected for bromodichloromethane and dibromochloromethane. As expected, increasing metabolism strongly affected the concentration of the parent THM in the liver.

Increasing the value of KM, the Michaelis constant for metabolism that represents the THM concentration that yields one-half the Vmax, decreased the values of CAM and increased the values of AUCL for chloroform and bromoform (Figures 59-62). Similar results are expected for bromodichloromethane and dibromochloromethane. The effect of increasing KM is to essentially decrease the initial rate of metabolism V/K. The sensitivity of CAM and AUCL to KM also reflects the relatively low levels of THM exposure in the water usage exposure scenario, such that the THM tissue concentrations are well below metabolic saturation.

Figures 63-66 show the effects of varying QCC on the CAM for each of the four THMs. Figures 67-70 show the effects of varying QCC on the AUCL for each of the four THMs. In general, as QCC increased, the values of CAM and AUCL for each of the four THMs increased. This is because increased blood flow increased the amount of each THM in the liver. This is further illustrated by the effects of varying liver blood flow, QLC (Figures 53-56, 71-74). As liver blood flow increases, more of each THM is brought to the liver, increasing both CAM and AUCL.

The CAM for both chloroform and bromoform was not sensitive to changes in VmaxC in the range of 2 to 20 mg/hr/kg (Figures 51 and 52). Similar results are expected for bromodichloromethane and dibromochloromethane. These results are consistent with the interpretation that the rate of THM metabolism in the liver is limited by the rate of hepatic blood flow (Figures 53-56). Figures 51 and 52 clearly demonstrate that VmaxC values greater than 2 mg/hr/kg do not significantly increase CAM. Thus, interindividual variability in VmaxC (a reflection of variability in enzyme content) at values greater than approximately 2 mg/hr/kg would not translate to interindividual variability in THM metabolism or CAM (a risk-related endpoint), as has been previously been demonstrated in PBPK simulations for chloroform (EPA, 2004). In contrast, the AUCL for parent chloroform (Figure 57) and bromoform (Figure 58)

decreased with increasing VmaxC. Similar results are expected for bromodichloromethane and dibromochloromethane. As expected, increasing metabolism strongly affected the concentration of the parent THM in the liver.

Increasing the value of KM, the Michaelis constant for metabolism that represents the THM concentration that yields one-half the Vmax, decreased the values of CAM and increased the values of AUCL for chloroform and bromoform (Figures 59-62). Similar results are expected for bromodichloromethane and dibromochloromethane. The effect of increasing KM is to essentially decrease the initial rate of metabolism V/K. The sensitivity of CAM and AUCL to KM also reflects the relatively low levels of THM exposure in the water usage exposure scenario, such that the THM tissue concentrations are well below metabolic saturation.

6. DISCUSSION

This modeling study allows examination of several factors central to the manner in which people are exposed to the four THMs and how these chemicals are regulated. In this study, specific population groups were modeled to compare the effects of chemical-specific processes (including mass-transfer effects and their effects on route-specific exposures and uptake); the effects of physiological processes; and the effects of activity patterns. Because the entire population was subjected to the same water concentrations, the effects of differing activity patterns across the same population group provides insight into the role activities play in the eventual dose.

The four THMs represent a moderately broad range of volatilities, as evident in the range of values for the dimensionless Henry's Law constant (0.15 to 0.022) and the vapor pressures (160 mm Hg to 5.6 mm Hg) between chloroform and bromoform (see Table 4). These chemicals are found in the drinking water supply at considerably different concentrations. Generally, chloroform is found at the highest concentrations, while the other THMs are generally found at progressively lower concentrations as the number of chlorine atoms decreases and the number of bromine atoms increases. In addition to volatility, other chemical properties, such as partition and permeability coefficients, also impact the magnitude of route-specific exposure and uptake, as well as the removal rates of each of the THMs.

The variability in the predicted absorbed dose, given in Figures 23-34 and Tables 65-68 is largely due to differences in activity patterns across a given population group. Other effects, including variations in house size and interzonal airflows, have lesser effects on the variation in absorbed dose across the population. It is evident from the results in the figures that the variation across the population is largely attributable to the inhalation route, which has a far larger range of exposures and doses for all four THMs. Wilkes et al. (1996) closely examined the effect of activity patterns on the inhalation route in a modeling study. In that study, Wilkes et al. defined the potential inhalation dose (PID) as the amount of contaminant entering the lungs and available for uptake, by modeling a two-person household with a water supply contaminated with trichloroethylene (TCE). The parameters other than activity patterns were held constant

across each population group, including the configuration of the household, the size of rooms, the interzonal airflows, the whole-house air exchange rate, the appliance characteristics, and the breathing rate. Wilkes et al. found very strong correlations between a number of activities and the resultant PID. The strongest correlations were found with the following factors (in order of importance):

- Shower duration
- Time spent in the bathroom
- The fraction of time spent in the home multiplied by the total volume of water use in the home
- Bath duration

These correlations were found to be similar for households with one adult and households with two adults. Furthermore, the Wilkes et al. study found that the effect of two people sharing a household resulted in approximately a 20% increase in PID over a single person in the same household.

The Wilkes et al. study did not examine the effect of building-related parameters, such as the size of the house and the air-exchange rate, on the inhalation dose. However, some of these factors were also examined in the Wilkes et al. (2002) study (U.S. EPA, 2003). In that study, a sensitivity analysis was conducted to examine the sensitivity of the model to a variety of parameters, including behavior and activity factors (such as shower and bath durations) as well as a number of building related factors (such as air exchange rate and room volumes). For chloroform, the model was found to be relatively sensitive to these factors, in addition to confirming the earlier study's finding that the inhalation dose was very sensitive to several behavioral factors.

The exposure as a function of its route (i.e., ingestion, dermal, and inhalation) can be evaluated for each THM based on the predicted uptake. Since the four THMs are all present in the water supply, a comparison of route-specific contributions to the total absorbed dose will provide insight into the importance of volatility for each route. Since much of the Environmental Protection Agency's regulatory approach for setting maximum contaminant levels (MCLs) relies on using the ingestion route as an indicator

of exposure and dose, the relationship between the dose due to the ingestion route and overall dose warrants examination.

The total absorbed doses for chloroform and bromoform are shown in Figures 75 and 76 as functions of the percentile of the population. From these figures, it is clear that the highly exposed portions of the population (e.g., the population exposed at greater than the 90th percentile) are expected to be exposed to considerably more than the mean absorbed dose. For these simulation results given in Tables 65-68 and Figures 75 and 76, the absorbed dose for the 90th percentile case for all four THMs was typically 4 to 8 times the absorbed dose for the 50th percentile case for the adult male and female population groups. The absorbed dose for the 99th percentile case for the four THMs was typically 30 to 40 times the absorbed dose for the 50th percentile case. Similarly for the child population group, the absorbed dose for the 90th percentile case for all four THMs was typically approximately 4 times the absorbed dose for the 50th percentile case, while the absorbed dose for the 99th percentile case for the four THMs was typically approximately 10 times the absorbed dose for the 50th percentile case.

Examining the same data set for route-specific contributions yields Figures 77-82. In these figures, the contribution of each route is displayed in a cumulative fashion, such that the top line is the total absorbed dose, and each shaded area represents the respective contribution of the route it represents. This analysis indicates that the inhalation route contributes an increasing percentage as the total dose the increases. For chloroform in all population groups above the 20th percentile of total absorbed dose, inhalation is the dominant route of exposure. Above the 50th percentile in total dose, the inhalation route contributes more than 70%, and above the 90th percentile, the inhalation route contributes more than 90%. It is clear looking at Figures 77-79 that the contribution of the oral route has very little or no systematic increase with the increasing total dose, while nearly all the increase is due to the inhalation route.

Figure 83 compares the chloroform and bromoform contributions by the oral and inhalation routes for the female population group. From this comparison, it is apparent that the bromoform inhalation route fractional contribution is slightly smaller, but generally similar to the inhalation route contribution by chloroform. Bromoform is a borderline semi-volatile, based on the generally accepted definition for VOCs (boiling

point less than 150^{o}C and a vapor pressure of less than 0.1 mm Hg at standard temperature and pressure, refer to Table 4 for the properties of bromoform). The lower volatility results in a somewhat lower fraction by the inhalation route, however, the inhalation route still dominates exposure.

Exposure by the ingestion route is typically used as a basis for regulating drinking water contaminants. Figure 84 shows the amount of water that would need to be consumed if all of the exposure was from the ingestion route. This analysis assumes that the consumed water is at the same concentration as the tap water, and further assumes 100% uptake in the digestive system. This analysis suggests that using consumption as a predictor for overall dose is problematic and not acceptable for volatile chemicals. For volatile chemicals, consumption is not a significant portion of the overall dose nor can consumption can be used as a predictor of the overall dose. If the MCL is set based on the amount of tap water consumed, the vast majority of the dose will not be considered, leaving much of the population exposed to higher than expected doses.

7. CONCLUSIONS

The four THMs have a reasonably wide range of volatility, with vapor pressures ranging from 5.6 mm Hg for bromoform to 160 mm Hg for chloroform. As volatility increases, the relative importance of the inhalation route increases. This analysis indicates that exposure to waterborne THMs varies widely across a population, influenced by a variety of factors. These factors include THM concentrations in the water supply, building characteristics that impact ventilation and therefore airborne concentrations, water-use activities that lead to release of THMs into the air, activities that bring the subject into the vicinity of high airborne concentrations, dermal contact, consumption, and physiological factors that affect uptake such as breathing rate. Excluding the water concentration, the factors that have the largest impact across the population are the activity patterns that impact exposure to the occupants, including activities that use water and activities that bring the subject into the vicinity of the water uses. Furthermore, as discussed above, pairing two people in the same household results in approximately a 20% increase in inhalation dose over a single person occupying the same house, due to the water-use activities of other occupants. For all four THMs, the inhalation route plays an extremely large role in the total dose, especially for the highly exposed portions of the population. Since water-use behavior and other activity pattern exposure factors can vary substantially across the population, the dose by the inhalation route reflects this variability for volatile chemicals, and subsequently, the inhalation route is largely responsible for higher exposures in the population.

It is evident, based on the route-specific analysis and on the analysis of effective consumption presented in Figure 84, that the exposure and dose by the ingestion route is a poor proxy for the total exposure, and that the estimated dose by the ingestion route cannot be used in an effective manner for estimating total dose. The effective consumption for chloroform, a fairly volatile chemical, is very different than the effective consumption for bromoform, a borderline volatile, semi-volatile chemical. In the case of bromoform, 2 liters per day may properly represent the exposure and dose to over 75% of the population, whereas for chloroform, an effective consumption of more than 15

liters per day is likely warranted. It is evident from this analysis, that the route specific dose is very dependent of chemical properties and human activity patterns. Therefore, all routes of exposure must be considered when assessing exposure and dose to water-borne contaminants.

Just as external exposure to the THMs was dependent upon water use patterns, the internal dosimetry of the THMs was also dependent upon water use patterns. Since the THMs are all substrates for the same isoform of cytochrome P450, CYP2E1 (Guengerich et al., 1991; Raucy et al., 1993), the THMs are expected to be alternative substrate competitive inhibitors upon coexposure. Under the exposure conditions to the THMs from water use patterns (Table 69), significant inhibition of the metabolic activation of the THMs was not observed with the 95^{th} percentile water concentration scenarios for chloroform, BDCM, DBCM or bromoform. The reason that metabolic interactions were not evident between the four THMs was that the metabolic capacity of CYP2E1 was large enough to metabolize all of the THMs the subject was exposed to from the water-use scenarios. This conclusion was verified by lowering the amount of CYP2E1 in the simulations (Table 71). Decreasing Vmaxc one million times showed inhibition of THM metabolism by approximately 0.2% (Table 71). These results indicate that inhibitory interactions between the four CYP2E1 substrate THMs would not be expected to be significant under the low level, intermittent exposures encountered through water use in the home setting.

8. MODEL ASSUMPTIONS AND DATA QUALITY

This study is the implementation of a variety of stochastic and deterministic modeling techniques. The data used in calculations, methods and models used to derive quantitative measures, including those of internal exposure, tissue dosimetry, and risk were taken from publications and other sources subjected to peer review where possible. These publications include peer reviewed journals and other open literature. The sources of all data contained within this report have been documented by reference or footnote describing the source of the data. In addition, a discussion of shortcomings of data used in this study is included in the text of this report in the section where the data are introduced.

8.1. DATA QUALITY

Many diverse types of data are used in this study, including behavioral data, physical data, chemical data, and physiological data. These data are taken from a variety of sources including databases, peer-reviewed publications, and estimation techniques. In addition, numerous models are used to develop the exposure, dose and tissue concentrations, including fate and transport models, mass-transfer models, models to represent behavior, uptake and pharmacokinetic models. A general summary of the models and data utilized in this study are presented in Tables 72-75. The data fall into seven general categories, as described in Table 72. The sources of the major data utilized in this study are categorized and described in Table 73. The models and model algorithms utilized in this study are categorized and described in Tables 74 and 75.

8.2. ACTIVITY PATTERN DATABASE OVERVIEW

This report uses data that was analyzed by Wilkes et al. (2004) for water-use behavioral characteristics. Wilkes et al. analyzed four primary data sources: (1) NHAPS, (2) REUWS, (3) RECS, and (4) CSFII. The survey conducted to compile NHAPS (Tsang and Klepeis, 1996) was designed to gather exposure-related information, and as such, quantifying duration and frequency of appliance use was a goal of the survey. REUWS (Mayer et al., 1998) and RECS (U.S. DOE, 1995) were gathered for other purposes, but also contain useful information. REUWS was

conducted to better understand how much water is used by the various household appliances and issues related to water conservation. RECS was conducted with a primary focus on energy consumption. CSFII (U.S. EPA, 2000b) is a study of food intake, which is analyzed for tap-water consumption.

The National Human Activity Pattern Survey (NHAPS) database contains the results from a two-year, nationwide, activity pattern survey. The NHAPS study was commissioned by the EPA National Exposure Research Laboratory. During the period from October 1992 through September 1994, 9386 persons residing in the 48 contiguous United States were interviewed over the phone. The households were chosen using a telephone random-digit dial method such that the database would statistically represent the U.S. population. The interview was composed of two parts, which will hereafter be referred to as the "Diary" and the "Main Questionnaire." NHAPS data was analyzed by Wilkes et al. (2004) for a variety of household water uses. In addition, the database was sampled in this study for activity pattern (location and activity), as described in Section 2.2.

The Residential End Use Water Study (REUWS) database contains water-use data obtained from 1188 volunteer households throughout North America. The REUWS study was funded by the American Water Works Association Research Foundation. During the period from May 1996 through March 1998, approximately 100 single-family detached homes in each of 12 different municipalities (located in California, Colorado, Oregon, Washington, Florida, Arizona, and Ontario) were outfitted with a data-logging device (Meter Master 100 EL, manufactured by F.S. Brainard and Co.[1]) attached to their household water meter (on only magnetic-driven water meters). The data logger recorded the water quantities at 10-second intervals for a total of 4 weeks (2 in warm weather and 2 in cool weather) at each household. Following the study, the data were retrieved and analyzed by a flow-trace analysis software program, called Trace Wizard©, developed by Aquacraft Engineering, Inc.,[2] (DeOreo et al., 1996), which disaggregated the total water volumes into individual end uses (i.e., toilet, shower, faucet, dishwasher, clothes washer, etc.) (Mayer et al., 1998). In addition to identifying

[1] F.S. Brainard and Company, P.O. Box 366, Burlington, NH 08016.
[2] Aquacraft Engineering, Inc., 2709 Pine Street, Boulder, CO 80304.

the type of water use (e.g., shower, faucet, toilet), Trace Wizard© identified the event durations, volumes, peak flows, and mode measurements for each water-using event. REUWS data was analyzed by Wilkes et al. (2004) for a variety of household water uses.

The Residential Energy Consumption Survey is a nationwide survey conducted in 1997 to obtain household energy-use information. The resultant RECS database contains energy-usage characteristics of 5900 residential housing units. The information was acquired through on-site personal interviews with residents; telephone interviews with rental agents of units where energy use was included in the rent; and mail questionnaires to energy suppliers to the units. The database contains information on physical characteristics of the housing units, demographic information of the residents, heating and cooling appliances used, clothes washer and dishwasher-use frequency information, fuel types, and energy consumption. The RECS database was analyzed by Wilkes et al. (2004) to quantify estimates on household clothes-washer and dishwasher usage.

The 1994-96 USDA's Continuing Survey of Food Intake by Individuals (CSFII) is the most recent and comprehensive consumption database available. CSFII was conducted over the 3-year period between January 1994 and January 1997. A nationally representative total of 15,303 persons in the United States were interviewed on two non-consecutive days with questions about what drinks and foods they consumed in the previous 24 hours. The dietary recall information was collected by an interviewer who came to the participants' homes and provided instructions and standard measuring cups and spoons to assist in recalling consumption quantities. The U.S. EPA (2000b) report, "Estimated Per Capita Water Ingestion in the United States," explains the details of the study and presents the results. The CSFII data were analyzed by Wilkes et al. (2004) for purposes of quantifying estimates of per capita water ingestion for both direct water (plain water consumed as a beverage) and indirect water (water used to prepare foods and beverages).

These data sources had a number of shortcomings. For NHAPS, the frequency was calculated in one of two ways, depending upon how the data were gathered. Some of the frequency data was reported in the form of a range of values, while others gave a

specific number of events over a given time period, and in some cases, the frequency range is truncated. For example, the clothes-washer frequency data was provided as daily, 3-5 times per week, 1-2 times per week, or less than once per week, and showers, where the frequencies of 10 and greater reported as "greater than 10." In the Wilkes et al. (2004) analysis for binned data, the midpoint of the range was assumed in the calculation. For truncated data, the calculation for overall frequency assumed the first number in the truncated range (i.e., 11 was assumed for the truncated range "greater than 10").

Though REUWS offers a tremendous amount of useful information, the database is not a statistically representative sample of our nation's population (as is NHAPS). The sampled households were located within only six U.S. states (five of which are in the western U.S.) and one Canadian province, and the participants were all volunteers who may not be representative of the entire population. The REUWS database presents a potentially significant data source toward the understanding of household water-use behavior. However, the quality of the data relies heavily on the disaggregation algorithms employed by the Trace Wizard© software. In a recent small, evaluation study of Trace Wizard© (see Wilkes et al., 2004, Appendix A), flaws in Trace Wizard's© analysis techniques were uncovered. Though fairly acceptable in classifying single, non-overlapping water-uses, the software quite often misclassified water-uses when two or more water uses overlapped. In the evaluation study, over 83% of single water uses were classified correctly, and less than 25% of multiple, overlapping water-uses were classified correctly.

8.3. OTHER ASSUMPTIONS

There are a number of other issues that are likely to be important, but they are poorly understood. Below is a partial list of issues that were not addressed in this study:

1. Water Heater. The water heater, as a storage device that maintains a relatively high temperature, represents an opportunity for further reactions. It is possible that the THM content of the water leaving the water-heater is substantially higher than the water entering the water heater
2. Dishwasher. The dishwasher, like the water heater, contains water that is heated and provided an opportunity for further reactions, thereby generating additional THMs.

3. Furthermore, chlorinated detergent is often added and is in the presences of waste food matter, providing additional reactants.
4. Activity Pattern Databases. The NHAPS activity pattern data base does not include specific demarcation in its time-activity records. As discussed earlier in this report, this shortcoming is addressed by appropriately simulating water-uses consistent with the population groups' characteristics in appropriate places in the time-activity pattern (see Section 2.2). Although there is every expectation that this generates realistic exposure scenarios, it is not possible to be sure. In addition, the activity patterns are independent, and therefore when a family is simulated, the correlation in activities that likely exists in actual families, is most likely not captured. Wilkes et al. (1996) discusses this issue.
5. The house volumes, room volumes, air exchange rates, interzonal air flows, and other building-related parameters are developed from a variety of sources, as discussed in Section 2.4. These represent general population characteristics; however individual nuances and peculiarities, such as whole-house fans, opening and closing of windows and doors, etc., are unlikely to have been captured.
6. Dermal Contact. Dermal contact is assumed to be a constant fraction of the skin for each activity. The following factors are not considered:
    - variations in amount of skin in contact with the water throughout a given activity,
    - the impact of water and air temperature on dermal uptake,
    - the dermal uptake rate is averaged over all areas of the body and there is no difference in the location of dermal contact.
7. Ingestion. Ingestion is randomly distributed throughout the day, as described in Section 2.3. The manner in which actual consumption behavior is distributed throughout the day is not well quantified.

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APPENDIX

PBPK Model Code

```
$TARGET_FUNCTION
#include "ia.hpp"
$END
PROGRAM THM
! PBPK model for THMs in water, interactions between 4 THMs
! THMs: 1=CF, 2=BDCM, 3=DBCM, 4=BF
! 2/6-23/04 GLK based on volatiles
INITIAL
CONSTANT  SUBNUM = 1 !SUBJECTNUMBER 1=MALE,2=FEMALE,3=CHILD
CONSTANT  QPC = 15. !alveolar ventilation rate (L/hr/kg)
CONSTANT  QCC = 15. !CARDIAC OUTPUT (l/HR/KG)
CONSTANT  QLC = 0.26 !FRACTIONAL BLOOD FLOW TO LIVER
CONSTANT  QFC = 0.05 !FRACTIONAL BLOOD FLOW TO FAT
CONSTANT  QKC = 0.034 !FRACTIONAL BLOOD FLOW TO KIDNEY
CONSTANT  QGC = 0.013 !FRACTIONAL BLOOD FLOW TO GENITALS
CONSTANT  BW = 70 !BODY WEIGHT (KG)
CONSTANT  VLC = 0.026 !FRACTION LIVER TISSUE
CONSTANT  VFC = 0.19 !FRACTION FAT TISSUE
CONSTANT  VKC = 0.004 !FRACTION KIDNEY TISSUE
CONSTANT  VGC = 0.0004 !FRACTION GENITAL TISSUE
CONSTANT  BVC = 0.06 !FRACTION BLOOD VOL
CONSTANT  VABC = 0.35 !FRACTION ARTERIAL BLOOD VOL
CONSTANT  VVBC = 0.65 !FRACTION VENOUS BLOOD VOL
CONSTANT  PL1 = 1.6 !LIVER/BLOOD PARTITION COEFF CF
CONSTANT  PL2 = 1.15 !LIVER/BLOOD PARTITION COEFF BDCM
CONSTANT  PL3 = 2.56 !LIVER/BLOOD PARTITION COEFF DBCM
CONSTANT  PL4 = 2.06 !LIVER/BLOOD PARTITION COEFF BF
CONSTANT  PF1 = 31.0 !FAT/BLOOD PARTITION COEFF CF
CONSTANT  PF2 = 19.8 !FAT/BLOOD PARTITION COEFF BDCM
CONSTANT  PF3 = 39.0 !FAT/BLOOD PARTITION COEFF DBCM
CONSTANT  PF4 = 40.4 !FAT/BLOOD PARTITION COEFF BF
CONSTANT  PK1 = 1.3 !KIDNEY/BLOOD PARTITION COEFF CF
CONSTANT  PK2 = 1.24 !KIDNEY/BLOOD PARTITION COEFF BDCM
CONSTANT  PK3 = 2.56 !KIDNEY/BLOOD PARTITION COEFF DBCM
CONSTANT  PK4 = 1.69 !KIDNEY/BLOOD PARTITION COEFF BF
CONSTANT  PG1 = 1.1 !GENITAL/BLOOD PARTITION COEFF CF
CONSTANT  PG2 = 0.69 !GENITAL/BLOOD PARTITION COEFF BDCM
CONSTANT  PG3 = 1.5 !GENITAL/BLOOD PARTITION COEFF DBCM
CONSTANT  PG4 = 1.18 !GENITAL/BLOOD PARTITION COEFF BF
CONSTANT  PS1 = 1.5 !SLOWLY PERF/BLOOD PART COEFF CF
CONSTANT  PS2 = 0.47 !SLOWLY PERF/BLOOD PART COEFF BDCM
CONSTANT  PS3 = 1.13 !SLOWLY PERF/BLOOD PART COEFF DBCM
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CONSTANT  PS4 = 1.12 !SLOWLY PERF/BLOOD PART COEFF BF
CONSTANT  PR1 = 1.6 !RICHLY PERF/BLOOD PART COEFF CF
CONSTANT  PR2 = 1.15 !RICHLY PERF/BLOOD PART COEFF BDCM
CONSTANT  PR3 = 2.56 !RICHLY PERF/BLOOD PART COEFF DBCM
CONSTANT  PR4 = 2.06 !RICHLY PERF/BLOOD PART COEFF BF
CONSTANT  PB1 = 11.34 !BLOOD/AIR PARTITION COEFF CF
CONSTANT  PB2 = 26.6 !BLOOD/AIR PARTITION COEFF BDCM
CONSTANT  PB3 = 49.2 !BLOOD/AIR PARTITION COEFF DBCM
CONSTANT  PB4 = 102.3 !BLOOD/AIR PARTITION COEFF BF
CONSTANT  MW1 = 119.4 !CF MOLECULAR WEIGHT (G/MOL)
CONSTANT  MW2 = 163.83 !BDCM MOLECULAR WEIGHT (G/MOL)
CONSTANT  MW3 = 208.29 !DBCM MOLECULAR WEIGHT (G/MOL)
CONSTANT  MW4 = 252.75 !BF MOLECULAR WEIGHT (G/MOL)
CONSTANT  VMAXC1 = 8.956 !CF MAXIMAL VELOCITY (MG/HR/KG)
CONSTANT  VMAXC2 = 8.01 !BDCM MAXIMAL VELOCITY (MG/HR/KG)
CONSTANT  VMAXC3 = 13.7 !DBCM MAXIMAL VELOCITY (MG/HR/KG)
CONSTANT  VMAXC4 = 10.4 !BF MAXIMAL VELOCITY (MG/HR/KG)
CONSTANT  KM1 = 0.012 !CF MICHAELIS-MENTEN CONSTANT (MG/L)
CONSTANT  KM2 = 0.302 !BDCM MICHAELIS-MENTEN CONSTANT (MG/L)
CONSTANT  KM3 = 0.72 !DBCM MICHAELIS-MENTEN CONSTANT (MG/L)
CONSTANT  KM4 = 0.42 !BF MICHAELIS-MENTEN CONSTANT (MG/L)
CONSTANT  ODOSE1 = 0. !CF ORAL DOSE (MG/KG)
CONSTANT  ODOSE2 = 0. !BDCM ORAL DOSE (MG/KG)
CONSTANT  ODOSE3 = 0. !DBCM ORAL DOSE (MG/KG)
CONSTANT  ODOSE4 = 0. !BF ORAL DOSE (MG/KG)
CONSTANT  KA = 2.0 !ORAL UPTAKE RATE (/HR)
CONSTANT  DDOSE1 = 0. !CF DERMAL DOSE (MG TOTAL)
CONSTANT  DDOSE2 = 0. !BDCM DERMAL DOSE (MG TOTAL)
CONSTANT  DDOSE3 = 0. !DBCM DERMAL DOSE (MG TOTAL)
CONSTANT  DDOSE4 = 0. !BF DERMAL DOSE (MG TOTAL)
!CONSTANT IVDOSE = 0. !IV DOSE (MG/KG)
CONSTANT  CONC1 = 0. !CF INHALED CONC (PPM)
CONSTANT  CONC2 = 0. !BDCM INHALED CONC (PPM)
CONSTANT  CONC3 = 0. !DBCM INHALED CONC (PPM)
CONSTANT  CONC4 = 0. !BF INHALED CONC (PPM)
! TIMING COMMANDS
CONSTANT  TSTOP = 24. !LENGTH OF EXPT (HR)
CONSTANT  TCHNG = 24. !LENGTH OF EXPOSURE (HR)
!CONSTANT TINF = 0.002 !LENGTH OF IV INFUSION (HR)
CONSTANT  TDER = 0.167 !LENGTH OF DERMAL EXPOSURE (HR)
CONSTANT  POINTS = 17280 !NUMBER OF POINTS IN PLOT
CINT = TSTOP/POINTS !COMMUNICATION INTERVAL
!SCALED PARAMETERS
QC = QCC*BW**0.74
QP = QPC*BW**0.74
QL = QLC*QC
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QF = QFC*QC
QK = QKC*QC
QG = QGC*QC
QS = 0.24*QC - QF
QR = 0.76*QC - QL - QK - QG
VL = VLC*BW
VF = VFC*BW
VK = VKC*BW
VG = VGC*BW
VS = 0.82*BW - VF
VR = 0.09*BW - VL - VK - VG
BV = BVC*BW
VAB = BV*VABC
VVB = BV*VVBC
VMAX1 = VMAXC1*BW**0.7
VMAX2 = VMAXC2*BW**0.7
VMAX3 = VMAXC3*BW**0.7
VMAX4 = VMAXC4*BW**0.7
DOSE1 = ODOSE1*BW
DOSE2 = ODOSE2*BW
DOSE3 = ODOSE3*BW
DOSE4 = ODOSE4*BW
!IVR = IVDOSE*BW/TINF
END !OF INITIAL
DYNAMIC
IALG = 2 !GEAR METHOD FOR STIFF SYSTEMS
DERIVATIVE
!CI = CONC IN INHALED AIR (MG/L)
CIZONE = RSW(T.GT.TCHNG,0.,1.)
CI1 = CIZONE*CONC1*MW1/24450
CI2 = CIZONE*CONC2*MW2/24450
CI3 = CIZONE*CONC3*MW3/24450
CI4 = CIZONE*CONC4*MW4/24450
!AI = AMOUNT INHALED (MG)
RAI1 = QP*CI1
RAI2 = QP*CI2
RAI3 = QP*CI3
RAI4 = QP*CI4
AI1 = INTEG(RAI1,0.)
AI2 = INTEG(RAI2,0.)
AI3 = INTEG(RAI3,0.)
AI4 = INTEG(RAI4,0.)
!MR = AMOUNT REMAINING IN STOMACH (MG)
RMR1 = -KA*MR1
RMR2 = -KA*MR2
RMR3 = -KA*MR3
```

```
RMR4 = -KA*MR4
MR1 = DOSE1*EXP(-KA*T)
MR2 = DOSE2*EXP(-KA*T)
MR3 = DOSE3*EXP(-KA*T)
MR4 = DOSE4*EXP(-KA*T)
!CA = CONC IN SYSTEMIC ARTERIAL BLOOD (MG/L)
CA1 = (QC*CV1 + QP*CI1)/(QC + (QP/PB1)) + DE1/VAB
CA2 = (QC*CV2 + QP*CI2)/(QC + (QP/PB2)) + DE2/VAB
CA3 = (QC*CV3 + QP*CI3)/(QC + (QP/PB3)) + DE3/VAB
CA4 = (QC*CV4 + QP*CI4)/(QC + (QP/PB4)) + DE4/VAB
AUCB1 = INTEG(CA1,0.)
AUCB2 = INTEG(CA2,0.)
AUCB3 = INTEG(CA3,0.)
AUCB4 = INTEG(CA4,0.)
!AX = AMOUNT EXHALED (MG)
CX1 = CA1/PB1
CX2 = CA2/PB2
CX3 = CA3/PB3
CX4 = CA4/PB4
CXPPM1 = (0.7*CX1 + 0.3*CI1)*24450./MW1
CXPPM2 = (0.7*CX2 + 0.3*CI2)*24450./MW2
CXPPM3 = (0.7*CX3 + 0.3*CI3)*24450./MW3
CXPPM4 = (0.7*CX4 + 0.3*CI4)*24450./MW4
RAX1 = QP*CX1
RAX2 = QP*CX2
RAX3 = QP*CX3
RAX4 = QP*CX4
AX1 = INTEG(RAX1,0.)
AX2 = INTEG(RAX2,0.)
AX3 = INTEG(RAX3,0.)
AX4 = INTEG(RAX4,0.)
!AS = AMOUNT IN SLOWLY PERFUSED TISSUES (MG)
RAS1 = QS*(CA1 - CVS1)
RAS2 = QS*(CA2 - CVS2)
RAS3 = QS*(CA3 - CVS3)
RAS4 = QS*(CA4 - CVS4)
AS1 = INTEG(RAS1,0.)
AS2 = INTEG(RAS2,0.)
AS3 = INTEG(RAS3,0.)
AS4 = INTEG(RAS4,0.)
CVS1 = AS1/(VS*PS1)
CVS2 = AS2/(VS*PS2)
CVS3 = AS3/(VS*PS3)
CVS4 = AS4/(VS*PS4)
CS1 = AS1/VS
CS2 = AS2/VS
```

```
CS3 = AS3/VS
CS4 = AS4/VS
!AMOUNT IN RAPIDLY PERFUSED TISSUES (MG)
RAR1 = QR*(CA1 - CVR1)
RAR2 = QR*(CA2 - CVR2)
RAR3 = QR*(CA3 - CVR3)
RAR4 = QR*(CA4 - CVR4)
AR1 = INTEG(RAR1,0.)
AR2 = INTEG(RAR2,0.)
AR3 = INTEG(RAR3,0.)
AR4 = INTEG(RAR4,0.)
CVR1 = AR1/(VR*PR1)
CVR2 = AR2/(VR*PR2)
CVR3 = AR3/(VR*PR3)
CVR4 = AR4/(VR*PR4)
CR1 = AR1/VR
CR2 = AR2/VR
CR3 = AR3/VR
CR4 = AR4/VR
!AF = AMOUNT IN FAT (MG)
RAF1 = QF*(CA1 - CVF1)
RAF2 = QF*(CA2 - CVF2)
RAF3 = QF*(CA3 - CVF3)
RAF4 = QF*(CA4 - CVF4)
AF1 = INTEG(RAF1,0.)
AF2 = INTEG(RAF2,0.)
AF3 = INTEG(RAF3,0.)
AF4 = INTEG(RAF4,0.)
CVF1 = AF1/(VF*PF1)
CVF2 = AF2/(VF*PF2)
CVF3 = AF3/(VF*PF3)
CVF4 = AF4/(VF*PF4)
CF1 = AF1/VF
CF2 = AF2/VF
CF3 = AF3/VF
CF4 = AF4/VF
!AK = AMOUNT IN KIDNEY (MG)
RAK1 = QK*(CA1 - CVK1)
RAK2 = QK*(CA2 - CVK2)
RAK3 = QK*(CA3 - CVK3)
RAK4 = QK*(CA4 - CVK4)
AK1 = INTEG(RAK1,0.)
AK2 = INTEG(RAK2,0.)
AK3 = INTEG(RAK3,0.)
AK4 = INTEG(RAK4,0.)
CVK1 = AK1/(VK*PK1)
```

```
CVK2 = AK2/(VK*PK2)
CVK3 = AK3/(VK*PK3)
CVK4 = AK4/(VK*PK4)
CK1 = AK1/VK
CK2 = AK2/VK
CK3 = AK3/VK
CK4 = AK4/VK
!AG = AMOUNT IN GENITALS [TESTES, OVARIES] (MG)
RAG1 = QG*(CA1 - CVG1)
RAG2 = QG*(CA2 - CVG2)
RAG3 = QG*(CA3 - CVG3)
RAG4 = QG*(CA4 - CVG4)
AG1 = INTEG(RAG1,0.)
AG2 = INTEG(RAG2,0.)
AG3 = INTEG(RAG3,0.)
AG4 = INTEG(RAG4,0.)
CVG1 = AG1/(VG*PG1)
CVG2 = AG2/(VG*PG2)
CVG3 = AG3/(VG*PG3)
CVG4 = AG4/(VG*PG4)
CG1 = AG1/VG
CG2 = AG2/VG
CG3 = AG3/VG
CG4 = AG4/VG
!AL = AMOUNT IN LIVER (MG)
RAL1 = QL*(CA1 - CVL1) - RAM1 + RAO1
RAL2 = QL*(CA2 - CVL2) - RAM2 + RAO2
RAL3 = QL*(CA3 - CVL3) - RAM3 + RAO3
RAL4 = QL*(CA4 - CVL4) - RAM4 + RAO4
AL1 = INTEG(RAL1,0.)
AL2 = INTEG(RAL2,0.)
AL3 = INTEG(RAL3,0.)
AL4 = INTEG(RAL4,0.)
CVL1 = AL1/(VL*PL1)
CVL2 = AL2/(VL*PL2)
CVL3 = AL3/(VL*PL3)
CVL4 = AL4/(VL*PL4)
CL1 = AL1/VL
CL2 = AL2/VL
CL3 = AL3/VL
CL4 = AL4/VL
AUCL1 = INTEG(CL1,0.)
AUCL2 = INTEG(CL2,0.)
AUCL3 = INTEG(CL3,0.)
AUCL4 = INTEG(CL4,0.)
!AM = AMOUNT METABOLIZED, P450 SATURABLE PATHWAY (MG)
```

```
RAM1 = (VMAX1*CVL1)/(KM1*(1+CVL2/KM2+CVL3/KM3+CVL4/KM4)+CVL1)
RAM2 = (VMAX2*CVL2)/(KM2*(1+CVL1/KM1+CVL3/KM3+CVL4/KM4)+CVL2)
RAM3 = (VMAX3*CVL3)/(KM3*(1+CVL1/KM1+CVL2/KM2+CVL4/KM4)+CVL3)
RAM4 = (VMAX4*CVL4)/(KM4*(1+CVL1/KM1+CVL2/KM2+CVL3/KM3)+CVL4)
RAMM1 = RAM1*1000./MW1
RAMM2 = RAM2*1000./MW2
RAMM3 = RAM3*1000./MW3
RAMM4 = RAM4*1000./MW4
AM1 = INTEG(RAM1,0.)
AM2 = INTEG(RAM2,0.)
AM3 = INTEG(RAM3,0.)
AM4 = INTEG(RAM4,0.)
CAM1 = AM1/VL
CAM2 = AM2/VL
CAM3 = AM3/VL
CAM4 = AM4/VL
DM1 = CAM1*1000./MW1
DM2 = CAM2*1000./MW2
DM3 = CAM3*1000./MW3
DM4 = CAM4*1000./MW4
!AO = TOTAL MASS INPUT FROM STOMACH (MG)
RAO1 = KA*MR1
RAO2 = KA*MR2
RAO3 = KA*MR3
RAO4 = KA*MR4
AO1 = DOSE1 - MR1
AO2 = DOSE2 - MR2
AO3 = DOSE3 - MR3
AO4 = DOSE4 - MR4
!IV = IV INFUSION DOSE (MG)
!IV = IVR*(1. - STEP(TINF))
!DE = DERMAL DOSE (MG)
DDR1 = DDOSE1/TDER
DDR2 = DDOSE2/TDER
DDR3 = DDOSE3/TDER
DDR4 = DDOSE4/TDER
DE1 = DDR1*(1. - STEP(TDER))
DE2 = DDR2*(1. - STEP(TDER))
DE3 = DDR3*(1. - STEP(TDER))
DE4 = DDR4*(1. - STEP(TDER))
!CV = MIXED VENOUS BLOOD CONC (MG/L)
CV1 = (QF*CVF1+QL*CVL1+QS*CVS1+QR*CVR1+QK*CVK1+QG*CVG1)/QC
CV2 = (QF*CVF2+QL*CVL2+QS*CVS2+QR*CVR2+QK*CVK2+QG*CVG2)/QC
CV3 = (QF*CVF3+QL*CVL3+QS*CVS3+QR*CVR3+QK*CVK3+QG*CVG3)/QC
CV4 = (QF*CVF4+QL*CVL4+QS*CVS4+QR*CVR4+QK*CVK4+QG*CVG4)/QC
!TMASS = MASS BALANCE (MG)
```

```
TMASS1 = AF1+AL1+AS1+AR1+AK1+AG1+AM1+AX1+MR1
TMASS2 = AF2+AL2+AS2+AR2+AK2+AG2+AM2+AX2+MR2
TMASS3 = AF3+AL3+AS3+AR3+AK3+AG3+AM3+AX3+MR3
TMASS4 = AF4+AL4+AS4+AR4+AK4+AG4+AM4+AX4+MR4
TMASS = TMASS1 + TMASS2 + TMASS3 + TMASS4
TERMT(T.GE.TSTOP)
END !OF DERIVATIVE
discrete readdata
interval readinterval = 0.01667
QP = get_breathingrate(simulationnumber, SUBNUM, t)
CONC1 = get_airconcentration(simulationnumber, SUBNUM, 1, t)
CONC2 = get_airconcentration(simulationnumber, SUBNUM, 2, t)
CONC3 = get_airconcentration(simulationnumber, SUBNUM, 3, t)
CONC4 = get_airconcentration(simulationnumber, SUBNUM, 4, t)
DDOSE1 = get_dermaldose(simulationnumber,SUBNUM,1,t,-1)
DDOSE2 = get_dermaldose(simulationnumber,SUBNUM,2,t,-1)
DDOSE3 = get_dermaldose(simulationnumber,SUBNUM,3,t,-1)
DDOSE4 = get_dermaldose(simulationnumber,SUBNUM,4,t,-1)
TDER = get_dermaldose(simulationnumber,SUBNUM,1,t,1)
ODOSE1 = get_oraldose(simulationnumber,SUBNUM,1,t,BW)
ODOSE2 = get_oraldose(simulationnumber,SUBNUM,2,t,BW)
ODOSE3 = get_oraldose(simulationnumber,SUBNUM,3,t,BW)
ODOSE4 = get_oraldose(simulationnumber,SUBNUM,4,t,BW)
!call put_dataout(t,QP,CONC1,CONC2,CONC3,CONC4,simulationnumber,SUBNUM)
!call

put_dataout2(DDOSE1,DDOSE2,DDOSE3,DDOSE4,TDER,ODOSE1,ODOSE2,ODOS
E3,ODOSE4)
end ! of discrete readdata
discrete writedata
interval writeinterval = 0.083
call resultsoutput1(SUBNUM,simulationnumber,t,QP,QC)
call resultsoutput2(AM1,AM2,AM3,AM4)
call resultsoutput3(CAM1,CAM2,CAM3,CAM4)
call resultsoutput4(AUCL1,AUCL2,AUCL3,AUCL4)
call resultsoutput5(CL1,CL2,CL3,CL4)
call resultsoutput6(CF1,CF2,CF3,CF4)
call resultsoutput7(CS1,CS2,CS3,CS4)
call resultsoutput8(CR1,CR2,CR3,CR4)
call resultsoutput9(CK1,CK2,CK3,CK4)
call resultsoutput10(CG1,CG2,CG3,CG4)
call resultsoutput11(CA1,CA2,CA3,CA4)
call resultsoutput12(CV1,CV2,CV3,CV4)
call resultsoutput13(DM1,DM2,DM3,DM4)
end ! of discrete writedata
END !OF DYNAMIC
```

```
TERMINAL
call resultsoutput1(-1,-1,-1,-1,-1)
call put_dataout(-1,-1,-1,-1,-1,-1,-1,-1)
END !OF TERMINAL
END !OF PROGRAM
```

TABLE 1

Location Codes Recorded in the National Human Activity Pattern Survey (NHAPS)

Location Code	Name
100	Home - Other
101	Home - Kitchen
102	Home - Living / Family / Den
103	Home - Dining
104	Home - Bathroom
105	Home - Bedroom
106	Home - Study / Office
107	Home - Garage
108	Home - Basement
110	Home - Utility / Laundry
111	Home - Pool, spa (outdoors)
112	Home - Yard, other outdoors
113	Home - Room to room
114	Home - In / out of house
120	Home - Other (verified)
199	Home - Ref
200	Other's House - Other
201	Other's House - Kitchen
202	Other's House - Living / Family / Den
203	Other's House - Dining
204	Other's House - Bathroom
205	Other's House - Bedroom
206	Other's House - Study / Office
207	Other's House - Garage
208	Other's House - Basement
210	Other's House - Utility / Laundry
211	Other's House - Pool, spa (outdoors)
212	Other's House - Yard, other outdoors
213	Other's House - Room to room
214	Other's House - In / out of house
220	Other's House - Other (verified)
299	Other's House - Ref
300	Transit - Other
301	Transit - Car
302	Transit - Truck (Pick-up / Van)
303	Transit - Truck (Others)
304	Transit - Motorcycle / Moped / Scooter
305	Transit - Bus
306	Transit - Walking
307	Transit - Bicycle / Skateboard / RSkates
308	Transit - Stroller / Carried by adult
310	Transit - Train / Subway / Rapid transit
311	Transit - Airplane
312	Transit - Boat
313	Transit - Waiting for Bus, train, ride (stop)
314	Transit - Waiting for travel, indoors
320	Transit - Other (verified)

Location Code	Name
399	Transit - Ref
400	Indoor - Other
401	Indoor - Office Bldg / Bank / Post Office
402	Indoor - Industrial plant / Factory / Warehouse
403	Indoor - Grocery store / Convenience store
404	Indoor - Shopping mall / Non-grocery store
405	Indoor - Bar / Night club / Bowling alley
406	Indoor - Auto repair shop / Gas station
407	Indoor - Gym / Sports or health club
408	Indoor - Public Bldg / Library / Museum / Theater
409	Indoor - Laundromat
410	Indoor - Hospital / Health care facility / Dr's Office
411	Indoor - Beauty parlor / Barber shop / Hair dresser
412	Indoor - Work (no specific main location)
413	Indoor - School
414	Indoor - Restaurant
415	Indoor - Church
416	Indoor - Hotel / Motel
417	Indoor - Dry cleaner
418	Indoor - Other repair shop
419	Indoor - Indoor parking garage
420	Indoor - Other (verified)
499	Indoor - Ref
500	Outdoor - Other
501	Outdoor - Sidewalk / Street / Neighborhood
502	Outdoor - Parking lot
503	Outdoor - Service station / Gas station
504	Outdoor - Construction site
505	Outdoor - School grounds / Playground
506	Outdoor - Sports stadium
507	Outdoor - Park / Golf course
508	Outdoor - Pool, river, lake
510	Outdoor - Restaurant / picnic (outdoors)
511	Outdoor - Farm
520	Outdoor - Other (verified)
599	Outdoor - Ref

TABLE 2

Activity Codes Recorded in the National Human Activity Pattern Survey (NHAPS)

Activity Code	Description
1	Work - Main job
2	Work - Unemployment
3	Work - Travel
5	Work - Second job
8	Work - Break
9	Work - Travel to/from
10	Household work - Food preparation
11	Household work - Food cleanup
12	Household work - Cleaning house
13	Household work - Outdoor cleaning
14	Household work - Clothes care
15	Household work - Car repair/maintenance (by respondent)
16	Household work - Other repairs (by respondent)
17	Household work - Plant care
18	Household work - Animal care
19	Household work - Other
20	Child care - Baby care
21	Child care - Child care
22	Child care - Helping/Teaching
23	Child care - Talking/Reading
24	Child care - Indoor playing
25	Child care - Outdoor playing
26	Child care - Medical care
27	Child care - Other
28	Child care - Cleaning
29	Child care - Travel
30	Obtaining goods and services - Food shopping
31	Obtaining goods and services - Clothes/Household shopping
32	Obtaining goods and services - Personal services
33	Obtaining goods and services - Medical appointments
34	Obtaining goods and services - Government/Financial service
35	Obtaining goods and services - Car repair services
36	Obtaining goods and services - Other repair services
37	Obtaining goods and services - Other services
38	Obtaining goods and services - Errands
39	Obtaining goods and services - Travel
40	Personal needs and care - Bathing, etc.
41	Personal needs and care - Medical care
42	Personal needs and care - Help and care
43	Personal needs and care - Eating
44	Personal needs and care - Personal hygiene
45	Personal needs and care - Sleeping / Napping
47	Personal needs and care - Dressing, etc.
48	Personal needs and care - NA activity
49	Personal needs and care - Travel

Activity Code	Description
50	Education and Training - Student classes
51	Education and Training - Other classes
54	Education and Training - Homework
55	Education and Training - Library
56	Education and Training - Other
59	Education and Training - Travel
60	Organizational activities - Professional/Union
61	Organizational activities - Special interest
62	Organizational activities - Political/Civic
63	Organizational activities - Volunteer/Helping
64	Organizational activities - Religious groups
65	Organizational activities - Religious practice
66	Organizational activities - Fraternal
67	Organizational activities - Child/Youth/Family
68	Organizational activities - Other
69	Organizational activities - Travel
70	Social - Sports events
71	Social - Entertainment events
72	Social - Movies/Videos
73	Social - Theatre
74	Social - Museums
75	Social - Visiting
76	Social - Parties
77	Social - Bars/Lounges
78	Social - Other
79	Social - Travel
80	Recreation - Active sports
81	Recreation - Outdoor
82	Recreation - Exercise
83	Recreation - Hobbies
84	Recreation - Domestic Crafts
85	Recreation - Art
86	Recreation - Music/Drama/Dance
87	Recreation - Games
88	Recreation - Computer use
89	Recreation - Travel
90	Communication - Radio
91	Communication - Television
92	Communication - Records/Tape
93	Communication - Read books
94	Communication - Read magazines, etc.
95	Communication - Read newspaper
96	Communication - Conversations
97	Communication - Letters/Write/Paperwork
98	Communication - Think/Relax
99	Communication - Travel, Passive Leisure

TABLE 3

List of Chemicals for Exposure Assessment

DBP Subclass	Chemical Name	CAS Number
Trihalomethanes	Chloroform	67-66-3
(THMs)	Bromodichloromethane (BDCM)	75-27-4
	Dibromochloromethane (DBCM)	124-48-1
	Bromoform	75-25-2

TABLE 4

Physical Properties of Chemicals of Interest

Chemical	Henry's Law Constant				Diffusivity in Water			Diffusivity in Air			Octanol/H_2O Partition Coef.		Molecular Weight	Boiling Point		Vapor Pressure		
	Dimensionless H	Temp. (^oC)	$\frac{\Delta H}{RT}$ (^oK)	Reference	(cm^2/s)	Temp. (^oC)	Reference	(cm^2/s)	Temp. (^oC)	Reference	Log K_{ow}	Reference		T_b (^oC)	Reference	P_{vp} (mmHg)	Temp. (^oC)	Reference
Trihalomethanes (THMs)																		
Chloroform (CAS: 67-66-3) $CHCl_3$	0.150 0.150 (a) 0.151 (a) 0.163 (a)	25 24 25 25	4500	1 2 5a 5b	1.0×10^{-5}	b	1	0.1040	25	1	1.96 1.97	1 2	119.38	61.17	3	160 (vapor density 4.12)	20	4
Bromodichloro-methane (CAS: 75-27-4) $CHBrCl_2$	0.0656 0.0866 (a) 0.065 0.095 0.085 0.102	25 25 25 25 25	4700	1 2 5c 5c 5c 5d	1.06×10^{-5}	b	1	0.0298	b	1	1.88 2.00	1 2	163.83	90 90	3	50	20	6
Dibromochloro-methane (Chlorodibromo-methane) (CAS: 124-48-1) $CHBr_2Cl$	0.037 0.034 0.056	25 25 25	4700	5c 5c 5d	1.05×10^{-5}	b	1	0.0196	b	1	2.09 2.16 2.24	1 2 5	208.28	120 119-120	3 4	76	20	4
Bromoform (CAS: 75-25-2) $CHBr_3$	0.0219 0.0219 (a) 0.0255 (a) 0.0240 (a)	25 25 25 25	5200	1 2 5a 5b	1.03×10^{-5}	b	1	0.0149	b	1	2.30 2.40	1 2	252.73	149.1 150-151	3 4	5.6 (vapor density 8.7)	25	4

a. Henry's law constant is reported in the literature with concentration and partial pressure units. The value reported in the table was converted to dimensionless H.
b. Temperature at which diffusivity is measured is not reported.
REFERENCES: Risk Assessment Information System, 2001; HSDB, 2001; Lide, 2000; Gangolli, 1989; Sander, 2001; 6a Mackay, 1981; 6b Staudinger, 1996; 6c Nicholson, 1984; 6d Moore, 1995; 7 SRC, 2001.

TABLE 5

Estimated Values for Liquid Phase Diffusivity, Gas Phase Diffusivity, and Dimensionless Henry's Law Constant

Temp	Chloroform			BDCM			DBCM			Bromoform		
^{o}C	$D_L/(1E-6)$ (L^2/T)	D_G (L^2/T)	H*	$D_L/(1E-6)$ (L^2/T)	D_G (L^2/T)	H*	$D_L/(1E-6)$ (L^2/T)	D_G (L^2/T)	H*	$D_L/(1E-6)$ (L^2/T)	D_G (L^2/T)	H*
16	8.200	0.0894	0.1086	8.077	0.0849	0.0586	7.9588	0.0814	0.0245	7.8452	0.0787	0.0134
17	8.443	0.09	0.1105	8.316	0.0854	0.0618	8.1943	0.082	0.0259	8.0773	0.0792	0.0142
18	8.699	0.0906	0.1123	8.5685	0.086	0.0651	8.4431	0.0825	0.0274	8.3226	0.0797	0.0151
19	8.951	0.0912	0.1142	8.8162	0.0866	0.0686	8.6872	0.0831	0.0289	8.5632	0.0802	0.016
20	9.206	0.0917	0.1161	9.0674	0.0871	0.0722	8.9347	0.0836	0.0305	8.8072	0.0808	0.017
21	9.465	0.0923	0.1236	9.3226	0.0877	0.076	9.1862	0.0841	0.0322	9.055	0.0813	0.018
22	9.726	0.0929	0.131	9.5802	0.0882	0.0799	9.44	0.0847	0.0339	9.3052	0.0818	0.0191
23	9.992	0.0935	0.1384	9.8418	0.0888	0.0841	9.6978	0.0852	0.0358	9.5593	0.0823	0.0203
24	10.260	0.0941	0.1459	10.106	0.0894	0.0884	9.9579	0.0858	0.0377	9.8157	0.0829	0.0214
25	10.532	0.0947	0.1533	10.374	0.09	0.0929	10.222	0.0863	0.0397	10.076	0.0834	0.0227
26	10.807	0.0953	0.1617	10.645	0.0905	0.0976	10.489	0.0869	0.0418	10.339	0.0839	0.024
27	11.085	0.0959	0.1701	10.919	0.0911	0.1025	10.759	0.0874	0.044	10.606	0.0845	0.0254
28	11.368	0.0965	0.1785	11.197	0.0917	0.1076	11.034	0.088	0.0463	10.876	0.085	0.0269
29	11.653	0.0971	0.1869	11.478	0.0922	0.1129	11.31	0.0885	0.0487	11.149	0.0856	0.0284
30	11.942	0.0977	0.1953	11.763	0.0928	0.1185	11.59	0.0891	0.0512	11.425	0.0861	0.03
31	12.233	0.0983	0.2037	12.05	0.0934	0.1243	11.873	0.0897	0.0538	11.704	0.0866	0.0317
32	12.527	0.0989	0.2122	12.339	0.094	0.1303	12.159	0.0902	0.0565	11.985	0.0872	0.0335
33	12.825	0.0995	0.2207	12.633	0.0946	0.1366	12.448	0.0908	0.0594	12.27	0.0877	0.0353
34	13.126	0.1002	0.2291	12.929	0.0951	0.1431	12.74	0.0913	0.0624	12.558	0.0883	0.0373
35	13.431	0.1008	0.2376	13.229	0.0957	0.1499	13.035	0.0919	0.0654	12.849	0.0888	0.0393
36	13.739	0.1014	0.2475	13.533	0.0963	0.157	13.335	0.0925	0.0687	13.145	0.0894	0.0415
37	14.050	0.102	0.2575	13.839	0.0969	0.1643	13.637	0.093	0.072	13.442	0.0899	0.0437
38	14.362	0.1026	0.2674	14.147	0.0975	0.172	13.94	0.0936	0.0756	13.741	0.0905	0.0461
39	14.680	0.1032	0.2773	14.46	0.0981	0.1799	14.248	0.0942	0.0792	14.045	0.091	0.0485
40	15.001	0.1039	0.2872	14.776	0.0987	0.1882	14.559	0.0947	0.083	14.352	0.0916	0.0511
41	15.324	0.1045	0.2981	15.094	0.0993	0.1968	14.873	0.0953	0.087	14.661	0.0921	0.0538
42	15.649	0.1051	0.3093	15.415	0.0999	0.2057	15.189	0.0959	0.0911	14.972	0.0927	0.0566
43	15.976	0.1057	0.3209	15.736	0.1005	0.2149	15.506	0.0965	0.0954	15.285	0.0932	0.0595
44	16.310	0.1063	0.3328	16.065	0.1011	0.2245	15.83	0.097	0.0999	15.604	0.0938	0.0625
45	16.644	0.107	0.3451	16.394	0.1017	0.2345	16.154	0.0976	0.1045	15.924	0.0944	0.0657
46	16.981	0.1076	0.3577	16.727	0.1023	0.2449	16.482	0.0982	0.1093	16.247	0.0949	0.0691
47	17.322	0.1082	0.3707	17.062	0.1029	0.2556	16.812	0.0988	0.1143	16.572	0.0955	0.0726
48	17.668	0.1089	0.3841	17.403	0.1035	0.2667	17.148	0.0994	0.1195	16.903	0.0961	0.0762
49	18.012	0.1095	0.3979	17.742	0.1041	0.2782	17.482	0.0999	0.1249	17.233	0.0966	0.08
50	18.362	0.1101	0.4121	18.086	0.1047	0.2902	17.822	0.1005	0.1306	17.567	0.0972	0.084

* Henry's law constants in this table are based on a combination of literature reported values and estimates derived from procedures presented in Section 2.1.2.1.

TABLE 6

Relevant Chemical Properties for the THMs

Property	Chloroform	BDCM	DBCM	Bromoform
Molecular Weight	119.38	163.8	208.03	252.77
Liquid Diffusivity (cm^2/sec)	9.21E-06 (20^oC) 1.50E-05 (40^oC)	9.07E-06 (20^oC) 1.48E-05 (40^oC)	8.94E-06 (20^oC) 1.46E-05 (40^oC)	8.81E-06 (20^oC) 1.44E-05 (40^oC)
Gas Diffusivity (cm^2/sec)	0.09175 (20^oC); 0.10386 (40^oC)	0.0871 (20^oC) 0.104 (40^oC)	0.0836 (20^oC) 0.0947 (40^oC)	0.0808 (20^oC) 0.0916 (40^oC)
Vapor Pressure (mm Hg)	160 (B)	57.4 (A)	15.6 (A)	5.4 (A)
Solubility (mg/L)	8000 (B)	3030 (A)	2700 (B)	3100 (A)
Henry's Law Constant	0.116 (20^oC) 0.287 (40^oC)	0.0722 (20^oC) 0.188 (40^oC)	0.0305 (20^oC) 0.0830 (40^oC)	0.0170 (20^oC) 0.0511 (40^oC)

Notes: Liquid-phase diffusivity, and gas-phase diffusivity are estimated based on the Hayduk and Laudie method (Lyman et al., 1990, pg. 17-200) and the Wilke and Lee Method (Lyman et al., 1990, pg 17-13), respectively. The Henry's law constant is estimated based on the method described in section 2.1.3.1, above.

Vapor pressure and solubility data are from the following sources:

a Risk Assessment Information System, 2001.

b Verschueren, 1983. Value reported at 20^oC.

TABLE 7

Relevant Chemical Properties for the Predictor Chemicals

Property	Acetone	Ethylacetate	Toluene	Ethylbenzene	Cyclohexane
Molecular Weight	58.08	88.1	92.1	106.17	84.16
Liquid-phase diffusivity @ 20°C (cm²/sec)	1.05E-05	8.36E-06	7.96E-06	7.19E-06	7.96E-06
Liquid-phase diffusivity @ 40°C (cm²/sec)	1.71E-05	1.36E-05	1.30E-05	1.17E-05	1.30E-05
Gas-phase diffusivity @ 20°C (cm²/sec)	0.110	0.0880	0.0831	0.0753	0.0853
Gas-phase diffusivity @ 40°C (cm²/sec)	0.124	0.0997	0.0942	0.0853	0.0966
Vapor pressure (mm Hg)	231 (A)	72.8 (B)	22 (B)	7 (B)	77 (B)
Solubility (mg/L)	1 E 06 (A)	8.6E04 (B)	515 (B)	152 (B)	55 (B)
Henry's law const @ 20°C	0.0011	0.00445	0.215	0.252	6.18
Henry's law const @ 40°C	0.00298	0.0132	0.456	0.642	11.62

Notes: Liquid-phase diffusivity, and gas-phase diffusivity are estimated based on the Hayduk and Laudie method (Lyman et al., 1990, pg 17-200 and the Wilke and Lee Method (Lyman et al., 1990, pg 17-13), respectively. The Henry's law constant is estimated based on the method described in section 2.1.3.1, above.
Vapor pressure and solubility data are from the following sources:

a Risk Assessment Information System, 2001.
b Verschueren, 1983. Value reported at 20°C.

TABLE 8

Summary of Normalized Percent Difference (Equation 9) for the THMs as a Function of Predictor Chemical

Property	Acetone	Ethylacetate	Toluene	Ethylbenzene	Cyclohexane
Chloroform					
Liquid Diffusivity	14.0%	9.2%	13.6%	21.9%	13.6%
Gas Diffusivity	19.9%	4.1%	9.4%	17.9%	7.0%
Henry's Law Constant	99.1%	96.2%	85.3%	117.2%	5227.6%
BDCM					
Liquid Diffusivity	15.8%	7.8%	12.2%	20.7%	12.2%
Gas Diffusivity	26.3%	1.0%	4.6%	13.5%	2.1%
Henry's Law Constant	98.5%	93.8%	197.8%	249.0%	8459.6%
DBCM					
Liquid Diffusivity	17.4%	6.5%	11.0%	19.6%	11.0%
Gas Diffusivity	31.6%	5.3%	0.6%	9.9%	2.0%
Henry's Law Constant	96.4%	85.4%	604.9%	726.2%	20162.3%
Bromoform					
Liquid Diffusivity	19.2%	5.1%	9.6%	18.4%	9.6%
Gas Diffusivity	36.1%	8.9%	2.8%	6.8%	5.6%
Henry's Law Constant	93.5%	73.8%	1164.7%	1382.4%	36252.9%

Note: Values evaluated at 20°C

TABLE 9

Estimated Values for Overall Mass Transfer Coefficient ($K_{OL}A$) based on Toluene

Appliance	Temp °C	Estimated $K_{OL}A$ (m^3/hr)			
		Chloroform	BDCM	DBCM	Bromoform
Shower	40	0.432	0.428	0.415	0.402
Bath:					
Fill	35	0.245	0.228	0.186	0.153
Bathing	35	0.0780	0.0735	0.0625	0.0531
Clothes Washer					
Fill	35	0.317	0.265	0.174	0.124
Wash	35	0.113	0.0637	0.0293	0.0177
Rinse	35	0.403	0.265	0.122	0.0735
Toilets	25	0.00468	0.00368	0.00312	0.00265
Faucets					
Kitchen	35	0.128	0.116	0.0913	0.0731
Bathroom	35	0.128	0.116	0.0913	0.0731
Laundry Room	30	0.117	0.104	0.0792	0.0613

TABLE 10

Shower Frequency Values from NHAPS and REUWS Analyses

Statistic	Population				
	Children 5-12 years (NHAPS)	Men 18-48 years (NHAPS)	Women 18-48 years (NHAPS)	All Households (NHAPS)	All Households (REUWS)
Shower Frequency per person-day	0.6	1.2	1.1	1.0	0.8

TABLE 11

Summary Statistics for Shower Duration, Volume and Flowrate from REUWS Analyses

Statistic for All Households (REUWS)	Geometric Mean	Geometric Standard Deviation	Arithmetic Mean
Shower Duration	6.8 minutes	1.64 minutes	7.7 minutes
Shower Volume (adults only)	15.8 gallons/shower	1.75 gallons	18.6 gallons/shower
Shower Flowrate	2.0 gallons/minute	1.58 gallons/min	2.4 gallons/minute

TABLE 12

Selected Model Parameters for Showers

Statistic	Value
Shower Frequency per person per day	
Children 6 years	0.6
Men 15-45 years	1.2
Women 15-45 years	1.1
Shower Duration (Geometric Mean)	6.8 minutes
Shower Duration (Geometric Standard Deviation)	1.64 minutes
Shower Flowrate	2.4 gallons/minute

TABLE 13

Bath Frequency and Duration Values from NHAPS Analyses

Statistic (NHAPS)	Population			
	Men 18-48 years	Women 18-48 years	Children 5-12 years	All Households
Bath frequency (events per person per day)	0.2	0.4	0.5	0.3
Bath Duration				
Geometric Mean (minutes)	17.2	17.8	18.6	17.6
Geometric Standard Deviation (minutes)	1.99	2.05	1.66	1.88
Arithmetic Mean (minutes)	20.8	21.5	20.8	20.9

TABLE 14

Bath Volume and Flowrate Values from REUWS Analyses

Statistic for All Households (REUWS)	Geometric Mean	Geometric Standard Deviation	Arithmetic Mean
Bath Flowrate	4.4 gallons/minute	1.71 gallons/minute	4.9 gallons/minute

TABLE 15

Selected Model Parameters for Bathing

Statistic	Men 15-45 years	Women 15-45 years	Children 6 years
Bathing Frequency per person per day	0.2	0.4	0.5
Bathing Duration	20.8 minutes	21.5 minutes	20.8 minutes
Bath Volume	50 gallons	50 gallons	50 gallons
Bath Fill Duration	8 minutes	8 minutes	8 minutes

TABLE 16

Frequency of Clothes Washer Use for 3-Person Households: RECS

Frequency	3-Person Family
	%
15+ loads/wk	3.4
10-15 loads/wk	14.8
5-9 loads/wk	50.2
2-4 loads/wk	28.8
1 load or less/wk	2.9
Total	100.0
Estimated Mean Frequency	6.7 loads per week

TABLE 17

Typical Clothes Washer Parameters: Based on REUWS and Experimental Data

Parameter	Typical Top-Loaded Clothes Washer	Comments
Cycle 1	Wash	
Volume	16.6 gallons	Mean volume for first fills (REUWS)
Time to Fill	3.8 minutes	Based on experimental data[a] on time to fill for a typical wash cycle[b]
Time to Agitate	12.0 minutes	Based on experimental data on time to agitate for a typical wash cycle[b]
Time to Drain/Spin	4.0 minutes	Based on experimental data on time to drain and spin for a typical wash cycle[b]
Cycles 2, 3 and 4	Rinse	
Volume	15.3 gallons	Mean volume for second fills (REUWS)
Time to Fill	7.5 minutes	Based on experimental data on time to fill for a typical rinse cycle[b]
Time to Agitate	4.0 minutes	Based on experimental data on time to agitate for a typical rinse cycle[b]
Time to Drain/Spin/Spray	8.0 minutes	Based on experimental data on time to drain, spin and spray for a typical rinse cycle[1]
Cycle 2 is 100% likely to occur Cycle 3 is 18.7% likely to occur Cycle 4 is 0.8% likely to occur		Based on REUWS data
Average Total Time for Washing Event (for this configuration)	43.1 minutes	Time for 1st cycle (19.8 minutes) plus (1.0 + 0.187 + 0.008) multiplied by time for rinse cycle (19.5 minutes)

1 Average calculated using only settings to high-water level.

2 For experimental data see Wilkes et al., 2004

TABLE 18

Selected Model Parameters for Clothes Washer Use

Parameter	Value Used in Modeling
Temperature	35˚C
Wash	
Fill Duration	3.3 minutes
Agitation Duration	7.4 minutes
Volume	16.6 gallons
Rinse	
Fill Duration	4.2 minutes
Agitation Duration	9.8 minutes (5 min. added for spin rinse)
Volume	21.0 gallons
Frequency	1.0 events per day for 3 person household

Note: The model is currently set up to handle 2 complete cycles. The first event is the wash cycle, consisting of the wash fill and the wash agitation and drain, the second event is a combination of all the rinse activities, which are represented as 1.2 rinse cycles.

TABLE 19

Frequency of Dishwasher Use for 3-person Households: U.S. DOE (1999)

Frequency	3-Person Family (%)
Daily	17.7
4-6 times/week	29.9
Less than 4 times/week	52.4
Total	100.0
Estimated Mean Frequency	3.8 times/week

TABLE 20

Manufacturer Supplied Dishwasher Information Summary

Condition	Total Volume, gal	Number of Fills	Average Volume per Fill, gal
Dishwasher Model: Whirlpool GU980SCG[a]			
Rinse Only -- Heavy Soil	4.3	2	2.15
Rinse Only – Light Soil	2.2	2	1.1
Quick Wash - Heavy Soil	6.9	2	3.45
Quick Wash - Light Soil	4.8	2	2.4
China – Heavy Soil	8.6	3	2.87
China - Light Soil	6.5	3	2.17
Low Energy - Heavy Soil	8.6	3	2.87
Low Energy - Light Soil	6.5	3	2.17
Normal - Heavy Soil	10.8	3 or 4	3.60-2.7
Normal - Medium Soil[b]	8.6	3 or 4	2.87-2.15
Normal – Light Soil	6.9	3 or 4	2.30-1.725
Heavy - Heavy Soil	10.8	5	2.16
Heavy - Medium Soil	10.8	5	2.16
Heavy - Light Soil	8.6	5	1.72
Dishwasher Model: Whirlpool DU920PFG[a]			
Rinse Only	2.2	2	1.1
Low Energy/China	6.5	3	2.17
Normal[b]	6.9	3	2.3
Heavy	8.6	5	1.72
Pots-N-Pans	8.6	5	1.72

TABLE 20 cont.			
Condition	Total Volume, gal	Number of Fills	Average Volume per Fill, gal
Dishwasher Model: Whirlpool DU850DWG[a]			
Rinse Only	2.9	2	1.45
Light Wash	5.8	4	1.45
Normal[b]	7.2	5	1.44
Pots-N-Pans	8.6	6	1.43
Dishwasher Model: GE Potscrubber[c]			
Rinse and Hold	3	2	1.5
Short Wash	7	5	1.4
Water Saver Cycle	6.1	4	1.53
China/Crystal Cycle	7.3	5	1.46
Light Wash Cycle	7	5	1.4
Normal Wash Cycle[b]	8.5	6	1.42
Potscrubber Cycle	10.1	7	1.44

[a] whirlpool@in-response.com 9/2000
[b] Normal cycles used for calculations in following table of selected model parameters.
[c] answerctr@exchange.appl.ge.com 2001

TABLE 21

Selected Model Parameters for Dishwasher Use

Characteristic	Average*
Volume of Water	8.5 gallons
Number of Cycles (without drying)	2 Cycles
Volume of Water per Cycle	4.3 gallons
Duration per Cycle	30 minutes
Frequency	0.5 events per day for 3 person households

*Based on the average of the "normal" cycles of selected dishwashers

TABLE 22

Summary of Reported Toilet Use Characteristics from Literature

Toilet Type	Reported Frequency (fpcd)[a]	Volume (gal/flush)	Population/ Sample Size	Reference	Special Study Conditions
Low-Flow (Avg. 3.6 gpf)	Mean = 3.8 Min =1.8 Max = 8.4	Mean =3.6 Min = 1.7 Max = 5.6	Tampa, Florida, 25 single family homes	Konen and Anderson, 1993	Study comparison of low flow to ultra-low flow retrofit (average 2.9 persons/ home)
Ultra-low Flow (rated 1.6 gpf)	Mean = 4.5 Min = 1.7 Max = 12.8	Mean = 1.6 Min = 1.1 Max =3.0	Tampa, Florida 25 single family homes	Konen and Anderson, 1993	
Low-Flow (Avg. 4.0 gpf)	Mean = 3.2 or 12.8 fphd[b]	Mean = 4.0	Oakland, California, 25 single family homes	Aher et al.,1991	Study comparison of low flow to ultra-low flow retrofit (average 4.4 persons/ home)
Ultra-low Flow (rated 1.6 gpf)	Mean = 3.7 or 15.9 fphd	Mean = 1.8 Min = 1.3 Max = 2.4	Oakland, California, 25 single family homes	Aher et al.,Oct. 1991	
Variety of toilets (33% low volume models or devices)	Mean = 4.0		CA, CO, D.C., VA, WA, 196 households, 545 persons, 356 toilets	HUD, 1984	Study subjects recorded toilet flush counts

[a]fpcd: Flushes per capita day
[b]fphd: Flushes per home per day

TABLE 23

Statistics for Toilet Flushes from REUWS

	All Flushes			Single Flushes Only		
	Frequency (flushes/ person/day)	Family Size	Sampling Days	Duration of Tank Fill (seconds)	Volume (gallons)	Mode Flow (gallons per minute)
Minimum	0.0	0.0	1.0	10.0	0.3	0.0
Maximum	42.7	9.0	16.0	2,720.0	9.8	14.1
Mean	5.2	2.8	10.7	71.4	3.5	3.9
Standard Deviation	3.15	1.37	1.63	29.77	1.18	1.31
Number of Records or Households[a]	2,145[b]	2,158	2,158	245,328	245,331	245,331

[a]Number of households reflects the combined total of homes participating in the first sampling period (1,173) and second sampling period (985).
[b]13 surveys indicated "0" for Q.31 or Q.30 regarding the number of people in selected age groups (households aggregated from 295,660 records).

TABLE 24

Selected Parameters for Toilet Use

Statistics	Value
Frequency	6 flushes/person/day
Volume of water used per flush	3.5 gallons/flush

Note: model assumes instant filling

TABLE 25

Summary of Reported Faucet Frequency and Volume of Use Characteristics in Literature

Type of Appliance	Location	Frequency	Volume (gpm)	Population/ Sample Size	Reference
Conventional	Kitchen	Not given	Maximum flow[a] Mean = 2.4 Min = 1.5 Max = 3.8	Tampa, Florida, 25 single family homes (avg. 2.9 persons/home)	Konen and Anderson, March 1993
Conventional	Bathroom	Not given	Maximum flow[a] Mean = 3.4 Min = 0.9 Max = 7.9	Tampa, Florida, 25 single family homes (avg. 2.9 persons/home)	Konen and Anderson, March 1993
Conventional	Not given	Not given	9.0 gal/person/ day[b]	Nationwide	HUD, 1984

[a]Measured flowrates with faucets in fully open position
[b]Estimated value

TABLE 26

Summary Statistics for Faucet Use from REUWS

	Duration (minutes)	Volume (gallons)	Mode Flow (gpm)	Frequency of Use per day per person
Minimum	0.0	0.01	0.0	2.3
Maximum	90.0	37.6	10.7	143.0
Mean	0.6	0.7	1.2	17.4
Standard Deviation	0.76	0.98	0.68	11.6
Number of Records	973,717	973,717	973,717	965 (households)

TABLE 27

Selected Parameters for Faucet Use

Statistic	Value
Faucet Use Duration	Range from 1.1 to 1.7 minutes
Flowrate	1.20 gallons per minute
Frequency of Faucet Use	15.5 events per person per day

TABLE 28

Tap Water Consumption Characteristics

Population	Average Consumption (units)
Canadian Department of Health[a]: 970 individuals, 295 households	
Children, 3-5 Years	48 mL/kg
Children, 6-17 Years	26 mL/kg
Females, 18-34 Years	23 mL/kg
Females, 35-54 years	25 mL/kg
Males, 18-54 Years	19 mL/kg
Average Daily Consumption, (All) 90th Percentile	1.34 L/day 2.36 L/day
1978 Drinking Water Consumption in Great Britain[b]: N = 3,564 People	
Females, 5-11 Years	0.533 L/day
Females, 18-30 Years	0.991 L/day
Females, 31-54 Years	1.091 L/day
Males, 5-11 Years	0.550 L/day
Males, 18-30 Years	1.006 L/day
Males, 31-54 Years	1.201 L/day
1987 National Cancer Institute Study[c]: N = 8,000 White Adults	
Females, 21-84 Years	1.35 L/day
Males, 21-84 Years	1.4 L/day
Females and Males, 18-44 Years	1.3 L/day
1977 – 78 USDA Nationwide Food Consumption Survey (NFCS)[d]: N = 26,000	
Adults, 20 to 75 or older Years 90th Percentile	1.2 L/day 2.1 L/day

TABLE 28 cont.

Population	Average Consumption (units)
Adults, 15-19 Years[e]	999 mL/day (N = 2998)
Adults, 20-44 Years[e]	1,255 mL/day (N = 7171)
Children, 4-6 Years[e]	37.9 mL/kg-day (N = 1702)
Pregnant Women[f]	2,076 mL/day (N = 188)
Lactating Women[f]	2,242 mL/day (N = 77)
Non-Pregnant, Non-Lactating Women, 15-49 Years[f]	1,940 mL/day (N = 6201)

All references discussed and cited in Exposure Factors Handbook, U.S. EPA (1997a)
[a]Canadian Ministry of National Health and Welfare (1981)
[b]Hopkins and Ellis (1980)
[c]Cantor et al. (1987)
[d]Ershow and Cantor (1989)
[e]Ershow and Cantor (1989)
[f]Ershow et al. (1989)

TABLE 29

Parameters of Fitted Lognormal Distribution for Water Ingestion in the United States

Population	Geometric Mean ml/day	Geometric Standard Deviation
Women, direct (20+ years)	394	2.52
Women, indirect (20+ years)	384	2.20
Men, direct (20+ years)	389	2.69
Men, indirect (20+ years)	418	2.33
Children, direct (1-10 years)	188	2.50
Children, indirect (1-10 years)	97	2.51
All ages, direct	321	2.79
All ages, indirect	290	2.53

Source: Fitted to data from Table A1 in U.S. EPA (2000d)

TABLE 30

Comparison of Consumption for Raw Data and Fitted Distributions based on CSFII Data

Percentile	Men, 20+ years				Women, 20+ years				Children, 1-10 years				Total Population			
	Direct Consumption (ml/d)		Indirect Consumption (ml/d)		Direct Consumption (ml/d)		Indirect Consumption (ml/d)		Direct Consumption (ml/d)		Indirect Consumption (ml/d)		Direct Consumption (ml/d)		Indirect Consumption (ml/d)	
	Data	Fitted Lognormal Distribution	Data	Fitted Lognormal Distribution	Data	Fitted Lognormal Distribution	Data	Fitted Lognormal Distribution	Data	Fitted Lognormal Distribution	Data	Fitted Lognormal Distribution	Data	Fitted Lognormal Distribution	Data	Fitted Lognormal Distribution
1	---	39	---	58	---	46	---	61	---	22	---	11	---	30	---	33
5	---	77	---	104	---	86	---	105	---	42	---	21	---	60	---	63
10	---	110	---	142	---	121	---	140	---	58	---	30	---	87	---	88
50	352	390	412	419	349	394	365	385	174	189	84	97	290	322	262	290
90	1,450	1,380	1,210	1,235	1,395	1,285	1,080	1,057	696	611	352	316	1,270	1,193	1,008	952
95	1,891	1,980	1,597	1,682	1,865	1,799	1,394	1,410	919	854	457	441	1,769	1,734	1,334	1,336
99	3,773	3,897	3,094	3,000	3,062	3,386	2,367	2,421	1,415	1,601	734	828	3,240	3,499	2,373	2,523

TABLE 31

Selected Parameters for Tapwater Consumption Modeling Study

Statistic	Man (age 15-45 years)		Woman (age 15-45 years)		Child (age 6 years)	
	Direct Consumption	Indirect Consumption	Direct Consumption	Indirect Consumption	Direct Consumption	Indirect Consumption
Volume (Liters/day)						
Geometric Mean	0.3895	0.419	0.3943	0.3848	0.1889	0.0974
Geometric Standard Deviation	0.988	0.8449	0.9228	0.4894	0.9173	0.9187
Duration (minutes to consume water)						
Geometric Mean	2.236	3.162	2.236	3.162	2.236	3.162
Geometric Standard Deviation	1.269	1.517	1.269	1.517	1.269	1.517
Arithmetic Mean	5	10	5	10	5	10
Arithmetic Standard Deviation	10	30	10	30	10	30
Mean Frequency	8	8	8	8	8	8
Time of Day	5 am-10 pm	5 am-10 pm	5 am-10 pm	5 am-10 pm	5 am-10 pm	5 am-10 pm

TABLE 32

Analysis of RECS for Total House Volume for 3-Person U.S. Households
(U.S. DOE, 1999)

Percentile	Area, ft^2	Area, m^2	Volume, ft^3	Volume, m^3*
4.1	0-600	55.7	4800	135.9
22.3	601-999	92.8	7992	226.3
60.4	1000-1599	148.6	12792	362.3
79.7	1600-1999	185.7	15992	452.9
90.5	2000-2399	222.9	19192	543.5
96.6	2400-2999	278.6	23992	679.5

*Volumes were calculated by assuming an 8 ft ceiling height

TABLE 33

Estimated Range of Dimensions of Water-Use Zones Based on Hoke (1988, 1994)

Zone	Dimension	Small	Large
Hall Bath	Area (m^2)	3.2	6.1
	Volume (m^3)	7.9	14.9
Master Bath	Area (m^2)	2.0	3.5
	Volume (m^3)	4.9	8.5
Kitchen	Area (m^2)	6.3	7.4
	Volume (m^3)	15.4	18.1
Laundry	Area (m^2)	5.5	10.4
	Volume (m^3)	13.5	25.4
Shower	Area (m^2)	1.2	1.8
	Volume (m^3)	2.9	4.5

Source: Hoke (1988, 1994)

TABLE 34

Summary Statistics for U.S. Residential Air Exchange Rates

	West Region	North Central Region	Northeast Region	South Region	All Regions
Arithmetic Mean (h^{-1})	0.66	0.57	0.71	0.61	0.63
Arithmetic Standard Deviation (h^{-1})	0.87	0.63	0.60	0.51	0.65
Geometric Mean (h^{-1})	0.47	0.39	0.54	0.46	0.46
Geometric Standard Deviation	2.11	2.36	2.14	2.28	2.25
10^{th} Percentile (h^{-1})	0.20	0.16	0.23	0.16	0.18
50^{th} Percentile (h^{-1})	0.43	0.35	0.49	0.49	0.45
90^{th} Percentile (h^{-1})	1.25	1.49	1.33	1.21	1.26
Maximum (h^{-1})	23.32	4.52	5.49	3.44	23.32

Source: U.S. EPA (1997b)

TABLE 35

Summary of Volume and Ventilation Parameters for Case 48

Parameter	Value	Units
WHACH	0.11	hr^{-1}
Whole House Volume	311.1	m^3
Laundry Volume	18.3	m^3
Kitchen Volume	17.3	m^3
Hall Bath Volume	12.6	m^3
Master Bath Volume	8.4	m^3
Shower Volume	4.4	m^3
ROH Volume	250.0	m^3
ROH to Outdoor Flowrate	35.4	m^3/hr
Laundry to ROH Flowrate	2.08	m^3/hr
Kitchen to ROH Flowrate	1.96	m^3/hr
Hall Bath to ROH Flowrate	1.43	m^3/hr
Master Bath to ROH Flowrate	0.95	m^3/hr
Shower to Master Bath Flowrate	50	m^3/hr

TABLE 36

Pearson Correlation Coefficients between Chloroform and BDCM, DBCM, and Bromoform based on all samples in the 85th to 95th Percentile in the Cumulative Chloroform Concentrations

		BDCM	DBCM	Bromoform
CHLOROFORM	Pearson Correlation	0.528	0.001	-0.183
	Sig. (2-tailed)	0.000	0.857	0.000
	N	15974	15950	15926

TABLE 37

Pearson Correlation Coefficients between BDCM and Chloroform, DBCM, and Bromoform based on all samples in the 85th to 95th Percentile in the Cumulative BDCM Concentrations

		Chloroform	DBCM	Bromoform
BDCM	Pearson Correlation	0.528	0.685	0.149
	Sig. (2-tailed)	0.000	0.000	0.000
	N	15974	16089	16057

TABLE 38

Pearson Correlation Coefficients between DBCM and Chloroform, BDCM, and Bromoform based on all samples in the 85th to 95th Percentile in the Cumulative DBCM Concentrations

		Chloroform	BDCM	Bromoform
DBCM	Pearson Correlation	0.001	0.685	0.640
	Sig. (2-tailed)	0.857	0.000	0.000
	N	15950	16089	16022

TABLE 39

Pearson Correlation Coefficients between Bromoform and Chloroform, BDCM, and DBCM based on all samples in the 85th to 95th Percentile in the Cumulative Bromoform Concentrations

		Chloroform	BDCM	DBCM
Bromoform	Pearson Correlation	-0.183	0.149	0.640
	Sig. (2-tailed)	0.000	0.000	0.000
	N	15926	16057	16022

TABLE 40

95th Percentile Chloroform (66 ppb) Values for ICR Surface Water Treatment Plants

EVENT ID	$CHCl_3$	BDCM	DBCM	$CHBr_3$	Disinfectant	Utility Name
1406409	66	2.6	0.5	0.5	CL2	East Bay Municipal Utility District
1439209	66	2.8	0.5	0.5	CL2_CLM	East Bay Municipal Utility District
6755111	66	10	1	0.5	CL2_CLM	Newport News Waterworks
2041103	66	11	1.2	0.5	CL2	City of Sacramento
3265607	66	12	1.3	0.5	CLX	Cobb County-Marietta Water Auth
4030312	66	9.3	1.4	0.5	CL2	City of New Bedford Water Depart
6765611	66	11	1.6	0.5	CL2	City of Norfolk, Dept. of Utilities
1417215	66	14	3.1	0.5	O3	East Bay Municipal Utility District
3277801	66	15	3.6	0.5	CLX	Cobb County-Marietta Water Auth
5855003	66	19	4.1	0.5	CL2	PRASA - Aguadilla Urbano
5589303	66	19.3	5	0.5	CL2_CLM	Philadelphia Water Department
5400913	66	22	6.5	0.5	CL2_CLM	Lawton Water Treatment Plant
4075701	66	29	12	0.5	CL2	Washington Suburban Sanitary Com.
5401316	66	24	11	1.1	CL2_CLM	Lawton Water Treatment Plant

Note: the shaded row indicates the row selected based on the stated criteria.

TABLE 41

95th Percentile BDCM (23.8 ppb) Values for ICR Surface Water Treatment Plants

Event ID	$CHCl_3$	BDCM	DBCM	$CHBr_3$	Disinfectant	Utility Name
5971217	26.1	23.8	17.7	2.6	CLM	Charleston
5971117	26.5	23.8	17.4	2.6	CLM	Charleston
6783101	59.5	23.8	5.1	0.5	CL2	City of Portsmouth, DPU

Note: the shaded row indicates the row selected based on the stated criteria.

TABLE 42

95th Percentile DBCM (17 ppb) Values for ICR Surface Water Treatment Plants

Event ID	$CHCl_3$	BDCM	DBCM	$CHBr_3$	Disinfectant	Utility Name
6380918	1.2	5.2	17	11	CL2_CLM	City of Lubbock Water Utilities
6381018	1.4	5.3	17	11	CL2_CLM	City of Lubbock Water Utilities
6385218	1.7	5.7	17	11	CL2_CLM	City of Lubbock Water Utilities
1461008	1.3	6	17	17	CL2_CLM	Contra Costa Water District
6385109	3.7	7.8	17	7.9	CL2_CLM	City of Lubbock Water Utilities
6385312	2.3	7.9	17	9.9	CL2_CLM	City of Lubbock Water Utilities
6381009	4.4	8.9	17	7.6	CL2_CLM	City of Lubbock Water Utilities
6385303	3.1	9.1	17	8.3	CL2_CLM	City of Lubbock Water Utilities
6385203	3	9.2	17	8.1	CL2_CLM	City of Lubbock Water Utilities
6261102	4.6	9.3	17	8.6	CLX	El Paso Water Utilities
6411009	6	9.7	17	24	CL2_CLM	City of Corpus Christi
6571607	8.7	10	17	7.8	CL2_CLM	City of Laredo, Texas
6571707	6	11	17	8.2	CL2_CLM	City of Laredo, Texas
6571310	7.4	13	17	6.4	CL2_CLM	City of Laredo, Texas
6540810	8.1	13	17	6.8	CL2_CLM	City of Austin
6540710	8.6	13	17	6.1	CL2_CLM	City of Austin
5640602	10.2	14.7	17	5	CL2	Pittsburgh Water and Sewer Authority
2085603	11	16	17	4.3	CL2	Cucamonga County Water District
2165004	12	18	17	4.1	CL2_CLM	Helix Water District
2161013	12	20	17	3.4	CL2_CLM	Helix Water District
6392606	13	20	17	3.3	CLM	City of Waco Utility Department
6392206	13	20	17	3.6	CLM	City of Waco Utility Department
2165013	14	20	17	3.3	CL2_CLM	Helix Water District
6393006	14	20	17	3.3	CLM	City of Waco Utility Department
1715402	17	20	17	3	CL2_CLM	Metro Water Dist of So Calif

TABLE 42 cont.

Event ID	$CHCl_3$	BDCM	DBCM	$CHBr_3$	Disinfectant	Utility Name
6545404	20	20	17	4.4	CL2_CLM	City of Austin
6391406	13	21	17	3.5	CLM	City of Waco Utility Department
1295114	14	21	17	4.1	CL2	City of Scottsdale
1720805	15	21	17	2.4	CL2_CLM	Metro Water Dist of So Calif
1295211	24	21	17	3.8	CL2	City of Scottsdale
2155102	20	23	17	3.2	CL2	City of Escondido
6401215	22	23	17	3.9	CLM	City of Waco Utility Department
6401615	22	23	17	4.1	CLM	City of Waco Utility Department
6401715	22	23	17	4.1	CLM	City of Waco Utility Department
5971214	27.9	23.9	17	2.4	CLX	Charleston
2155202	21	24	17	3	CL2	City of Escondido
1271116	29	25	17	2	CL2	City of Glendale
1271216	31	25	17	1.9	CL2	City of Glendale
2190703	23	26	17	1.7	CL2_CLM	City of San Diego Water Utilities
2155105	23	26	17	2.7	CL2	City of Escondido
6392412	26	26	17	1.8	CLM	City of Waco Utility Department
1271513	29	26	17	2.3	CL2	City of Glendale
2155005	26	27	17	2.8	CL2	City of Escondido
6393012	28	27	17	1.6	CLM	City of Waco Utility Department
1242211	45	27	17	4.2	CL2	Chandler Municipal Water Department
1271610	39	28	17	2	CL2	City of Glendale
3790804	58.7	31.7	17	1.5	CL2	Evansville Water & Sewer Utility
6402418	27	34	17	1.8	CLM	City of Waco Utility Department
1261813	140	44	17	3.7	CL2	City of Glendale

Note: the shaded row indicates the row selected based on the stated criteria.

TABLE 43

95th Percentile Bromoform (5.6 ppb) Values for ICR Surface Water Treatment Plants

Event ID	$CHCl_3$	BDCM	DBCM	$CHBr_3$	Disinfectant	Utility Name
6530613	5.9	12.4	5.4	5.6	CLX	City of Abilene Water Utilities
6145313	1.4	4	6.2	5.6	CLX	Brownsville Public Utilities Board
6571716	7.1	15	13	5.6	CL2_CLM	City of Laredo, Texas
1201012	35.9	24.4	17.2	5.6	CL2	Phoenix Municipal Water System
1285101	10.1	15.3	20.9	5.6	CLX	City of Mesa, Utility
5609803	23.4	30.4	25.4	5.6	CL2_CLM	Philadelphia Water Department
1321404	13	25	26	5.6	CL2	City of Tempe
1321604	14	25	26	5.6	CL2	City of Tempe

Note: the shaded row indicates the row selected based on the stated criteria.

TABLE 44

Summary of THM Concentrations Paired with the 95th Percentile for Each THM for All ICR Samples

Variable Subgroup	Description	Concentration, ppb (percentile)			
		Chloroform	BDCM	DBCM	Bromoform
All Reported Samples	Chloroform 95th Percentile	65.9 (95)	18.1 (90)	3.4 (65)	0.5 (0)
	BDCM 95th Percentile	10.0 (37)	23.0 (95)	42.0 (1)	24.0 (99)
	DBCM 95th Percentile	120.0 (1)	58.0 (1)	16.0 (95)	0.5 (0)
	Bromoform 95th Percentile	36.0 (79)	46.0 (1)	37.0 (1)	6.1 (95)
	MEAN	21.9	8.2	4.1	1.6
Number of Reported Samples		15987	16144	16109	16103

Note: The ICR database contained 18,214 records of analyzed THM samples. Some records were incomplete for a variety of quality control reasons. No records containing reported values were excluded from this analysis.

TABLE 45

Description of Variables Used in Analysis and Their Associated Attributes

ICR Database Variable Name	Variable Definition	Variable Attribute to be Analyzed
MSRC_CAT	Characterization of the plant water resource type	o Surface Water Intake
		o Ground Water Intake
WTP_DIS	Categorical description of disinfection practices in the treatment plant	o Ozonation
		o All chlorine-based disinfection systems
		o Chlorine Only
		o Chloramine
		o Chlorine dioxide
		o Chlorine followed by chloramine
SAMP_QTR	Definition of the sampling quarter	o July-September of 1997 & 1998
		o October-December of 1997 & 1998
		o January-March 1998
		o April-June 1998

TABLE 46

Summary of THM Concentrations Paired with the 95th Percentile for the Analyzed THM Based on Analysis of the ICR Database.

Variable Subgroup	THM Analysis Description	Concentration, ppb (Percentile)			
		Chloroform	BDCM	DBCM	Bromoform
All Systems Using Surface Water Intake (N = 12,440)	Chloroform 95th Percentile	66.0 (95)	29.0 (98)	12.0 (90)	0.5 (0)
	BDCM 95th Percentile	26.1 (62)	23.8 (95)	17.7 (95)	2.6 (89)
	DBCM 95th Percentile	140.0 (100)	44.0 (100)	17.0 (95)	3.7 (92)
	Bromoform 95th Percentile	14.0 (34)	25.0 (96)	26.0 (98)	5.6 (95)
All Systems Using Ground Water Intake (N = 4,318)	Chloroform 95th Percentile	44.8 (95)	7.2 (83)	0.5 (0)	0.5 (0)
	BDCM 95th Percentile	42.6 (94)	15.3 (95)	5.1 (84)	0.5 (0)
	DBCM 95th Percentile	0.5 (0)	3.6 (67)	12.0 (95)	23.0 (99)
	Bromoform 95th Percentile	3.5 (64)	9.0 (87)	17.0 (98)	8.3 (95)
All Systems Using Ozonation as Primary Disinfectant (N = 645)	Chloroform 95th Percentile	65.2 (95)	16.0 (91)	2.5 (49)	0.5 (0)
	BDCM 95th Percentile	71.0 (95)	20.0 (95)	4.9 (76)	0.5 (0)
	DBCM 95th Percentile	40.0 (87)	18.0 (93)	9.7 (95)	0.5 (0)
	Bromoform 95th Percentile	2.0 (27)	5.3 (57)	7.8 (90)	5.8 (95)
Systems Using any type of Chlorine Disinfectant Process (N = 14,015)	Chloroform 95th Percentile	66.0 (95)	29.0 (98)	12.0 (90)	0.5 (0)
	BDCM 95th Percentile	9.1 (26)	24.0 (95)	46.0 (100)	34.0 (100)
	DBCM 95th Percentile	140.0 (100)	44.0 (100)	17.0 (95)	3.7 (91)
	Bromoform 95th Percentile	5.5 (18)	12.3 (76)	6.0 (78)	6.0 (95)

TABLE 46 cont.

Variable Subgroup	THM Analysis Description	Concentration, ppb (Percentile)			
		Chloroform	BDCM	DBCM	Bromoform
Systems Using Chlorine as Primary Disinfectant (N = 9,137)	Chloroform 95th Percentile	69.1 (95)	24.9 (96)	5.8 (82)	0.5 (0)
	BDCM 95th Percentile	9.1 (27)	24.0 (95)	46.0 (100)	34.0 (100)
	DBCM 95th Percentile	14.0 (38)	6.6 (48)	15.0 (95)	45.0 (100)
	Bromoform 95th Percentile	21.0 (52)	29.0 (98)	20.0 (97)	4.2 (95)
Systems Using Chlorine followed by Chloramine (N = 3,242)	Chloroform 95th Percentile	59.7 (95)	9.4 (53)	0.5 (0)	0.5 (0)
	BDCM 95th Percentile	13.0 (28)	24.0 (95)	33.0 (99)	11.0 (97)
	DBCM 95th Percentile	35.0 (77)	40.0 (100)	20.0 (95)	3.3 (89)
	Bromoform 95th Percentile	22.0 (54)	37.0 (99)	31.0 (99)	6.6 (95)
Systems Using Chloramine as Primary Disinfectant	Chloroform 95th Percentile	47.2 (95)	13.3 (77)	1.8 (46)	0.5 (0)
	BDCM 95th Percentile	30.0 (87)	27.6 (95)	21.0 (97)	2.3 (74)
	DBCM 95th Percentile	27.0 (83)	34.0 (98)	17.2 (95)	1.8 (69)
	Bromoform 95th Percentile	0.5 (0)	1.5 (15)	5.1 (59)	12.0 (95)
Systems Using Chlorine Dioxide as Primary Disinfectant	Chloroform 95th Percentile	70.0 (95)	8.7 (56)	0.5 (0)	0.5 (0)
	BDCM 95th Percentile	16.0 (53)	22.0 (95)	23.0 (97)	9.9 (90)
	DBCM 95th Percentile	5.8 (31)	10.5 (67)	18.4 (95)	5.3 (79)
	Bromoform 95th Percentile	11.0 (42)	24.0 (97)	35.0 (99)	13.9 (95)

TABLE 46 cont.

Variable Subgroup	THM Analysis Description	Concentration, ppb (Percentile)			
		Chloroform	BDCM	DBCM	Bromoform
Systems Sampled between July and September (1997 and 1998)	Chloroform 95th Percentile	74.8 (95)	17.6 (84)	4.0 (65)	0.5 (0)
	BDCM 95th Percentile	14.0 (40)	27.0 (95)	43.0 (100)	23.0 (99)
	DBCM 95th Percentile	170.0 (100)	70.0 (100)	20.0 (95)	1.6 (77)
	Bromoform 95th Percentile	30.0 (64)	37.0 (99)	33.0 (99)	6.5 (95)
Systems Sampled between October and December (1997 and 1998)	Chloroform 95th Percentile	55.0 (95)	29.0 (99)	17.0 (97)	2.3 (86)
	BDCM 95th Percentile	22.1 (67)	21.7 (95)	14.7 (95)	2.6 (87)
	DBCM 95th Percentile	38.8 (87)	30.8 (99)	14.6 (95)	2.3 (86)
	Bromoform 95th Percentile	20.0 (62)	36.0 (99)	30.0 (99)	6.4 (95)
Systems Sampled between January and March (1998)	Chloroform 95th Percentile	49.0 (95)	32.0 (99)	5.3 (80)	0.5 (0)
	BDCM 95th Percentile	11.0 (46)	19.0 (95)	20.0 (98)	5.5 (95)
	DBCM 95th Percentile	1.5 (16)	5.2 (50)	14.1 (95)	40.0 (100)
	Bromoform 95th Percentile	14.1 (57)	23.0 (98)	16.9 (97)	5.3 (95)
Systems Sampled between April and July (1998)	Chloroform 95th Percentile	70.3 (95)	6.9 (55)	0.5 (0)	0.5 (0)
	BDCM 95th Percentile	24.0 (59)	21.0 (95)	17.0 (97)	3.8 (92)
	DBCM 95th Percentile	60.0 (92)	23.0 (96)	14.0 (95)	5.8 (95)
	Bromoform 95th Percentile	75.0 (96)	37.0 (100)	32.0 (100)	5.0 (95)

TABLE 47

Chemical Properties of Compounds (24ºC) Studied by Howard and Corsi (1996)

Chemical	H (unitless)	D_L (cm^2/sec)[a]	D_G (cm^2/sec)[b]
Cyclohexane	7.1	9.0 E –6	0.088
Toluene	0.27	9.1 E –6	0.085
Acetone	0.0012	1.1 E –5	0.11

[a]D_L is estimated using the Hayduk and Laudie method (Lyman et al., 1990, pp 17-20).
[b]D_G is estimated using the Wilke and Lee method (Lyman et al., 1990, pp 17-13).

TABLE 48

Chemical properties of Compounds Being Modeled (24º C)

Chemical	H (unitless)	D_L (cm^2/sec)[a]	D_G (cm^2/sec)[b]
Chloroform	0.15	1.03 E –5	0.094
BDCM	0.088	1.01 E –5	0.089
DBCM	0.038	9.96 E –6	0.086
Bromoform	0.021	9.82 E –6	0.083

[a]D_L is estimated using the Hayduk and Laudie method (Lyman et al., 1990, pp 17-20)
[b]D_G is estimated using the Wilke and Lee method (Lyman et al., 1990, pp 17-13).

TABLE 49

Summary of Experimental Stripping Efficiencies for Cyclohexane, Toluene, and Acetone

Flowrate	Aerator	Stripping Efficiency (%)*		
		Cyclohexane	Toluene	Acetone
4.8	None	24	21	4.9
7.9	None	19	17	2.2
4.8	Screen	19	13	1.7
7.9	Screen	18	14	1.1
4.8	Bubble Aerator	33	23	1.4
6.3	Bubble Aerator	35	22	1.5
7.9	Bubble Aerator	44	23	1.6

*Measured by Howard and Corsi (1996) for Kitchen Sink Experiments; water temperature approximately 23ºC.

TABLE 50

Estimated Rate Constants for Removal of THMs from a Storage Container Based on Batterman et al.

Condition	Chloroform		BDCM		DBCM		Bromoform	
	k (h^{-1})	R^2	k (h^{-1})	R^2	k (h^{-1})	R^2	k (h^{-1})	R^2
Tall glass, full, water at 4°C	0.088	0.77	0.076	0.78	0.080	0.75	0.080	0.84
Tall glass, full, water at 25°C	0.055	0.63	0.046	0.53	0.047	0.47	0.044	0.33
Tall glass, half full, water at 25°C	0.070	0.77	0.064	0.64	0.063	0.76	0.062	0.56
Wide mouth glass, full, water at 25°C	0.180	0.59	0.110	0.30	0.108	0.61	0.140	0.71
Tall glass, full, water at 30°C	0.183	0.69	0.135	0.65	0.142	0.74	0.158	0.85
Tall glass, half full, water at 30°C	0.248	0.83	0.205	0.90	0.177	0.90	0.193	0.89
Wide mouth glass, full, water at 30°C	0.411	0.62	0.427	0.80	0.392	0.82	0.332	0.76
Coffee mug, full, water at 100°C	1.50	0.86	1.52	0.82	1.41	0.80	1.40	0.85

TABLE 51

Estimated Fractional Volatilization from a Storage Container as a Function of Time for THMs for Cold, Room Temperature, and Hot Water

Condition	Chemical	Rate Const, k (h^{-1})	Fraction Volatilized													
			Time, minutes													
			0	5	10	15	30	60	75	90	105	120	180	240	360	420	480
Cold Water (4°C)	Chloroform	0.09	0	0.007	0.015	0.022	0.044	0.086	0.11	0.13	0.15	0.16	0.24	0.30	0.42	0.47	0.51
	BDCM	0.076	0	0.006	0.013	0.019	0.037	0.073	0.091	0.11	0.13	0.14	0.20	0.26	0.37	0.41	0.46
	DBCM	0.080	0	0.07	0.013	0.020	0.039	0.077	0.095	0.11	0.13	0.15	0.21	0.27	0.38	0.43	0.47
	Bromoform	0.080	0	0.07	0.013	0.020	0.039	0.077	0.095	0.11	0.13	0.15	0.21	0.27	0.38	0.43	0.47
Room Temp (25°C)	Chloroform	0.18	0	0.015	0.030	0.044	0.086	0.16	0.20	0.24	0.27	0.30	0.42	0.51	0.66	0.72	0.76
	BDCM	0.11	0	0.009	0.018	0.027	0.054	0.104	0.13	0.15	0.18	0.20	0.28	0.36	0.48	0.54	0.59
	DBCM	0.108	0	0.009	0.018	0.027	0.053	0.102	0.13	0.15	0.17	0.19	0.28	0.35	0.48	0.53	0.58
	Bromoform	0.14	0	0.012	0.023	0.034	0.068	0.13	0.16	0.19	0.22	0.24	0.34	0.43	0.57	0.62	0.67
Hot Water (100°C)	Chloroform	1.50	0	0.12	0.22	0.31	0.53	0.78	0.85	0.89	0.93	0.95	0.99	1.0	1.0	1.0	1.0
	BDCM	1.52	0	0.12	0.22	0.32	0.53	0.78	0.85	0.90	0.93	0.95	0.99	1.0	1.0	1.0	1.0
	DBCM	1.41	0	0.11	0.21	0.30	0.51	0.76	0.83	0.88	0.92	0.94	0.99	1.0	1.0	1.0	1.0
	Bromoform	1.40	0	0.11	0.21	0.30	0.50	0.75	0.83	0.88	0.91	0.94	0.99	1.0	1.0	1.0	1.0

TABLE 52

THM Consumption Scenarios

Scenario	Chemical	Fraction Volatilized			
		Filling	Storage[a]	Processing	Total[b]
Glass of water, room temperature, immediate consumption (over 5-10 minutes)	Chloroform	0.12	0.013	0	0.13
	BDCM	0.075	0.008	0	0.08
	DBCM	0.044	0.008	0	0.05
	Bromoform	0.035	0.010	0	0.04
Glass of water, room temperature, consumption over 1 hour	Chloroform	0.12	0.084	0	0.19
	BDCM	0.075	0.053	0	0.12
	DBCM	0.044	0.052	0	0.09
	Bromoform	0.035	0.067	0	0.10
Glass of ice water, immediate consumption (over 5-10 minutes)	Chloroform	0.12	0.007	0	0.13
	BDCM	0.075	0.006	0	0.08
	DBCM	0.044	0.006	0	0.05
	Bromoform	0.035	0.006	0	0.04
Glass of ice water, consumption over 1 hour	Chloroform	0.12	0.044	0	0.16
	BDCM	0.075	0.037	0	0.11
	DBCM	0.044	0.039	0	0.08
	Bromoform	0.035	0.039	0	0.07
Hot beverage (e.g., coffee or tea), consumed immediately (over 5-10 minutes)	Chloroform	0.12	0.11	0.85[c]	0.88
	BDCM	0.075	0.11	0.80[c]	0.84
	DBCM	0.044	0.11	0.72[c]	0.76
	Bromoform	0.035	0.11	0.63[c]	0.68

TABLE 52 cont.

Scenario	Chemical	Fraction Volatilized			
		Filling	Storage[a]	Processing	Total[b]
Hot beverage (e.g., coffee or tea), consumed immediately (over 20 minutes)	Chloroform	0.12	0.23	0.85 [g]	0.90
	BDCM	0.075	0.23	0.80 [g]	0.86
	DBCM	0.044	0.22	0.72 [g]	0.79
	Bromoform	0.035	0.22	0.63 [g]	0.72
Prepared and stored beverages (e.g., pitcher of orange juice), prepared, stored cold (assume average = 4 hours), poured, consumed over 5-10 minutes	Chloroform	0.12[d] 0.12[e]	0.29[f] 0.007[g]	0	0.38
	BDCM	0.075[d] 0.075[e]	0.25[f] 0.006[g]	0	0.36
	DBCM	0.044[d] 0.044[e]	0.26[f] 0.006[g]	0	0.33
	Bromoform	0.035[d] 0.035[e]	0.26[f] 0.006[g]	0	0.32
Prepared and stored beverages (e.g., pitcher of orange juice), prepared, stored cold (assume average = 4 hours), poured, consumed over 30 minutes	Chloroform	0.12[e] 0.12[e]	0.29[f] 0.02[g]	0	0.39
	BDCM	0.075[d] 0.075[e]	0.25[f] 0.02[g]	0	0.37
	DBCM	0.044[d] 0.044[e]	0.25[f] 0.02[g]	0	0.33
	Bromoform	0.035[d] 0.035[e]	0.26[f] 0.02[g]	0	0.32

[a]Calculated using weighted averages for the appropriate time categories, with fractional volatilization as given in Table 48.
[b]Total is calculated in a consecutive manner by multiplying fraction remaining after each activity (i.e., for coffee, hot, consumed immediately; the initial concentration is reduced for filling by 18% to yield 82%, then the 82% is reduced by 85% because of heating to yield 12.3%, and finally the 12.3% is reduced by 23% to account for storage losses to yield 9%, or a fractional volatilization of 0.91).
[c]Taken from Batterman et al. (2002).
[d]Volatilization attributed to preparation.
[e]Volatilization attributed to pouring from the pitcher into the glass.
[f]Volatilization attributed to storage in the pitcher.
[g]Volatilization while in the glass.

TABLE 53

Recommended Consumption Model Inputs for the THMs

Chemical	Average Fraction Remaining Prior to Storage or Consumption		Volatilization Rate Constant (h^{-1})	
	Direct	Indirect	Direct	Indirect
Chloroform	0.80	0.15	0.07	0.4
BDCM	0.90	0.2	0.06	0.4
DBCM	0.95	0.25	0.06	0.4
Bromoform	0.95	0.3	0.06	0.4

TABLE 54

Alveolar Ventilation Rates by Demographic Group and Activity

Activity Level	Alveolar Ventilation Rate (Liters/Hour)*		
	Male (Age 15-45)	Female (Age 15-45)	Child (Age 6)
Rest	540	430	410
Sedentary	600	480	435

*From Exposure Factors Handbook, Table 5-6, U.S. EPA (1997b)

TABLE 55

Skin Permeability Coefficients

Chemical Name	Kp (cm/hr) (measured)	Kp (cm/hr) (Krishnan, 2001)	Kp[a] (cm/hr) (est. possible range)	Kp[b] Value Used as Model Input (cm/hr)
Chloroform	0.13	0.0156-0.0393	0.015-0.15	0.13
BDCM	---	0.0184-0.0478	0.018-0.18	0.0331
DBCM	---	0.0215-0.0577	0.021-0.22	0.0396
Bromoform	---	0.0247-0.0681	0.24-0.25	0.0464

[a]Range of possible Kp values estimated based on predictions and on measured/predicted values for other compounds in the same class. For classes other than the THMs, no measurements have been identified, so the range itself is somewhat uncertain.

[b]The midpoint of the estimate range by Krishnan was used unless alternative information was available.

TABLE 56

Partition Coefficients Required for Fundamental Uptake Modeling in TEM

Chemical Name	Skin/Blood	Blood/Air
Chloroform	1.62[a]	11.34 (adult)[b] 12.41 (child)[b]
BDCM	2.0[c]	26.6[d]
DBCM	3.82[c]	49.2[d]
Bromoform	5.51[c]	102.3[d]

[a]Estimates for $CHCl_3$ from Corley et al. (1990)
[b]Data from U.S. EPA (2003)
[c]Estimates from Krishnan (2001) and Lipscomb (2001)
[d]Data from Batterman et al. (2002)

TABLE 57

Definition of Some Terms Commonly Used in PBPK Modeling

Q_{alv} - alveolar ventilation C_{inh} - concentration of agent in inhaled air C_{alv} - concentration of agent in exhaled air
Q_c - cardiac output C_{ART} - concentration of the agent in arterial blood; C_A
Q_F - fraction of the cardiac output directed to the fat compartment Q_S - fraction of the cardiac output directed to the slowly perfused tissue compartment Q_R - fraction of the cardiac output directed to the rapidly perfused tissue compartment Q_T - fraction of the cardiac output directed to the testes Q_O - fraction of the cardiac output directed to the ovaries Q_K - fraction of the cardiac output directed to the kidneys Q_L - fraction of the cardiac output directed to the liver Q_P - fraction of the cardiac output directed to the pulmonary (alveolar) region; Q_C
C_{VF} - concentration of the agent in venous blood leaving the fat compartment C_{VS} - concentration of the agent in venous blood leaving the slowly perfused tissue compartment C_{VR} - concentration of the agent in venous blood leaving the rapidly perfused tissue compartment C_{VT} - concentration of the agent in venous blood leaving the testes C_{VO} - concentration of the agent in venous blood leaving the ovaries C_{VK} - concentration of the agent in venous blood leaving the kidneys C_{VL} - concentration of the agent in venous blood leaving the liver C_{VEN} - concentration of the agent in pooled venous blood
P_B - blood:air partition coefficient P_L - liver:blood partition coefficient P_K - kidney:blood partition coefficient P_T - testes:blood partition coefficient P_O - ovary:blood partition coefficient P_F - fat:blood partition coefficient P_R - rapidly perfused tissue:blood partition coefficient P_S - slowly perfused tissue:blod partition coefficient
V_{max} - theoretical maximal initial rate of the metabolic reaction V_{maxC} - V_{max} scaled as a function of body weight, i.e., $V_{max}*BW^{0.7}$ K_M - concentration of the agent producing a metabolic rate one-half that of V_{max}, concentration expressed in the C_{VL} compartment
RDD - a first-order rate equation describing dermal absorption RAM - rate of metabolism RAO - rate of oral absorption

TABLE 58

Physiological Parameters Used in the PBPK Models[a]

Parameter	Value[a]		
	Male	Female	Child[b]
Weights			
Body (kg)	70	60	21.7
Liver (% Body Weight)	2.6	2.6	2.9
Kidney (% Body Weight)	0.4	0.4	0.6
Fat (% Body Weight)	19.0	21.0	17.0
Testes (% Body Weight)	0.04	-	0.008[a]
Ovaries (% Body Weight)	-	0.014	-
Rapidly Perfused (% Body Weight)	5.96	5.986	5.492
Slowly Perfused (% Body Weight)	63.0	61.0	65.0
Flows (l/hr/kg)[c]			
QC_C (cardiac output)	15.0	15.0	15.0
QP_C (alveolar ventilation)	15.0	15.0	15.0
Liver (Q_L, % Cardiac Output)	26.0	26.0	7.95
Kidney (Q_K, % Cardiac Output)	3.4	3.4	5.1
Fat (Q_F, % Cardiac Output)	5.0	5.0	5.3
Testes (Q_T, % Cardiac Output)	1.3	-	0.07
Ovaries (Q_O, % Cardiac Output)	-	0.12	-
Rapidly Perfused (Q_R, % Cardiac Output)[d]	45.3	46.48	62.88
Slowly Perfused (Q_S, % Cardiac Output)[e]	19.0	19.0	18.7

[a]Values from ICRP (1975) unless otherwise indicated.
[b]From Price et al. (2003)
[c]QC = QCC * BW0.74; Qalv = QPC * BW0.74
[d]QR = 76 - QL - QK - QT - QO
[e]QS = 24 - QF

TABLE 59

Tissue Partition Coefficients for the THMs

Value	THM			
	Chloroform[a]	BDCM	CDBM	Bromoform
Blood:Air (P_B)	11.34 (adult) 12.41 (child)	26.6[b]	49.2[b]	102.3[b]
Liver:Blood (P_L)	1.6 (adult) 1.4 (child)	1.15[c]	2.56[c]	2.06[c]
Kidney:Blood (P_K)	1.3 (adult) 1.0 (child)	1.24[c]	2.56[c]	1.69[c]
Testes:Blood (P_T)[d]	1.1 (adult) 0.99 (child)	0.69	1.5	1.18
Ovaries:Blood (P_O)[d]	0.78	0.49	1.03	0.79
Fat:Blood (P_F)	31.0 (adult) 19.6 (child)	19.8[c]	39.0[c]	40.4[c]
Rapidly Perfused:Blood (P_R)	1.6 (adult) 1.4 (child)	1.15[c]	2.56[c]	2.06[c]
Slowly Perfused:Blood (P_S)	1.5 (adult) 2.8 (child)	0.47[c]	1.13[c]	1.12[c]

[a]Data from U.S. EPA (2003)
[b]Data from Batterman et al. (2002)
[c]Calculated from rat tissue:air data (da Silva et al., 1999) and human blood:air data (Batterman et al., 2002).
[d]Calculated based on tissue lipid and water content using the algorithms of Krishnan (2002) and human blood:air data (Batterman et al., 2002).

TABLE 60

Metabolic Parameters for the THMs[a]

THM	V_{maxc} (mg/hr/kg)[b]	K_M (mg/L)
Chloroform [c]	8.96 (adult) 7.6 (child)	0.012
BDCM	8.01	0.302
CDBM	13.7	0.72
Bromoform	10.4	0.42

[a]Data from da Silva et al. (1999) unless otherwise noted.
[b]$V_{max} = V_{maxc} * BW^{0.70}$
[c]Data from U.S. EPA (2003)

TABLE 61

Description of Transfer File Naming Conventions.

File Type	Naming Convention	Description
Breathing Rate Files	BXYYYY.pk	B indicates the file contains breathing rate data X identifies the subject; where A is subject 1, B is subject 2, etc. YYYY is the simulation number, for example 0005 is the 5th simulation
Dermal Data File	DXYZZZZ.pk	D indicates the file contains dermal data X identifies the subject; where A is subject 1, B is subject 2, etc. Y is the chemical identifier (e.g., A is for Chloroform, B for BDCM. Etc.) ZZZZ is the simulation number, for example 0005 is the 5th simulation
Ingestion Data File	GXYZZZZ.pk	G indicates the file contains ingestion data X identifies the subject; where A is subject 1, B is subject 2, etc. Y is the chemical identifier (e.g., A is for Chloroform, B for BDCM. Etc.) ZZZZ is the simulation number, for example 0005 is the 5th simulation
Inhalation Data File	IXYZZZZ.pk	I indicates the file contains inhalation data X identifies the subject; where A is subject 1, B is subject 2, etc. Y is the chemical identifier (e.g., A is for Chloroform, B for BDCM. Etc.) ZZZZ is the simulation number, for example 0005 is the 5th simulation

TABLE 62

Summary of THM Paired Concentrations for the Selected Factors
(Based on Analysis of the ICR Database)

Variable Subgroup	THM Analysis Description	Concentration, ppb (Percentile)			
		Chloroform	BDCM	DBCM	Bromoform
All Systems Using Surface Water Intake (N = 12,440)	Chloroform 95th Percentile	66.0 (95)	29.0 (98)	12.0 (90)	0.5 (0)
	BDCM 95th Percentile	26.1 (62)	23.8 (95)	17.7 (95)	2.6 (89)
	DBCM 95th Percentile	140.0 (100)	44.0 (100)	17.0 (95)	3.7 (92)
	Bromoform 95th Percentile	14.0 (34)	25.0 (96)	26.0 (98)	5.6 (95)
Systems Using any type of Chlorine Disinfectant Process (N = 14,015)	Chloroform 95th Percentile	66.0 (95)	29.0 (98)	12.0 (90)	0.5 (0)
	BDCM 95th Percentile	9.1 (26)	24.0 (95)	46.0 (100)	34.0 (100)
	DBCM 95th Percentile	140.0 (100)	44.0 (100)	17.0 (95)	3.7 (91)
	Bromoform 95th Percentile	5.5 (18)	12.3 (76)	6.0 (78)	6.0 (95)
Systems Sampled between July and September (1997 and 1998)	Chloroform 95th Percentile	74.8 (95)	17.6 (84)	4.0 (65)	0.5 (0)
	BDCM 95th Percentile	14.0 (40)	27.0 (95)	43.0 (100)	23.0 (99)
	DBCM 95th Percentile	170.0 (100)	70.0 (100)	20.0 (95)	1.6 (77)
	Bromoform 95th Percentile	30.0 (64)	37.0 (99)	33.0 (99)	6.5 (95)

TABLE 62 cont.

Variable Subgroup	THM Analysis Description	Concentration, ppb (Percentile)			
		Chloroform	BDCM	DBCM	Bromoform
All Samples (18,214 records)	Chloroform 95th Percentile	65.9 (95)	18.1 (90)	3.4 (65)	0.5 (0)
	BDCM 95th Percentile	10.0 (37)	23.0 (95)	42.0 (1)	24.0 (99)
	DBCM 95th Percentile	120.0 (1)	58.0 (1)	16.0 (95)	0.5 (0)
	Bromoform 95th Percentile	36.0 (79)	46.0 (1)	37.0 (1)	6.1 (95)

TABLE 63

Demographic Characteristics of Simulation Number 48.

NHAPS Record Number	Population Group	Sampled Occupant Age
2758	Male, Ages 15-45	18
2677	Female, Ages 15-45	39
4142	Child, Ages 1-9	8

TABLE 64

Water-Use Activity Pattern from the NHAPS Database for Simulation Number 48

Source Name	Model Location	Occupant	Time On, hours	Time Off, hours	Duration, min
Dishwasher	Kitchen	Female	10.279	11.527	74.9
Faucet -- Bathroom	Master Bathroom	Male	5.508	5.532	1.4
Faucet -- Bathroom	Master Bathroom	Female	9.512	9.550	2.3
Faucet -- Bathroom	Master Bathroom	Female	9.563	9.581	1.1
Faucet -- Bathroom	Master Bathroom	Female	9.592	9.629	2.2
Faucet -- Bathroom	Master Bathroom	Female	17.133	17.147	0.9
Faucet -- Bathroom	Master Bathroom	Female	17.157	17.164	0.4
Faucet -- Bathroom	Master Bathroom	Female	17.164	17.177	0.8
Faucet -- Bathroom	Master Bathroom	Female	17.177	17.213	2.2
Faucet -- Bathroom	Master Bathroom	Female	17.278	17.316	2.3
Faucet -- Bathroom	Master Bathroom	Female	17.367	17.386	1.1
Faucet -- Bathroom	Master Bathroom	Female	17.396	17.404	0.5
Faucet -- Bathroom	Master Bathroom	Female	17.404	17.412	0.5
Faucet -- Kitchen	Kitchen	Child	8.365	8.372	0.4
Faucet -- Kitchen	Kitchen	Female	10.271	10.279	0.5
Faucet -- Kitchen	Kitchen	Female	10.292	10.300	0.5
Faucet -- Kitchen	Kitchen	Female	10.387	10.411	1.5
Faucet -- Kitchen	Kitchen	Female	10.411	10.412	0.1
Faucet -- Kitchen	Kitchen	Female	10.412	10.428	1.0
Faucet -- Kitchen	Kitchen	Female	10.432	10.471	2.4

TABLE 64 cont.

Source Name	Model Location	Occupant	Time On, hours	Time Off, hours	Duration, min
Faucet -- Kitchen	Kitchen	Male	12.157	12.167	0.6
Faucet -- Kitchen	Kitchen	Male	12.203	12.210	0.4
Faucet -- Kitchen	Kitchen	Child	16.007	16.016	0.5
Faucet -- Kitchen	Kitchen	Child	16.123	16.131	0.5
Faucet -- Kitchen	Kitchen	Child	16.331	16.336	0.3
Faucet -- Kitchen	Kitchen	Child	16.481	16.500	1.2
Faucet -- Kitchen	Kitchen	Child	17.626	17.640	0.9
Faucet -- Kitchen	Kitchen	Child	17.729	17.733	0.2
Faucet -- Kitchen	Kitchen	Child	17.733	17.809	4.6
Faucet -- Kitchen	Kitchen	Child	17.956	17.967	0.7
Faucet -- Kitchen	Kitchen	Child	17.977	18.013	2.2
Faucet -- Kitchen	Kitchen	Male	18.020	18.063	2.6
Faucet -- Kitchen	Kitchen	Male	18.063	18.064	0.1
Faucet -- Kitchen	Kitchen	Male	18.064	18.077	0.8
Faucet -- Kitchen	Kitchen	Male	18.122	18.140	1.1
Faucet -- Kitchen	Kitchen	Male	18.235	18.248	0.8
Faucet -- Kitchen	Kitchen	Child	18.248	18.271	1.4
Faucet -- Kitchen	Kitchen	Male	18.271	18.288	1.0
Faucet -- Kitchen	Kitchen	Child	18.320	18.329	0.6
Faucet -- Kitchen	Kitchen	Male	18.499	18.518	1.1
Faucet -- Laundry	Laundry	Child	19.449	19.461	0.7

TABLE 64 cont.

Source Name	Model Location	Occupant	Time On, hours	Time Off, hours	Duration, min
Faucet -- Laundry	Laundry	Child	19.461	19.491	1.8
Faucet -- Laundry	Laundry	Child	19.491	19.504	0.8
Faucet -- Laundry	Laundry	Child	19.664	19.670	0.3
Faucet -- Laundry	Laundry	Child	20.25	20.380	7.8
Hall Bath	Hall Bath	Child	19.25	19.703	27.2
Hall Toilet	Hall Bath	Child	19.265	19.270	0.3
Hall Toilet	Hall Bath	Child	19.319	19.322	0.2
Hall Toilet	Hall Bath	Child	19.347	19.362	0.9
Hall Toilet	Hall Bath	Child	19.380	19.388	0.5
Hall Toilet	Hall Bath	Child	19.390	19.396	0.3
Hall Toilet	Hall Bath	Child	19.579	19.612	2.0
Hall Toilet	Hall Bath	Child	19.663	19.680	1.1
Hall Toilet	Hall Bath	Child	20.290	20.296	0.4
Shower	Master Bathroom	Male	5.532	5.620	5.3
Shower	Master Bathroom	Male	5.620	5.691	4.2
Shower	Master Bathroom	Female	17.004	17.122	7.1
Toilet	Master Bathroom	Male	5.511	5.537	1.6
Toilet	Master Bathroom	Male	5.716	5.781	4.0
Toilet	Master Bathroom	Female	9.594	9.630	2.1
Toilet	Master Bathroom	Female	9.655	9.692	2.2
Toilet	Master Bathroom	Female	9.694	9.721	1.6

TABLE 64 cont.					
Source Name	Model Location	Occupant	Time On, hours	Time Off, hours	Duration, min
Toilet	Master Bathroom	Female	17.220	17.263	2.6
Toilet	Master Bathroom	Female	17.308	17.325	1.0
Toilet	Master Bathroom	Female	17.364	17.420	3.4
Toilet	Master Bathroom	Female	17.428	17.459	1.8
Toilet	Master Bathroom	Female	17.465	17.566	6.0

TABLE 65

Predicted Chloroform Absorbed Dose Results

Percentile	Chloroform Absorbed Dose, mg			
	Total	Dermal	Ingestion	Inhalation
Female, Age 15-45				
1	0.021646	0*	0.006553	0.000838
5	0.045655	0*	0.009483	0.010973
10	0.073058	0.001117	0.011450	0.033892
25	0.149855	0.002829	0.016664	0.091219
50	0.310254	0.026129	0.027141	0.226843
75	0.630598	0.045304	0.047809	0.540248
90	1.145596	0.089087	0.084438	1.031325
95	1.649123	0.121611	0.106439	1.551581
99	8.393424	0.197200	0.248118	8.352551
Male, Age 15-45				
1	0.019457	0*	0.005736	0.000529
5	0.041836	0*	0.009278	0.011465
10	0.067577	0*	0.011848	0.024670
25	0.138960	0.002399	0.017798	0.073703
50	0.311573	0.024272	0.031017	0.237161
75	0.687820	0.046043	0.052064	0.590267
90	1.259366	0.082338	0.090232	1.131236
95	2.044970	0.121381	0.134513	1.975072
99	10.03811	0.237628	0.209462	9.968789

TABLE 65 cont.				
Percentile	Chloroform Absorbed Dose, mg			
	Total	Dermal	Ingestion	Inhalation
Child, Age 6				
1	0.009934	0 [a]	0.002120	0.000289
5	0.020267	0 [a]	0.003645	0.004391
10	0.034366	0 [a]	0.004697	0.013448
25	0.076542	0.000739	0.007633	0.043171
50	0.171478	0.006855	0.013569	0.137133
75	0.377213	0.027164	0.024119	0.337850
90	0.699450	0.051160	0.039602	0.634908
95	0.941091	0.065190	0.051362	0.876666
99	1.444239	0.088984	0.096345	1.424603

*The zeroes entered in the dermal category represent the portion of the population that has no dermal contact with the water supply during the simulated day. For the female (age 15-45) population group, 6.9% had no dermal contact. For the male (age 15-45) population group, 6.9% had no dermal contact. For the child (age 6) population group, 11.1% had no dermal contact.

TABLE 66

Predicted BDCM Absorbed Dose Results

Percentile	BDCM Absorbed Dose, mg			
	Total	Dermal	Ingestion	Inhalation
Female, Age 15-45				
1	0.008631	0*	0.002925	0.000267
5	0.016902	0*	0.004124	0.003761
10	0.025717	0.000189	0.004858	0.011244
25	0.048507	0.000466	0.007103	0.031282
50	0.099072	0.003149	0.011414	0.075642
75	0.203035	0.005263	0.019801	0.178904
90	0.370423	0.009307	0.034635	0.345126
95	0.523761	0.012348	0.043487	0.504863
99	2.814060	0.019722	0.101010	2.806662
Male, Age 15-45				
1	0.008356	0*	0.002559	0.000174
5	0.015445	0*	0.004011	0.003761
10	0.023455	0*	0.005106	0.008234
25	0.044175	0.000403	0.007653	0.024811
50	0.101447	0.002924	0.013053	0.079238
75	0.222273	0.005421	0.021847	0.195328
90	0.401879	0.008875	0.037423	0.366215
95	0.661688	0.012353	0.054970	0.649494
99	3.432694	0.023330	0.085477	3.419677

TABLE 66 cont.				
Percentile	BDCM Absorbed Dose, mg			
	Total	Dermal	Ingestion	Inhalation
Child, Age 6				
1	0.004433	0*	0.001296	9.2E-05
5	0.008829	0*	0.002031	0.001432
10	0.012558	0*	0.002667	0.004451
25	0.025508	0.000123	0.004103	0.014526
50	0.056992	0.000876	0.007079	0.045818
75	0.125885	0.002900	0.011615	0.110828
90	0.221136	0.005229	0.017947	0.209114
95	0.300591	0.006434	0.022104	0.290700
99	0.456096	0.008918	0.041569	0.449681

*The zeroes entered in the dermal category represent the portion of the population that has no dermal contact with the water supply during the simulated day. For the female (age 15-45) population group, 6.9% had no dermal contact. For the male (age 15-45) population group, 6.9% had no dermal contact. For the child (age 6) population group, 11.1% had no dermal contact.

TABLE 67

Predicted DBCM Absorbed Dose Results

Percentile	DBCM Absorbed Dose, mg			
	Total	Dermal	Ingestion	Inhalation
Female, Age 15-45				
1	0.006838	0*	0.002529	0.000170
5	0.012561	0*	0.003472	0.002202
10	0.018498	0.000210	0.004094	0.007019
25	0.034433	0.000521	0.005932	0.019891
50	0.066284	0.003221	0.009375	0.048070
75	0.133292	0.005348	0.015826	0.110357
90	0.232392	0.008948	0.027289	0.211710
95	0.333569	0.011876	0.034284	0.310299
99	1.794922	0.018525	0.079193	1.787844
Male, Age 15-45				
1	0.006539	0*	0.002196	0.000111
5	0.011250	0*	0.003388	0.002338
10	0.016953	0*	0.004283	0.005262
25	0.032167	0.000447	0.006285	0.016069
50	0.069418	0.002959	0.010803	0.049303
75	0.143467	0.005548	0.017817	0.120803
90	0.253583	0.008660	0.030253	0.223912
95	0.413262	0.012051	0.043168	0.402837
99	2.175275	0.021618	0.067179	2.124613

TABLE 67 cont.				
Percentile	DBCM Absorbed Dose, mg			
	Total	Dermal	Ingestion	Inhalation
Child, Age 6				
1	0.002988	0*	0.000765	5.93E-05
5	0.005530	0*	0.001253	0.000865
10	0.008306	0*	0.001663	0.002877
25	0.016842	0.000136	0.002652	0.009110
50	0.036099	0.000926	0.004543	0.028304
75	0.078574	0.002844	0.007909	0.069483
90	0.139613	0.005002	0.012820	0.128593
95	0.189552	0.006104	0.016558	0.179028
99	0.282424	0.008271	0.031030	0.276845

*The zeroes entered in the dermal category represent the portion of the population that has no dermal contact with the water supply during the simulated day. For the female (age 15-45) population group, 6.9% had no dermal contact. For the male (age 15-45) population group, 6.9% had no dermal contact. For the child (age 6) population group, 11.1% had no dermal contact.

TABLE 68

Predicted Bromoform Absorbed Dose Results

Percentile	Bromoform Absorbed Dose, mg			
	Total	Dermal	Ingestion	Inhalation
Female, Age 15-45				
1	0.002289	0*	0.000902	4.69E-05
5	0.003976	0*	0.001217	0.000591
10	0.005844	8.86E-05	0.001430	0.001928
25	0.010873	0.000219	0.002087	0.005638
50	0.019824	0.001330	0.003246	0.013413
75	0.038290	0.002190	0.005282	0.030515
90	0.065453	0.003593	0.008956	0.057593
95	0.092500	0.004765	0.011241	0.083673
99	0.505940	0.007186	0.025824	0.503191
Male, Age 15-45				
1	0.002211	0*	0.000760	3.22E-05
5	0.003744	0*	0.001189	0.000654
10	0.005498	0*	0.001484	0.001464
25	0.010434	0.000188	0.002187	0.004575
50	0.020922	0.001215	0.003725	0.013943
75	0.041260	0.002279	0.006019	0.033213
90	0.070014	0.003517	0.010251	0.061013
95	0.113307	0.004822	0.014303	0.109606
99	0.599301	0.008450	0.021969	0.571568

TABLE 68 cont.				
Percentile	Bromoform Absorbed Dose, mg			
	Total	Dermal	Ingestion	Inhalation
Child, Age 6				
1	0.000937	0*	0.000265	1.66E-05
5	0.001829	0*	0.000425	0.000249
10	0.002613	0*	0.000578	0.000792
25	0.005179	5.75E-05	0.000892	0.002564
50	0.010647	0.000383	0.001539	0.007748
75	0.021956	0.001144	0.002640	0.018976
90	0.039021	0.002008	0.004231	0.034882
95	0.053294	0.002387	0.005402	0.049472
99	0.077309	0.003211	0.010172	0.075052

*The zeroes entered in the dermal category represent the portion of the population that has no dermal contact with the water supply during the simulated day. For the female (age 15-45) population group, 6.9% had no dermal contact. For the male (age 15-45) population group, 6.9% had no dermal contact. For the child (age 6) population group, 11.1% had no dermal contact.

TABLE 69

Water Concentrations Used to Investigate THM Metabolic Interactions

95th Percentile	THM (µg/L)			
	Chloroform	BDCM	DBCM	Bromoform
Chloroform	74.8	17.6	4.0	0.5
BDCM	14.0	27.0	43.0	23.0
DBCM	170.0	70.0	20.0	1.6
Bromoform	30.0	37.0	33.0	6.5

TABLE 70

Inhibition of DBCM Bioactivation by THMs

Exposure	CM_{24} (mg/L liver)	% Inhibition
Chloroform alone	2.97977 e-3	0
Chloroform all	2.97977 e-3	0
BDCM alone	1.81045 e-3	0
BDCM all	1.81045 e-3	0
Bromoform alone	4.7322 e-5	0
Bromoform all	4.7322 e-5	0
DBCM alone	6.95279 e-4	0
DBCM all	6.95278 e-4	0.0001
DBCM + Chloroform	6.95279 e-4	0
DBCM + BDCM	6.95279 e-4	0
DBCM + Bromoform	6.95279 e-4	0
DBCM + Chloroform + BDCM	6.95278 e-4	0.0001
DBCM + Chloroform + Bromoform	6.95279 e-4	0
DBCM + BDCM + Bromoform	6.95279 e-4	0

TABLE 71

Effect of Decreasing Enzyme Content on the Metabolic Interactions of the THMs

Vmaxc (% control)	THM	CM_{24} Alone[a]	CM_{24} All[b]	% Inhibition
100	DBCM	6.95279 e-4	6.95278 e-4	0.0001
	Chloroform	2.97977 e-3	2.97977 e-3	0
	BDCM	1.81045 e-3	1.81045 e-3	0
	Bromoform	4.7322 e-5	4.7322 e-5	0
10	DBCM	4.7301 e-4	4.72992 e-4	0.004
	Chloroform	2.91157 e-3	2.91156 e-3	0.0003
	BDCM	1.30214 e-3	1.3021 e-3	0.003
	Bromoform	3.63856 e-5	3.63847 e-5	0.002
1	DBCM	1.11495 e-4	1.11452 e-4	0.04
	Chloroform	2.3686 e-3	2.36855 e-3	0.002
	BDCM	3.39948 e-4	3.39799 e-4	0.04
	Bromoform	1.08096 e-5	1.08062 e-5	0.03
0.1	DBCM	1.28725 e-5	1.28565 e-5	0.12
	Chloroform	8.24953 e-4	8.24895 e-4	0.007
	BDCM	4.04642 e-5	4.0431 e-5	0.08
	Bromoform	1.33922 e-6	1.33779 e-6	0.11
0.01	DBCM	1.30737 e-6	1.3053 e-6	0.16
	Chloroform	1.09647 e-4	1.09637 e-4	0.009
	BDCM	4.12475 e-6	4.11679 e-6	0.19
	Bromoform	1.37173 e-7	1.36985 e-7	0.14

TABLE 71 cont.				
Vmaxc (% control)	THM	CM_{24} Alone[a]	CM_{24} All[b]	% Inhibition
0.001	DBCM	1.30942 e-7	1.30728 e-7	0.16
	Chloroform	1.13375 e-5	1.13364 e-5	0.01
	BDCM	4.13275 e-7	4.12454 e-7	0.2
	Bromoform	1.37507 e-8	1.37313 e-8	0.14
0.0001	DBCM	1.30963 e-8	1.30748 e-8	0.16
	Chloroform	1.13761 e-6	1.13751 e-6	0.009
	BDCM	4.13355 e-8	4.12532 e-8	0.2
	Bromoform	1.3754 e-9	1.37346 e-9	0.14

[a]CM24 for each THM alone.
[b]CM24 for each THM in a mixture of all 4 THMs.

TABLE 72

Categories of Data Sources and Models

Category	Description
I	Taken from peer reviewed literature, used for the purpose intended by the measurement
II	Taken from peer reviewed literature, used for the purpose other than intended by the measurement.
III	Taken from peer-reviewed database compiled for the purposes in which it is being used.
IV	Taken from non peer-reviewed database compiled for the purposes other than those for which it is being used.
V	Taken from other non peer-reviewed source.
VI	Estimated based on peer-reviewed method or data.
VII	Estimated based on non peer-reviewed method.

TABLE 73

Quality and Sources of Data Used in the Models

Variables	Category	Description	Citation
Mass-Transfer Coefficient	VI	Predicted based on peer reviewed algorithms	Corsi and Howard, 2000
Gas- and liquid-phase diffusivities	I, VI	Diffusivities are used in the prediction algorithm for the mass transfer coefficient, as described in Section 3.1. The sources of the diffusivities vary. Several were obtained from the Department of Energy, Risk Assessment Information System (RAIS) database. The values for many of the diffusivities were estimated using peer reviewed prediction algorithms as described in Section 3.1.3.	Risk Assessment Information System, Oak Ridge National Laboratory Lyman et al., 1990
Henry's Law Constant	I, II, VI	Reported in literature or in databases at specific temperatures. A temperature adjustment was applied based on a peer-reviewed method as described in Section 3.1.3.	Various, see Table 2 and Section 2.1 for a listing of data sources and temperature adjustment algorithm
Exposure-Related Behavior	III	Activity patterns are sampled from the NHAPS database	Described in Section 2.2.1
Water Use Behavior	III, IV, V	Compiled from a variety of databases including REUWS, RECS, and NHAPS. NHAPS was compiled for this purpose; REUWS and RECS were compiled for other purposes.	Described in Section 2.2.2
Ingestion Behavior	III	Taken from the CSFII database	U.S. EPA, 2000d
House Volume	I, IV	Household volumes are based on an analysis of RECS data from 1993 and 1997. The 1993 data are analyzed and presented in the Exposure Factors Handbook.	U.S. DOE, 1995 U.S. DOE, 1997a U.S. EPA, 1997b
Water-Use Zones	VII	Volumes are estimated based on architectural design standards.	Hoke, 1988 Hoke, 1994
Whole House Air Exchange Rate	I	Sampled from the national distribution recommended by the Exposure Factors Handbook.	U.S. EPA, 1997b

TABLE 73 cont.

Variables	Category	Description	Citation
Interzonal Airflows	I	Interzonal airflows are based on several sources. The interzonal airflows between the non-water using zones and the kitchen and laundry room are based on a correlation from Koontz and Rector, 1995. The flows between the non-water using zones and the bathrooms are based on Giardino et al., 1992.	Koontz and Rector, 1995 Giardino et al., 1992
Water Concentrations	I	The water concentrations were characterized based on the published Information Collection Rule (ICR) measurement data.	McGuire et al., 2002
Ingestion Concentrations	I, VII	The ingestion concentrations were estimated for a plausible set of activities based on published results lab measurements.	Howard and Corsi, 1996 Batterman et al., 2000
Breathing Rates	I	Alveolar ventilation rates were assigned based on two assumed activity levels: resting and sedentary.	U.S. EPA, 1997b
Body Weight	I	Calculated from the Exposure Factors Handbook, Tables 7.2 and 7.3, adjusted for clothes	U.S. EPA, 1997a
Body Compartmental Blood Flow Rates	I	Taken from ICRP (1975). Child values from Price et al. (2003)	ICRP, 1975; Price et al., 2003
Body Compartmental Volumes	I	Taken from ICRP (1975). Child values from Price et al. (2003)	ICRP, 1975; Price et al., 2003
Skin Permeability Coefficients	VI	Taken from methods used by Krishnan -	Krishnan, 2001, 2002
Skin Partition Coefficients	VI	Krishnan, Personal Communication	Krishnan, 2001, 2002
	I	Chloroform -	Corley et al., 1990
	I	BDCM, DBCM, Bromoform	Batterman et al., 2002
Gastro-Intestinal Absorption Rate	VI	Estimated based on Corley et al (1990)	Corley et al., 1990

TABLE 73 cont.

Variables	Category	Description	Citation
Tissue Partition Coefficients	I	Chloroform partition coefficients from U.S. EPA (2003)	U.S. EPA, 2003
	I	BDCM, DBCM, Bromoform blood:air from Batterman et al.(2002)	Batterman et al., 2002
	VI	BDCM, DBCM, Bromoform calculated from rat tissue:air data (da Silva et al., 1999) and human blood:air data (Batterman et al., 2002).	da Silva et al., 1999; Batterman et al., 2002
	VII	Ovaries and Testes calculated based on tissue lipid and water content using the algorithms of Krishnan (2002).	Krishnan, 2002
Metabolism Rate Constants	I	Chloroform metabolic parameters are from EPA (2003)	U.S. EPA, 2003
	II	BDCM, DBCM and Bromoform metabolic parameters are from rat studies by da Silva et al. (1999)	da Silva et al., 1999

TABLE 74

Categories of Model Approaches and Algorithms

Category	Description
A	Widely accepted modeling approach
B	Approach similar to commonly used and accepted approaches, but adapted to satisfy project specific requirements
C	Novel approach addressing specific requirements of estimating exposure and uptake of water borne contaminants

TABLE 75

Quality of Modeling Approaches and Algorithms

Model	Category	Description
Representation of the building	B	Building is represented as a collection of water using zones and a lumped non-water using zones. Similar approaches are widely used in the literature.
Fate and transport modeling	A	Commonly accepted approach based on mass balance. Method assumes well mixed zones, each zone constrained by mass and volumetric balance.
Fate and Transport Model Integration Method	A	Model solves set of differential equations using the 4^{th} order Runge-Kutta method (Mathews, 1992). This method is widely cited, is very stable, self starting, and accurate.
Behavior Models	C	The behavior is sampled from the NHAPS database, but is modified to address known deficiencies in the dataset and to accommodate water-use related behavior not included in NHAPS.
Water Use Models	C, A	Approach to simulating water uses incorporate techniques for simulating water use occurrences as well as the duration of water uses. The occurrences of water uses are simulated based on survey data from NHAPS and REUWS using a Poisson process. The durations of the water uses are simulated by sampling from representative lognormal distributions. These techniques are used for similar purposes in peer-reviewed literature, but the implementation in this modeling effort is unique to exposure to water borne contaminants. This work has been published in several peer reviewed publications (Wilkes, 1999, Wilkes et al., 1996)
Exposure Models	A	The exposure model used in this study, TEM, has been published in several journal articles. The basic model algorithms have been validated (Wilkes, 1994).

TABLE 75 cont.

Model	Category	Description
Inhalation Uptake Model	A, C	The exposure model uptake algorithms are described in Section 2.7. These algorithms are taken from peer-reviewed literature (Olin, 1998), but there integration into an exposure model framework is unique to this exposure model.
Dermal Uptake Model	A, C	
Physiologically Based Pharmacokinetic Model	A, B	The physiologically based pharmacokinetic model is based on a model used for over 30 volatile organic chemicals (Gargas et al., 1986, 1990) including chloroform (Corley et al., 1990) and BDCM (Lilly et al., 1998). The model accounts for the potential metabolic interactions between the four THMs as competitive inhibitors of each others metabolism.

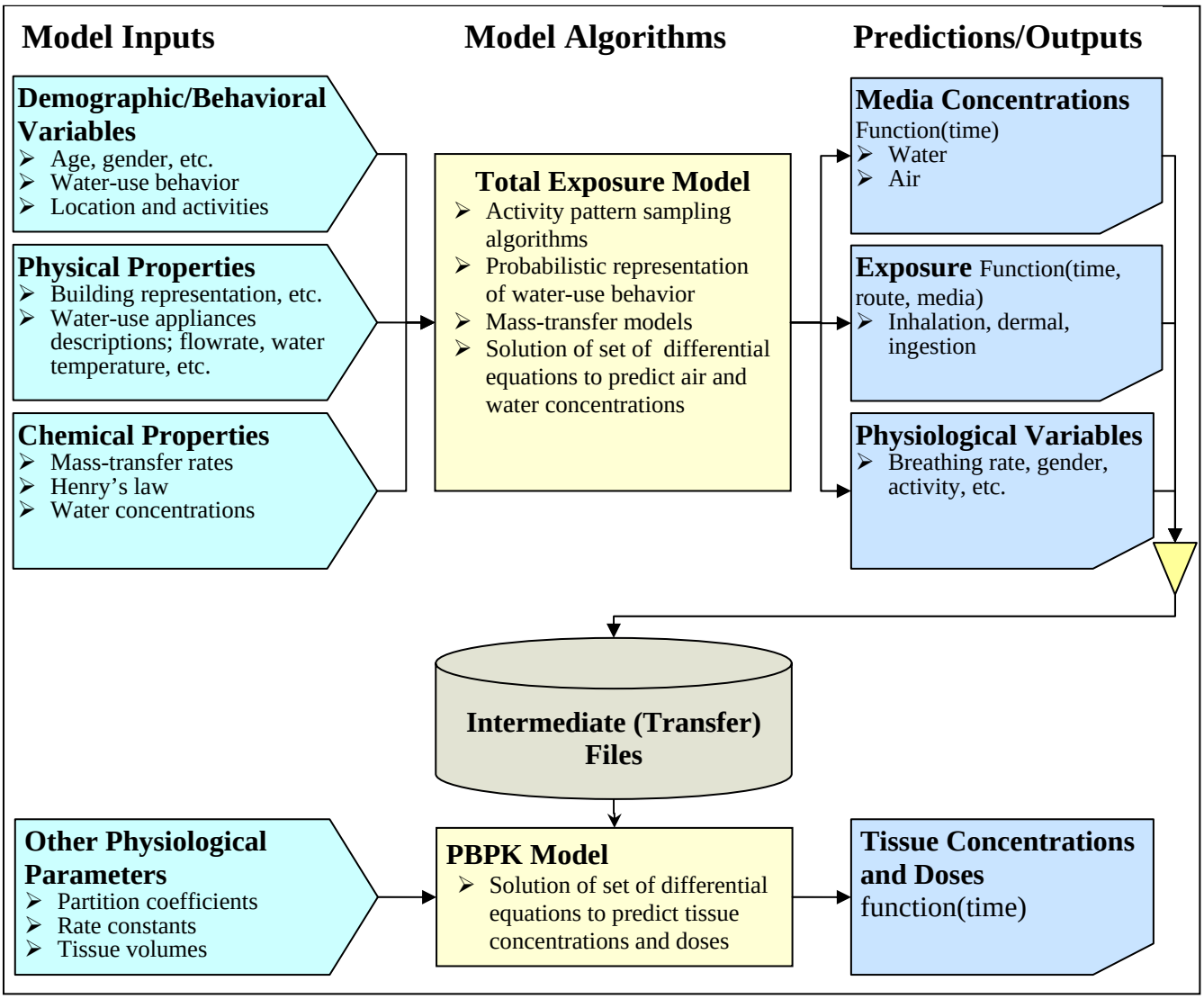


Figure 1 Population-Based Modeling Paradigm

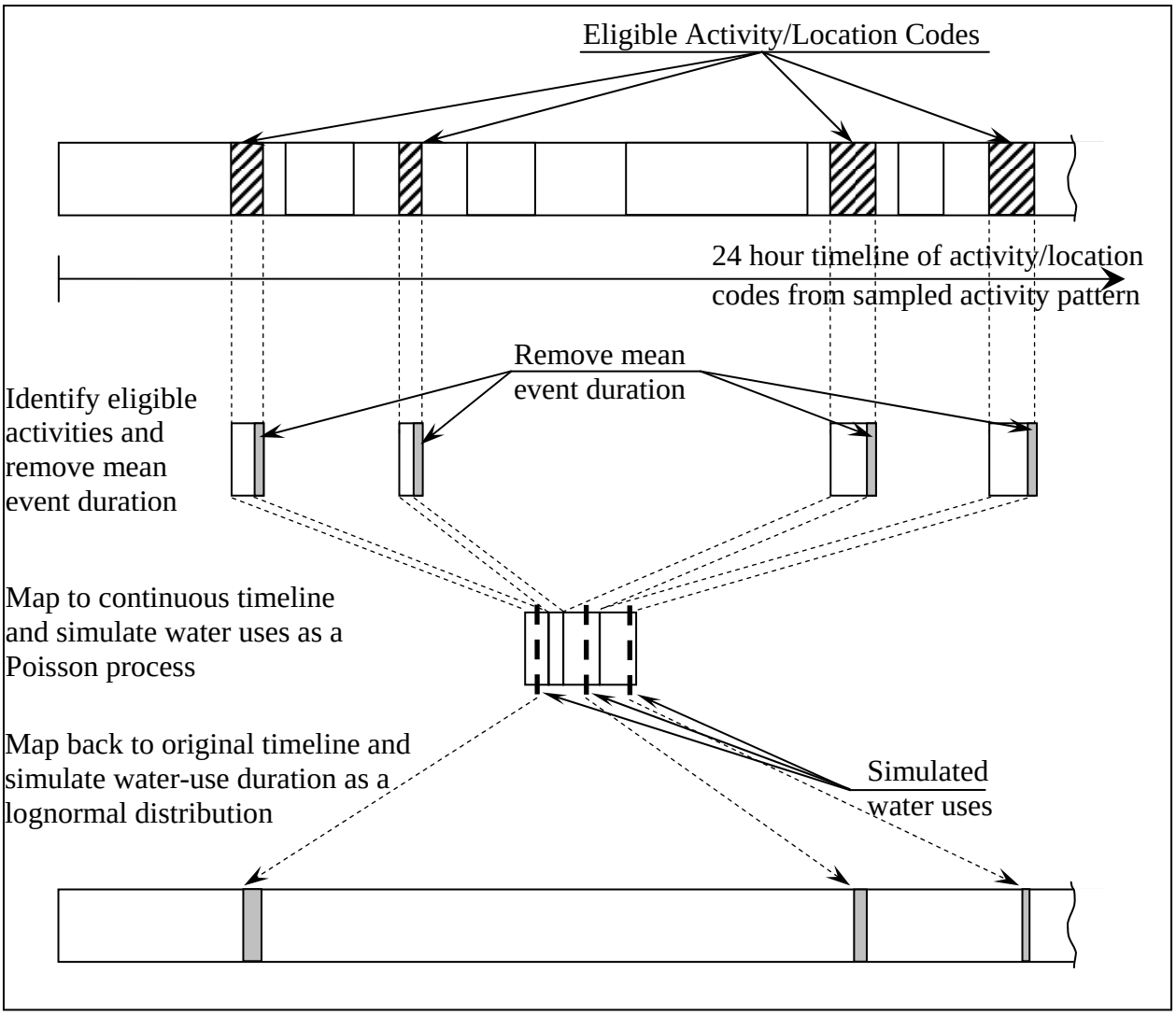


Figure 2 Schematic Representation of the Procedures Used for Simulating Water Uses Based on a Sampled Activity Pattern

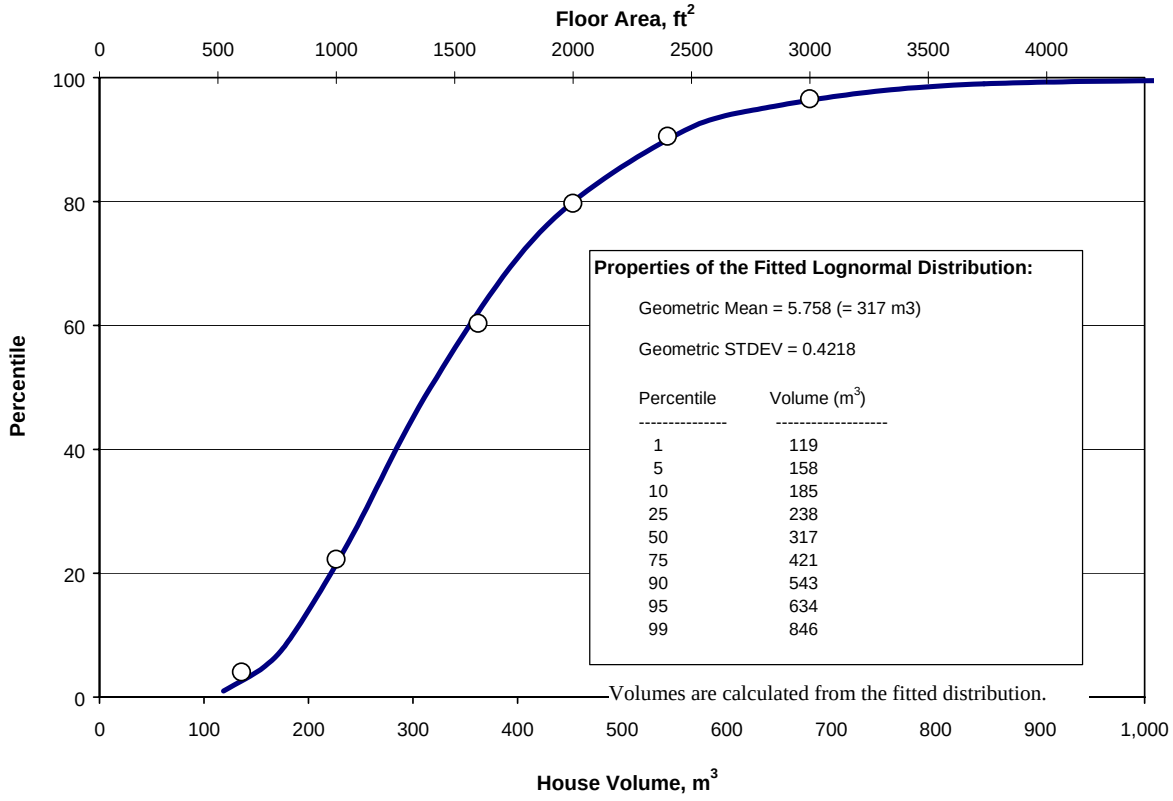


Figure 3. Cumulative Distribution Function of Volume for 3-Person Households. Source: Analysis of RECS 1997 data

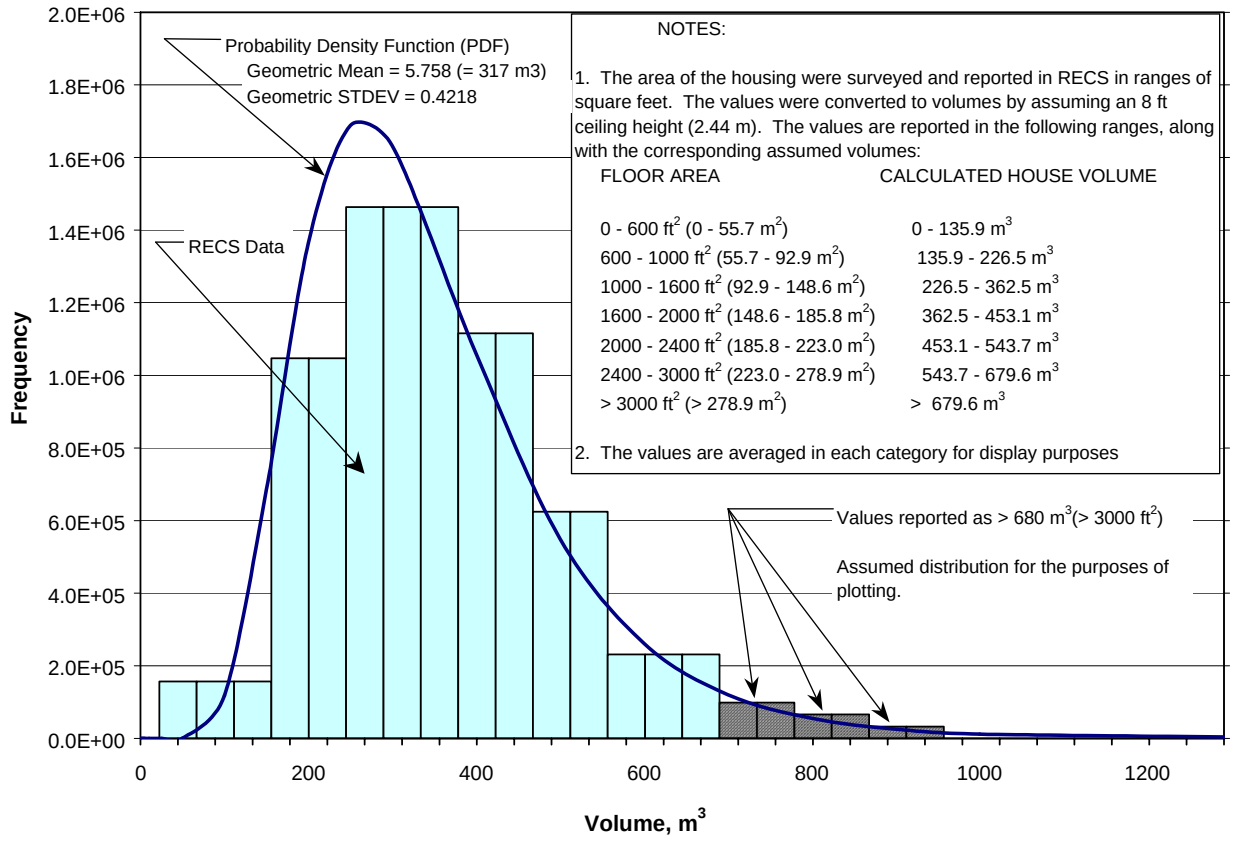
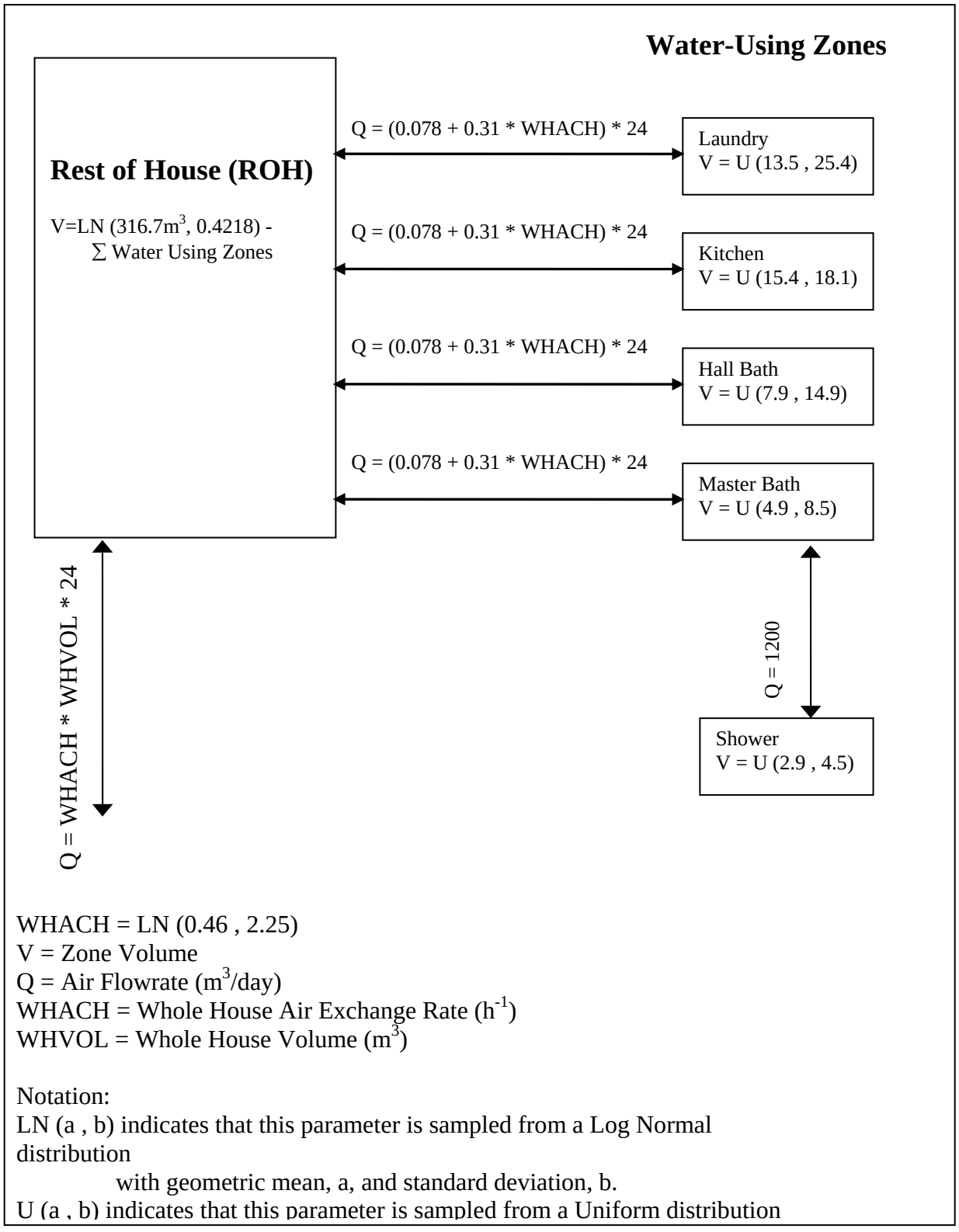


Figure 4. Comparison of RECS Data and the Fitted Probability Density Function of Volume for 3-Person Households.
Source: Analysis of RECS 1997 data



WHACH = LN (0.46 , 2.25)
V = Zone Volume
Q = Air Flowrate (m^3/day)
WHACH = Whole House Air Exchange Rate (h^{-1})
WHVOL = Whole House Volume (m^3)

Notation:
LN (a , b) indicates that this parameter is sampled from a Log Normal distribution
with geometric mean, a, and standard deviation, b.
U (a , b) indicates that this parameter is sampled from a Uniform distribution

Figure 5. Schematic Representation of House Interzonal Air Flows

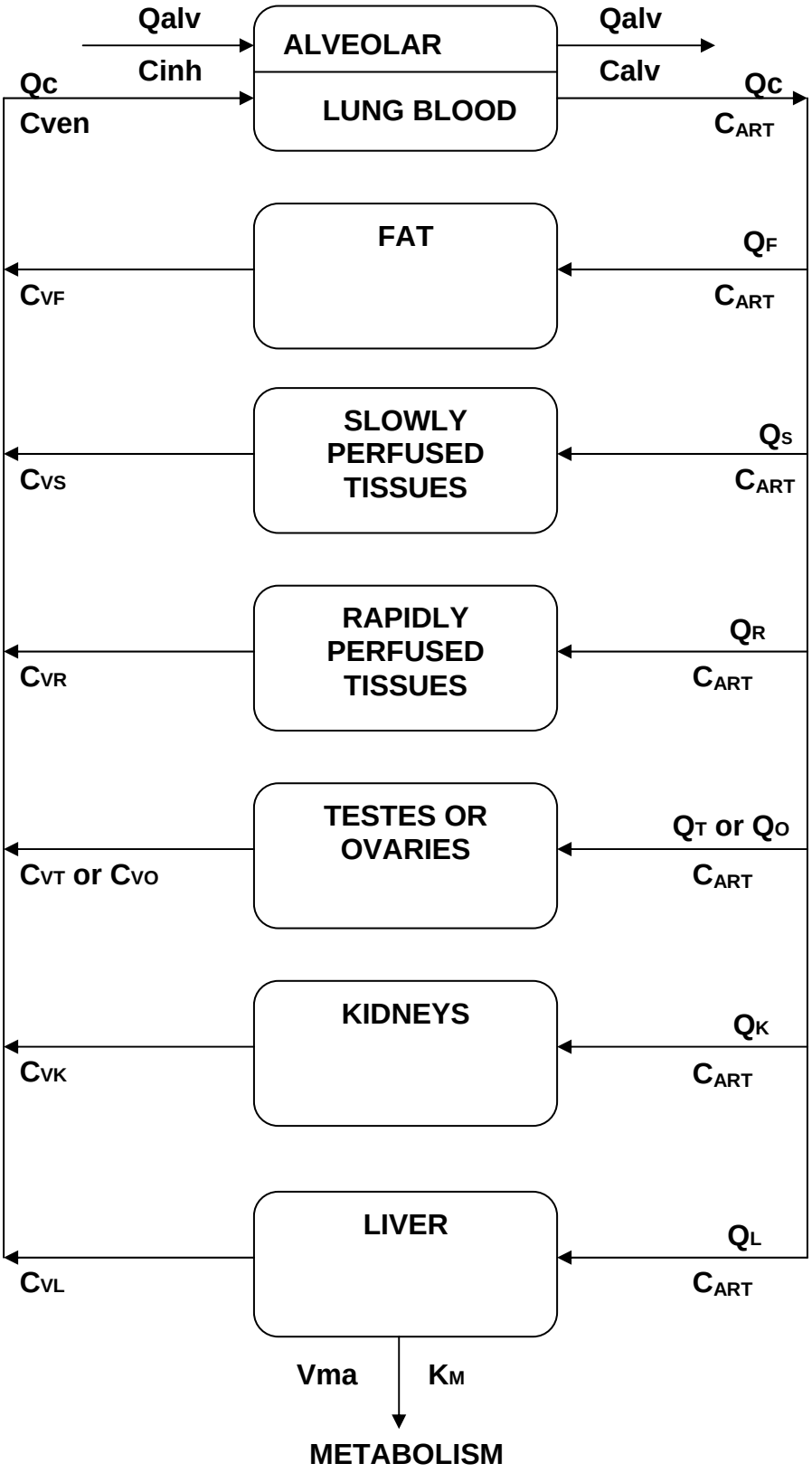


Figure 6. Structure of the PBPK model used to analyze human exposures to THMs.

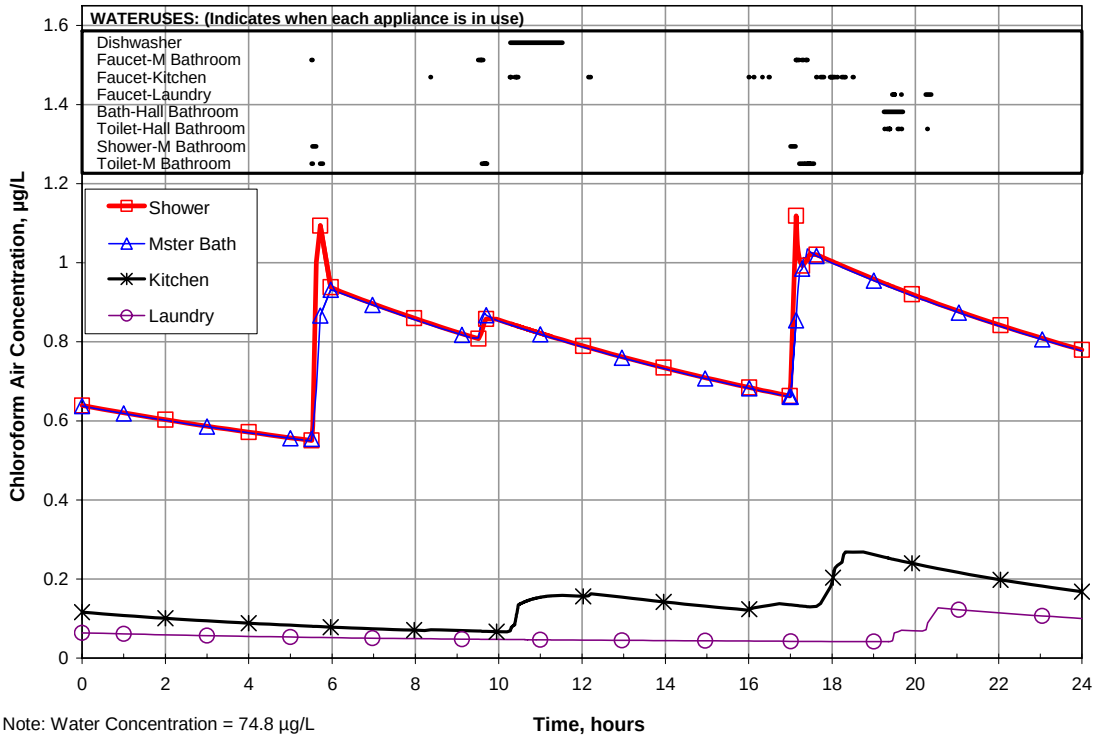


Figure 7. Predicted Chloroform Air Concentrations for the Example Case

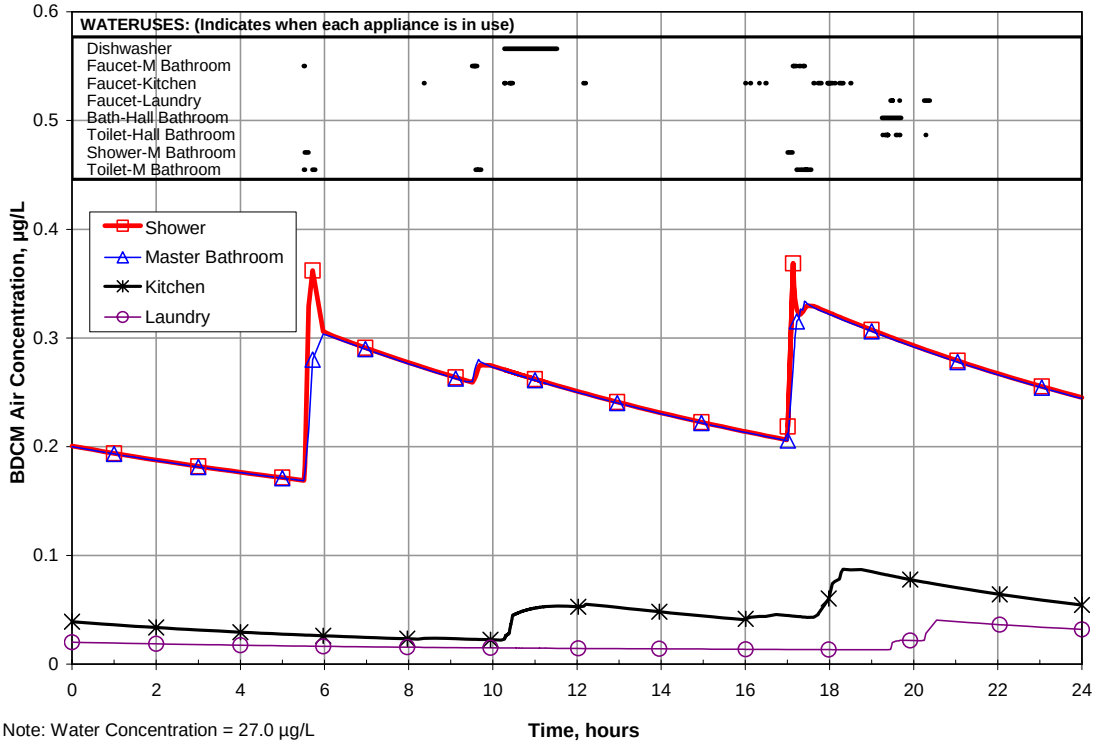
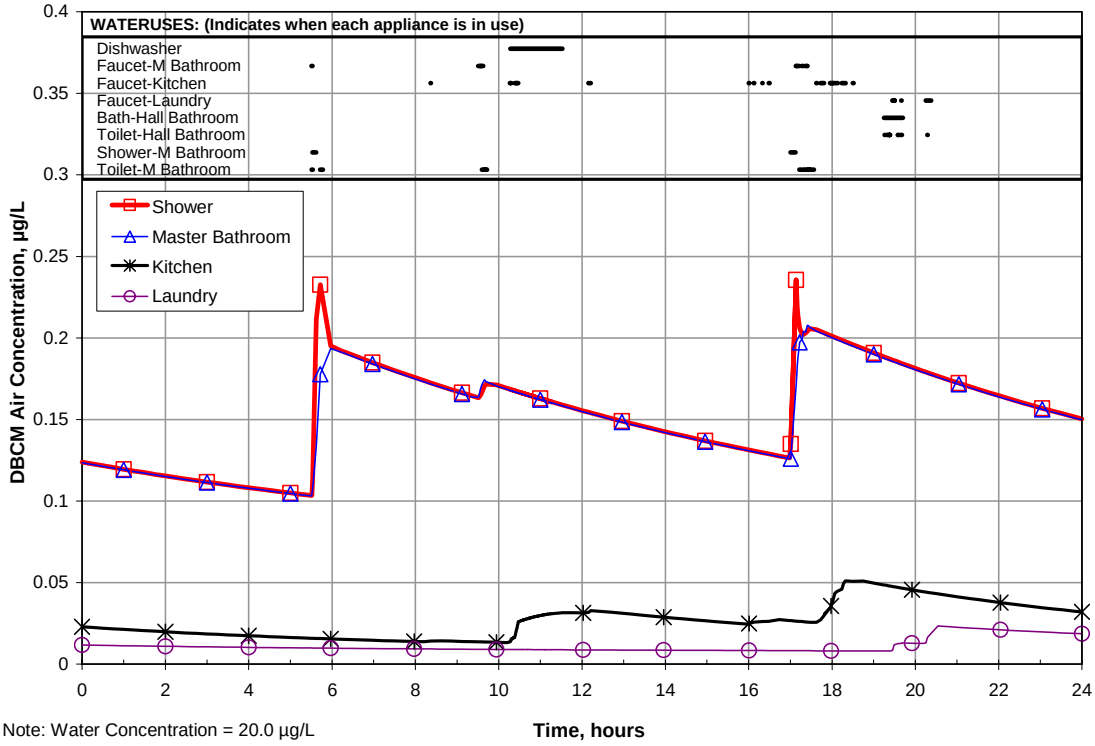
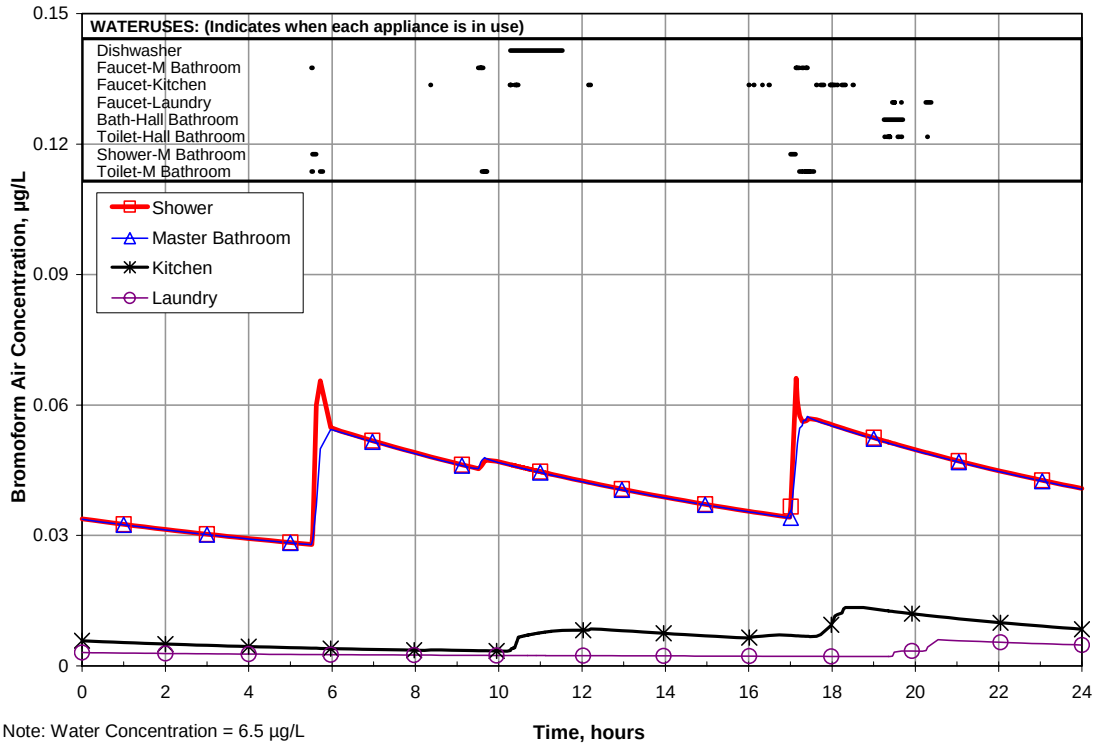


Figure 8. Predicted BDCM Air Concentrations for the Example Case



Note: Water Concentration = 20.0 µg/L

Figure 9. Predicted DBCM Air Concentrations for the Example Case



Note: Water Concentration = 6.5 µg/L

Figure 10. Predicted Bromoform Air Concentrations for the Example Case

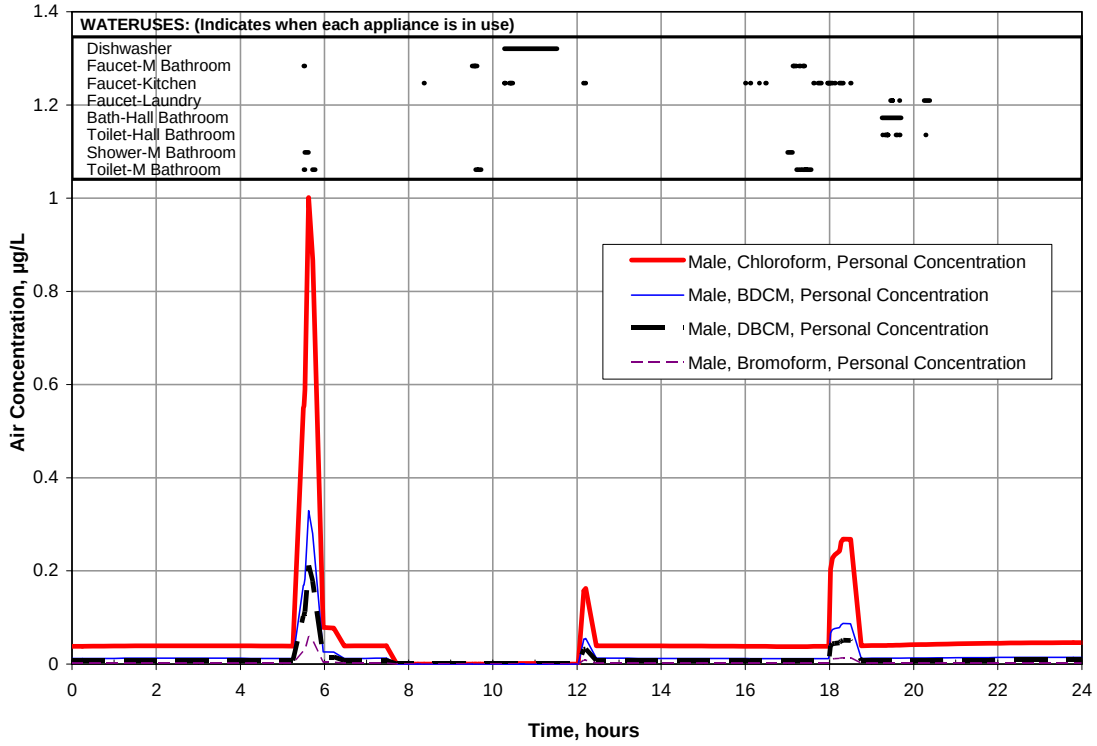


Figure 11. Predicted Personal Air Concentrations for the Adult Male for the Example Case

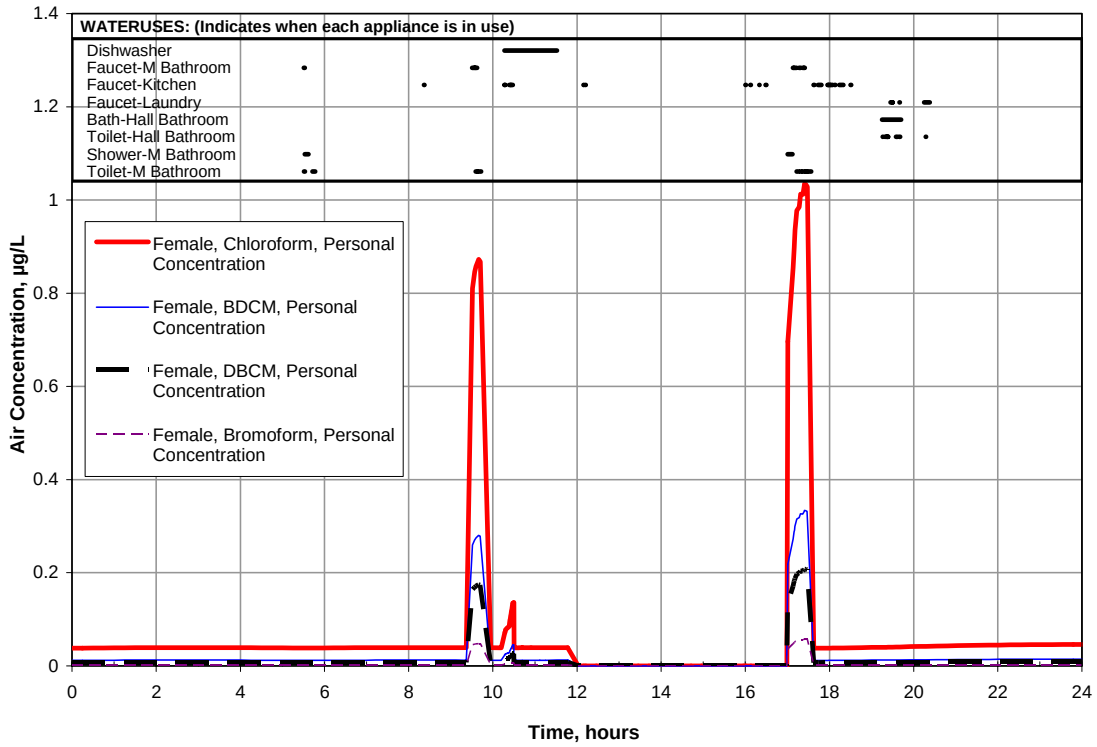


Figure 12. Predicted Personal Air Concentrations for the Adult Female for the Example Case

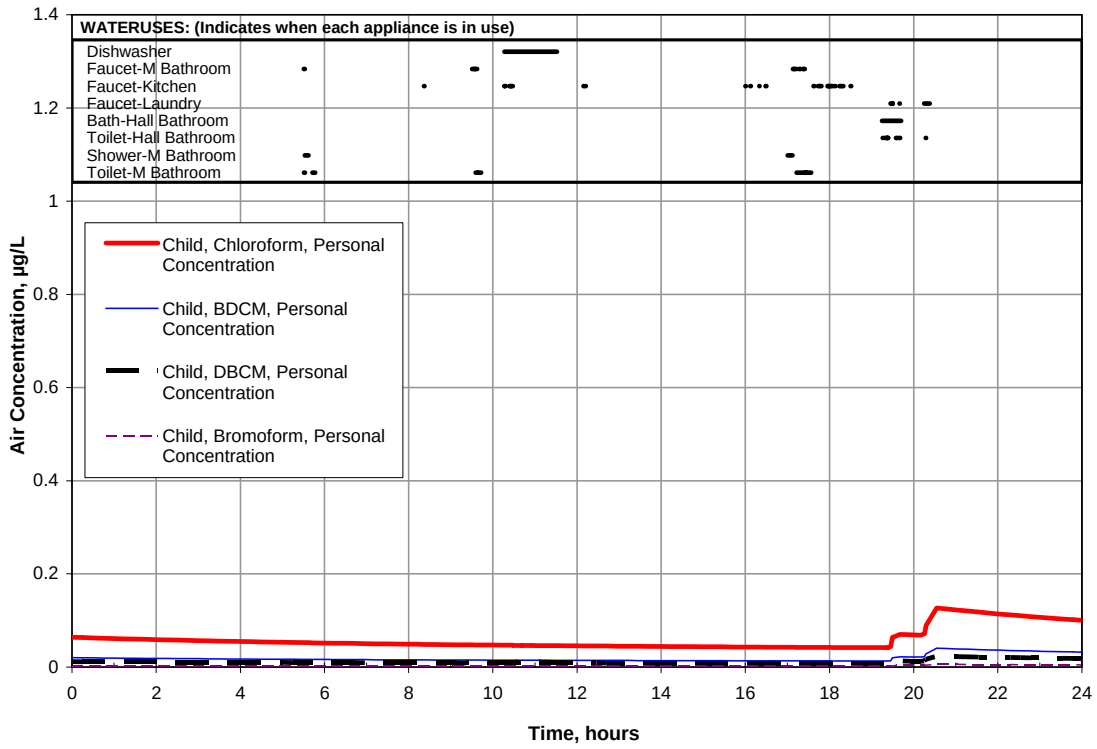


Figure 13. Predicted Personal Air Concentrations for the Child for the Example Case

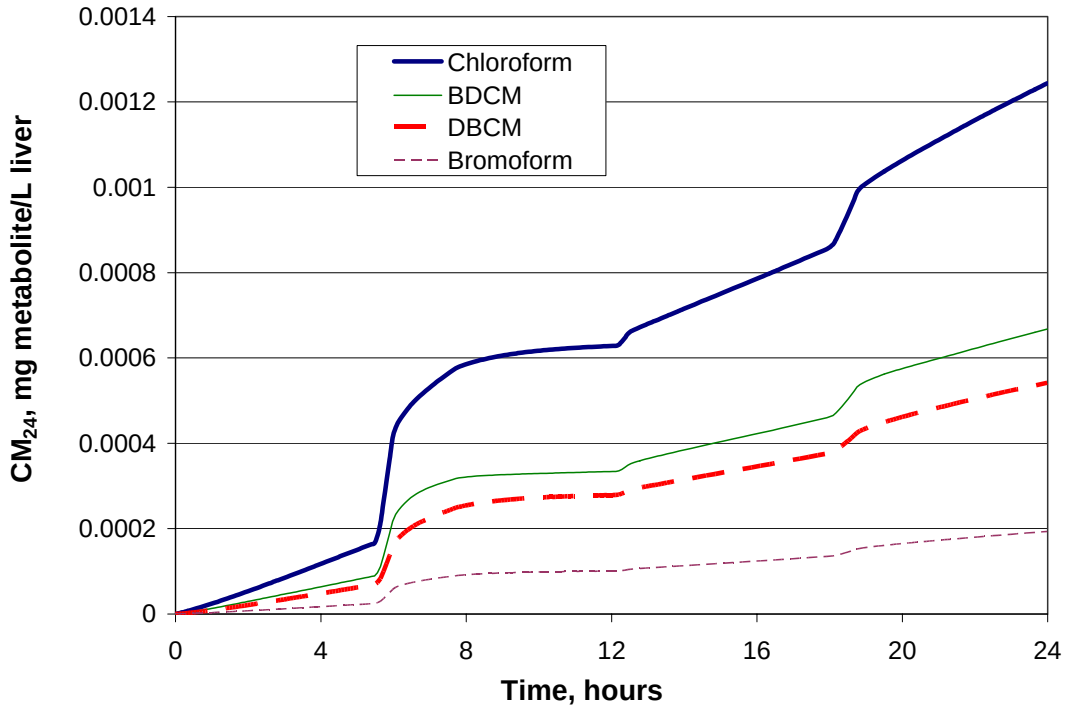


Figure 14. Predicted Concentrations of Metabolites Produced in the Liver over 24 hours (CM_{24}) for the Adult Male in the Example Case

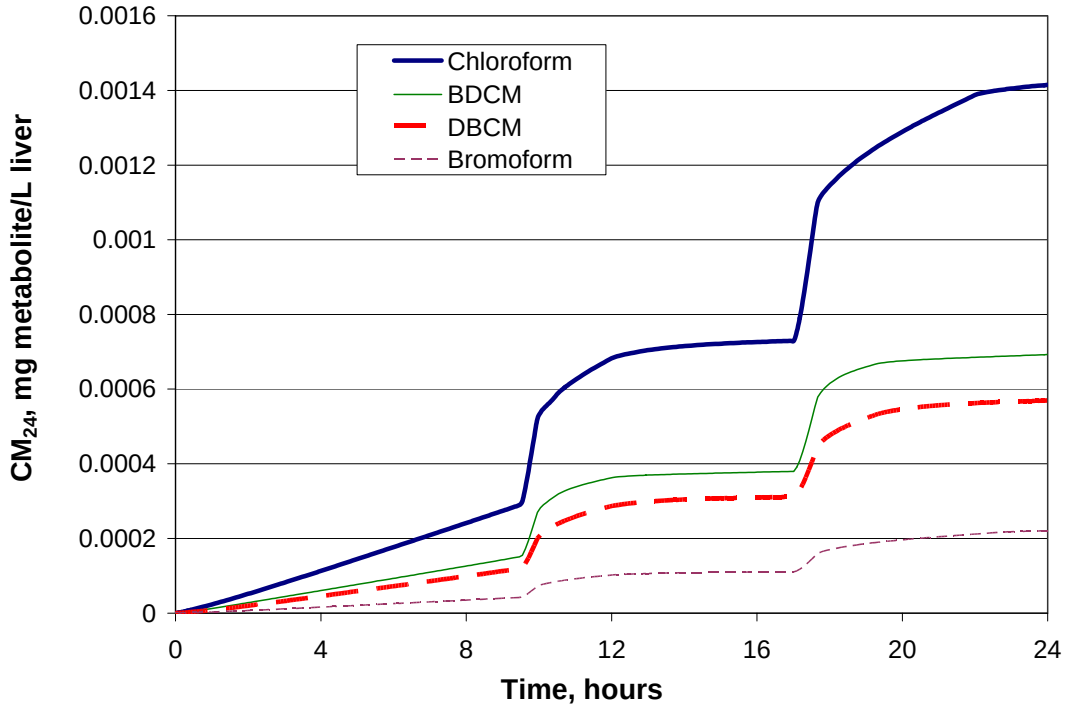


Figure 15. Predicted Concentrations of Metabolites Produced in the Liver over 24 hours (CM_{24}) for the Adult Female in the Example Case

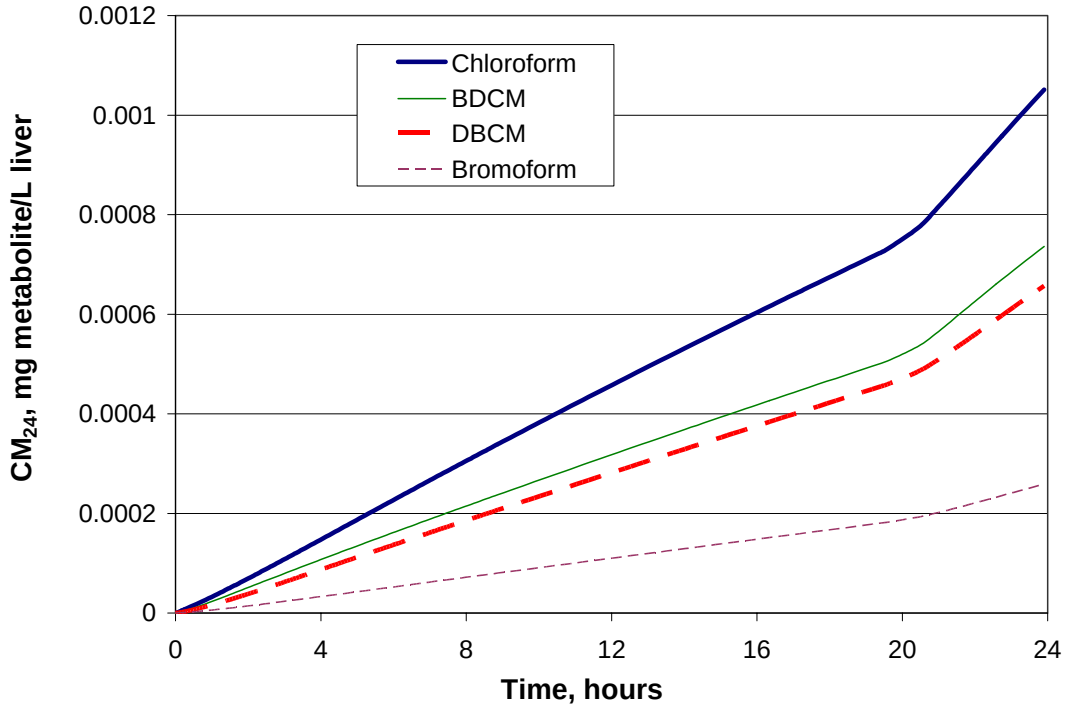


Figure 16. Predicted Concentrations of Metabolites Produced in the Liver over 24 hours (CM_{24}) for the Child in the Example Case

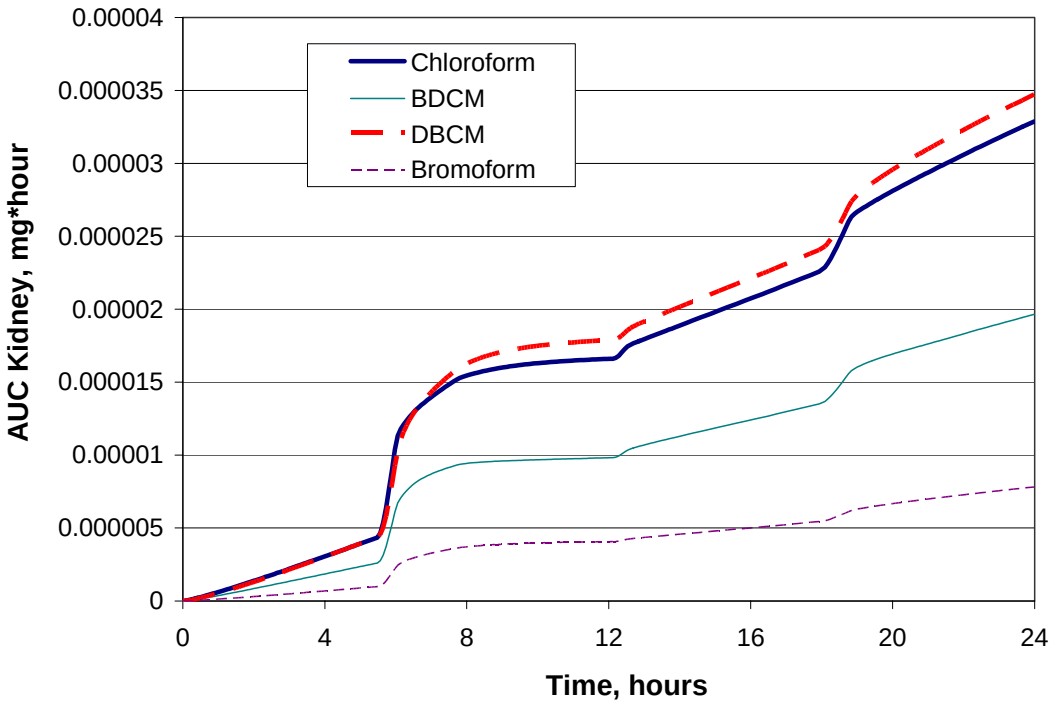


Figure 17. Predicted Area under the Curve (AUC) for the parent THMs Concentrations in the Kidney for the Adult Male in the Example Case

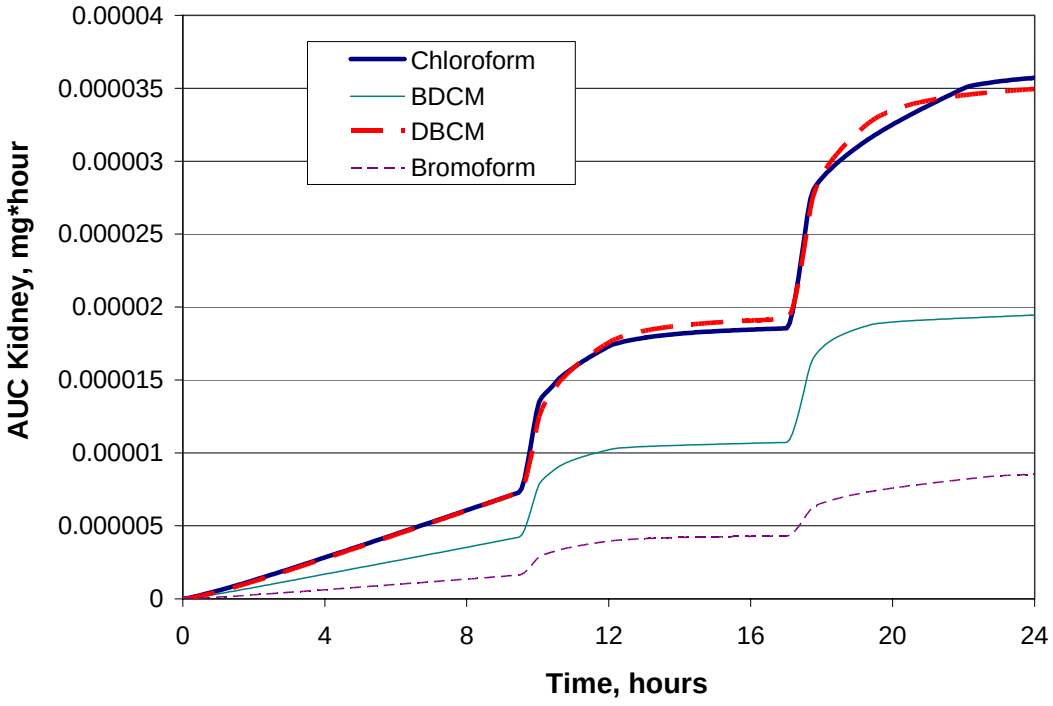


Figure 18. Predicted Area under the Curve (AUC) for the parent THMs Concentrations in the Kidney for the Adult Female in the Example Case

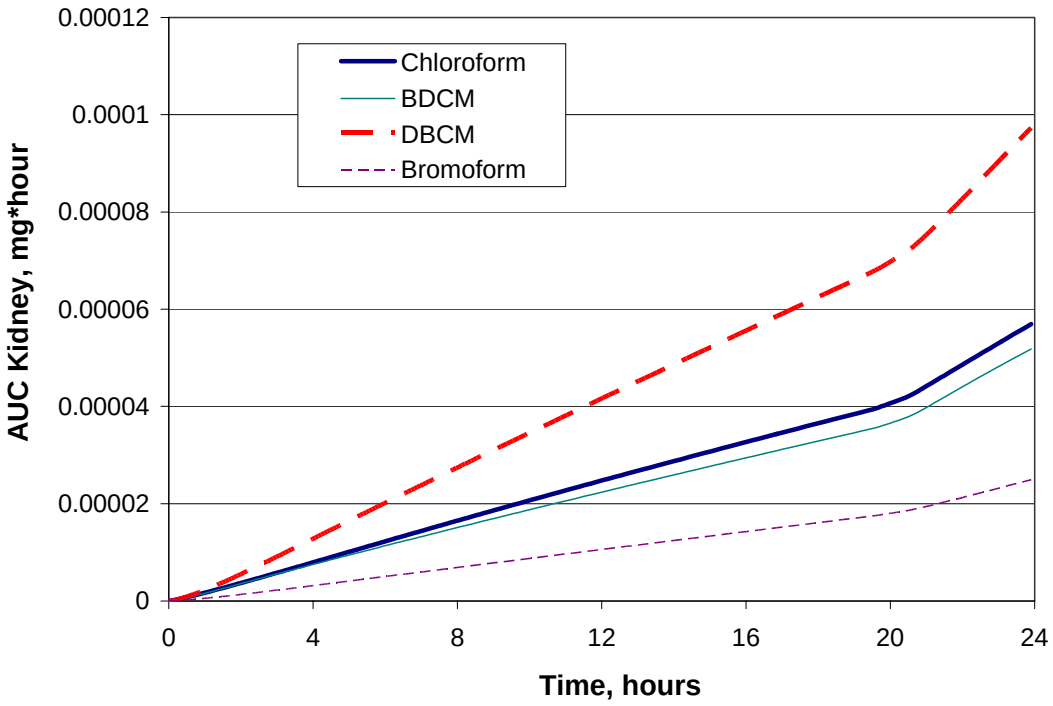


Figure 19. Predicted Area under the Curve (AUC) for the parent THMs Concentrations in the Kidney for the Child in the Example Case

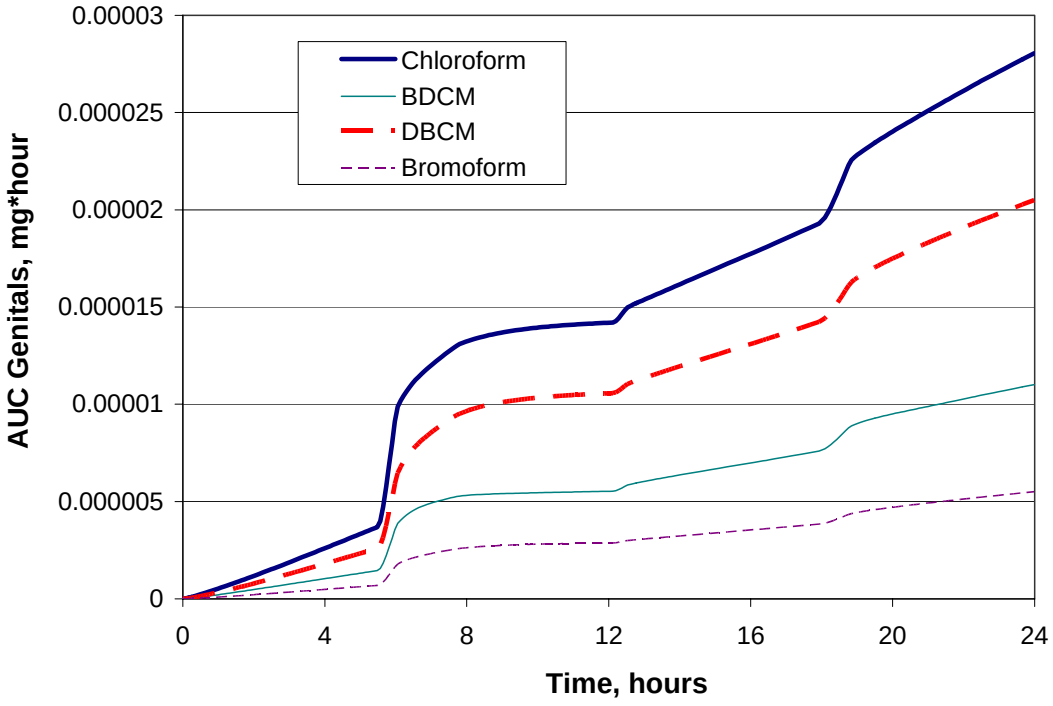


Figure 20. Predicted Area under the Curve (AUC) for the parent THMs Concentrations in the Genitals for the Adult Male in the Example Case

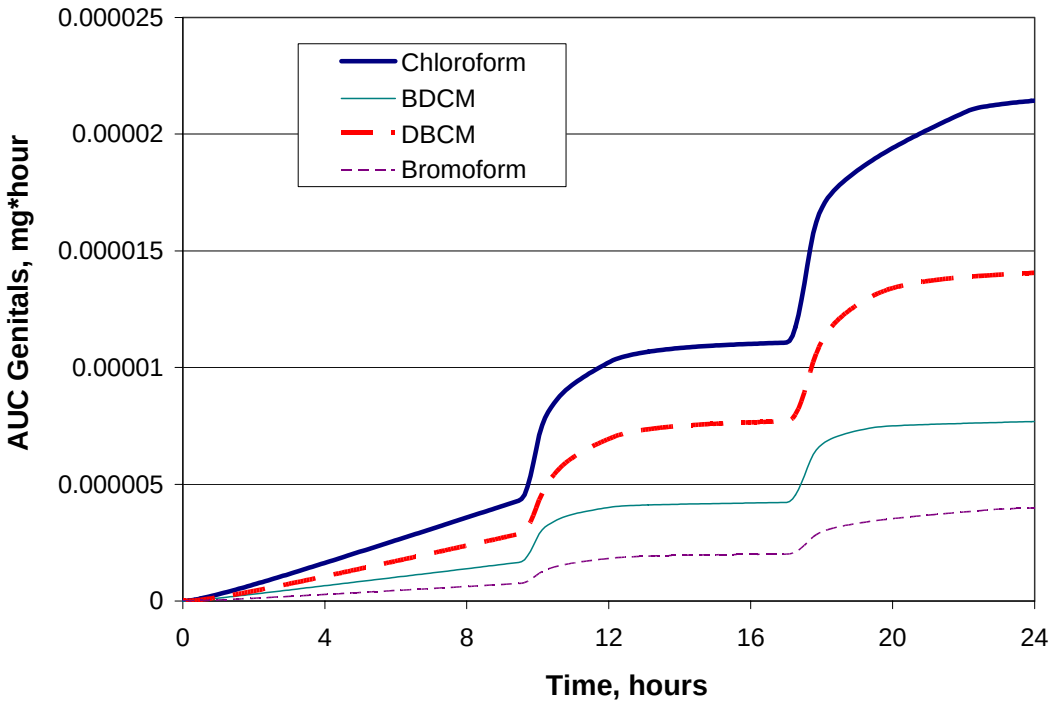


Figure 21. Predicted Area under the Curve (AUC) for the parent THMs Concentrations in the Genitals for the Adult Female in the Example Case

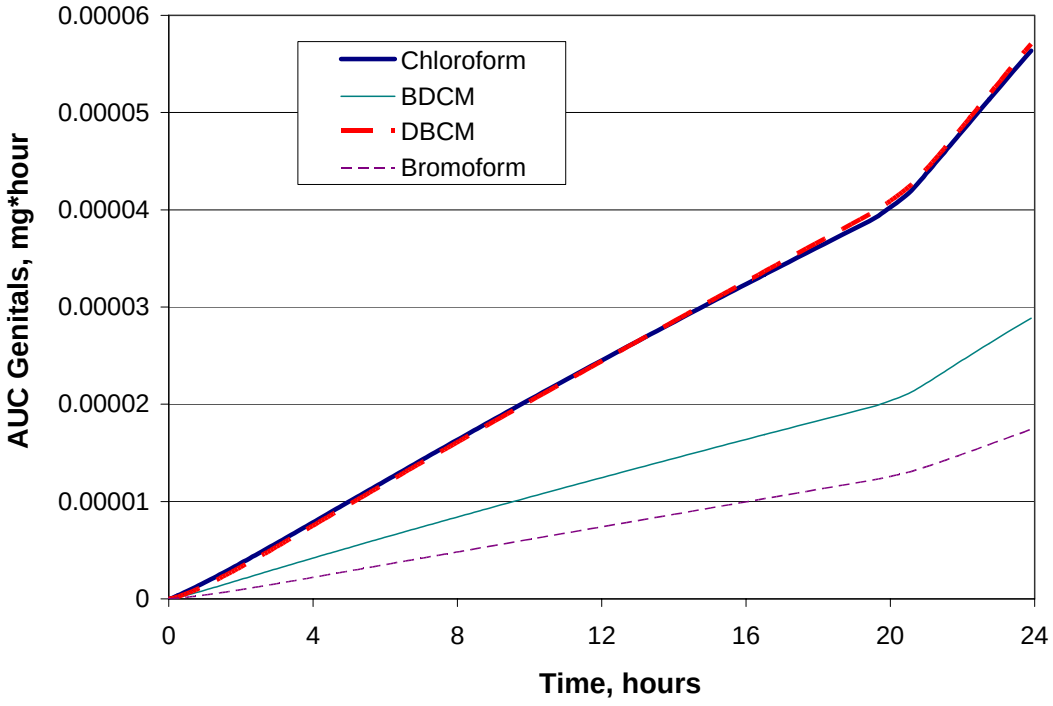


Figure 22. Predicted Area under the Curve (AUC) for the parent THMs Concentrations in the Genitals for the Child in the Example Case

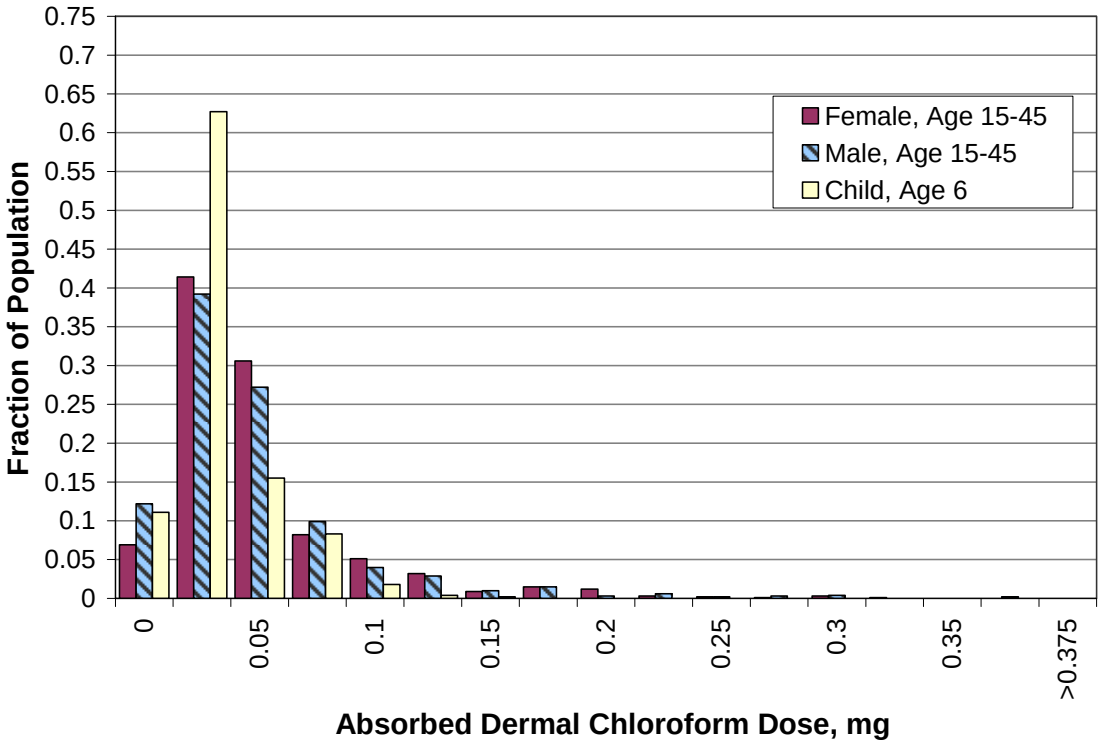


Figure 23. Histogram of Absorbed Chloroform Dermal Dose for Females, Males, and Children

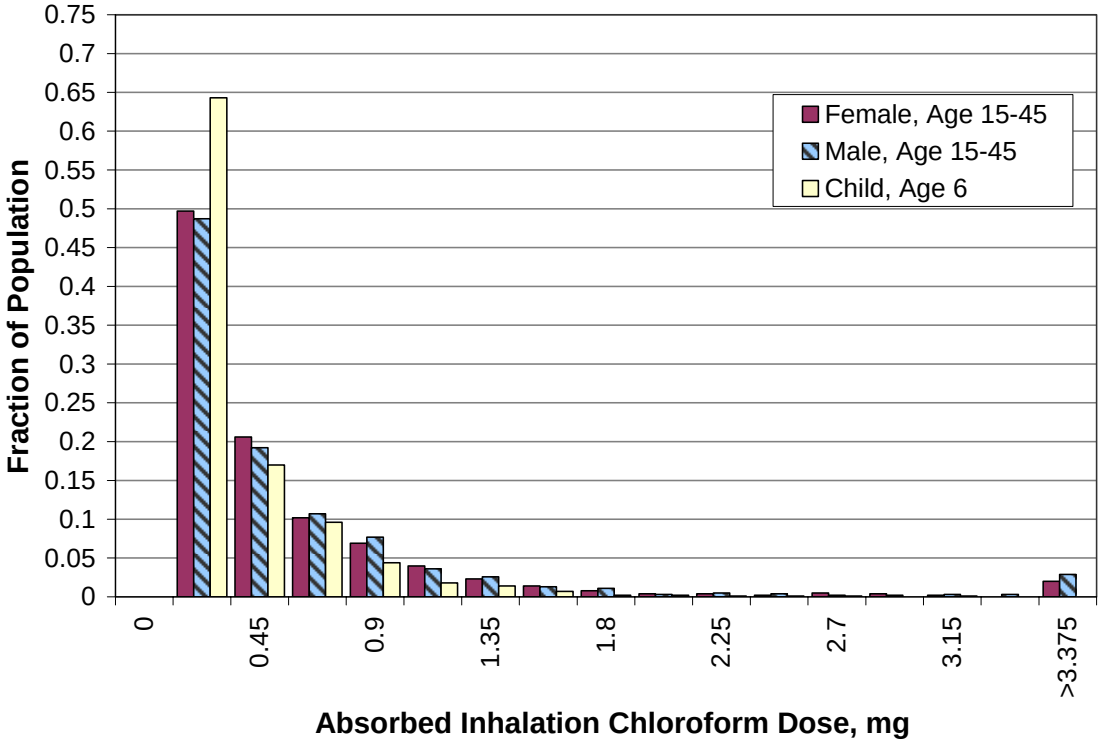


Figure 24. Histogram of Absorbed Chloroform Inhalation Dose for Females, Males, and Children

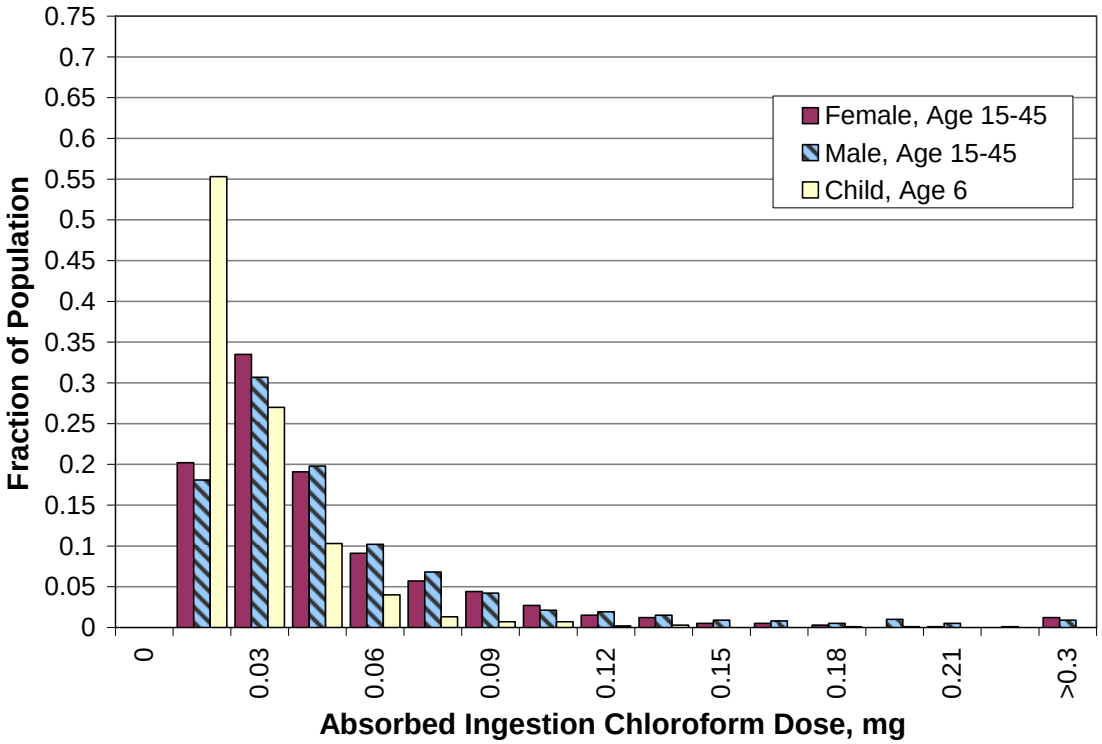


Figure 25. Histogram of Absorbed Chloroform Ingestion Dose for Females, Males, and Children

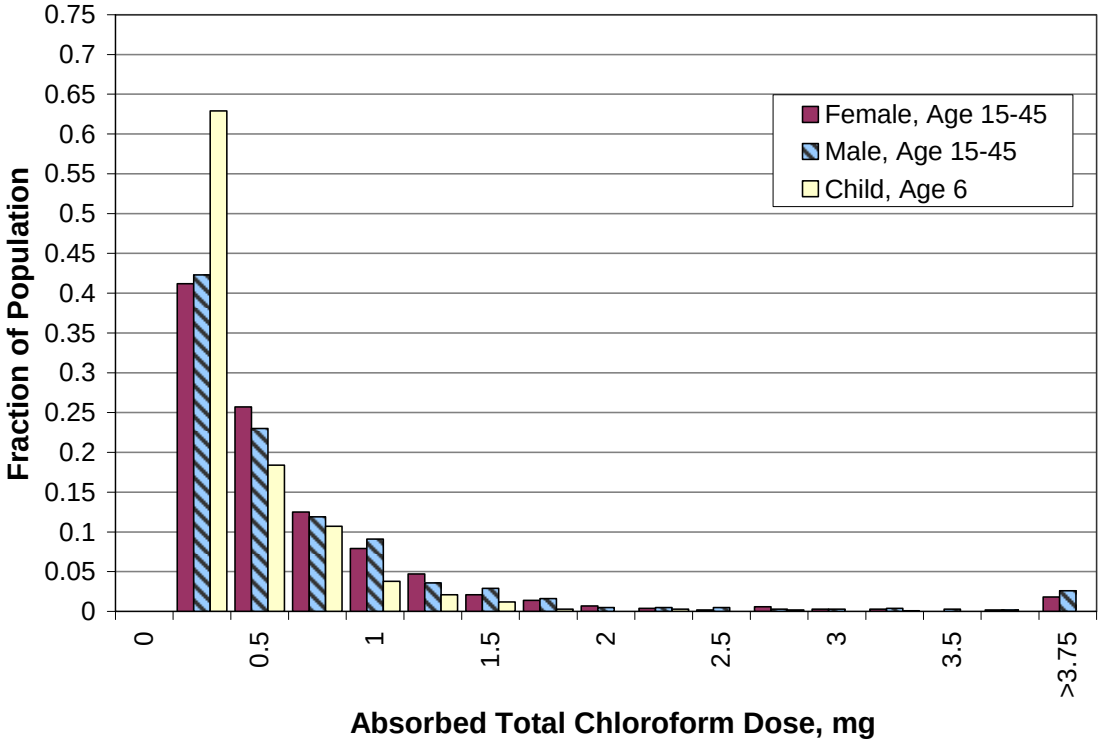


Figure 26. Histogram of Total Absorbed Chloroform Dose for Females, Males, and Children

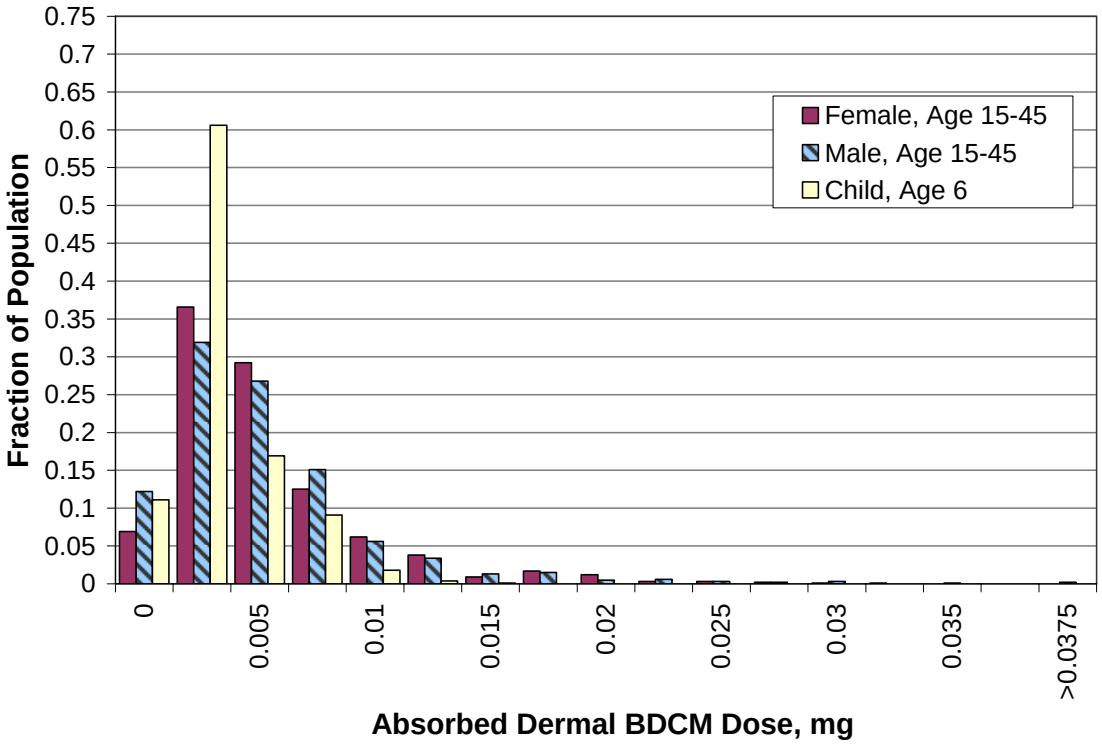


Figure 27. Histogram of Absorbed BDCM Dermal Dose for Females, Males, and Children

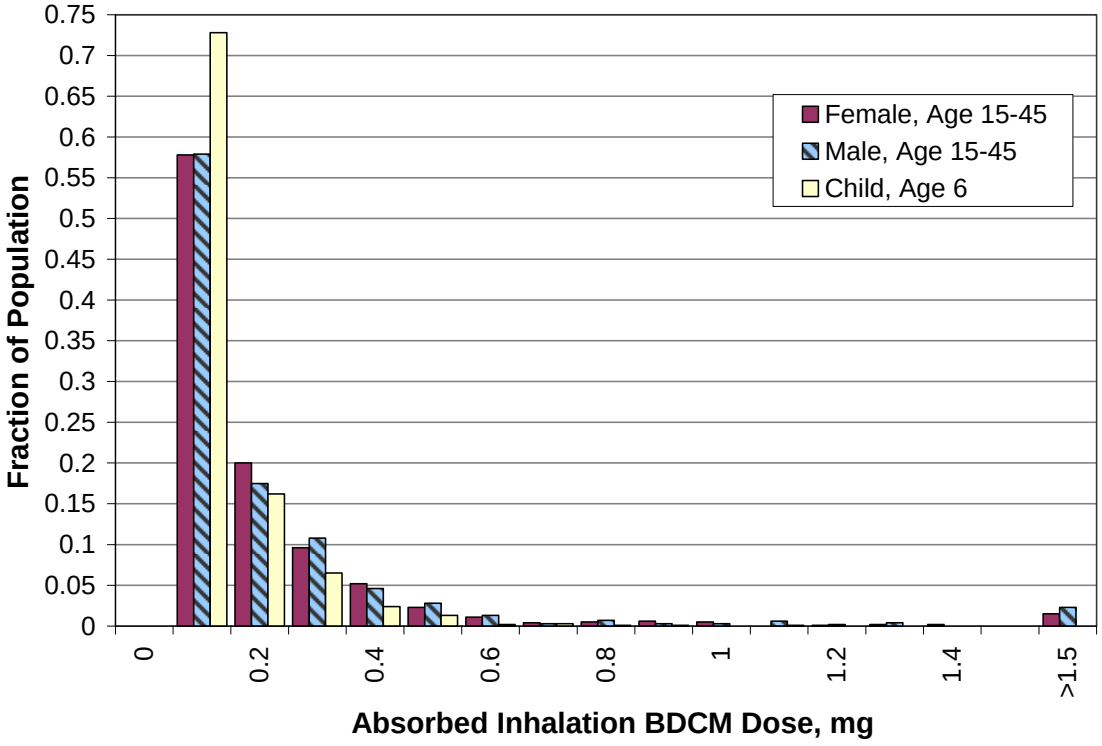


Figure 28. Histogram of Absorbed BDCM Inhalation Dose for Females, Males, and Children

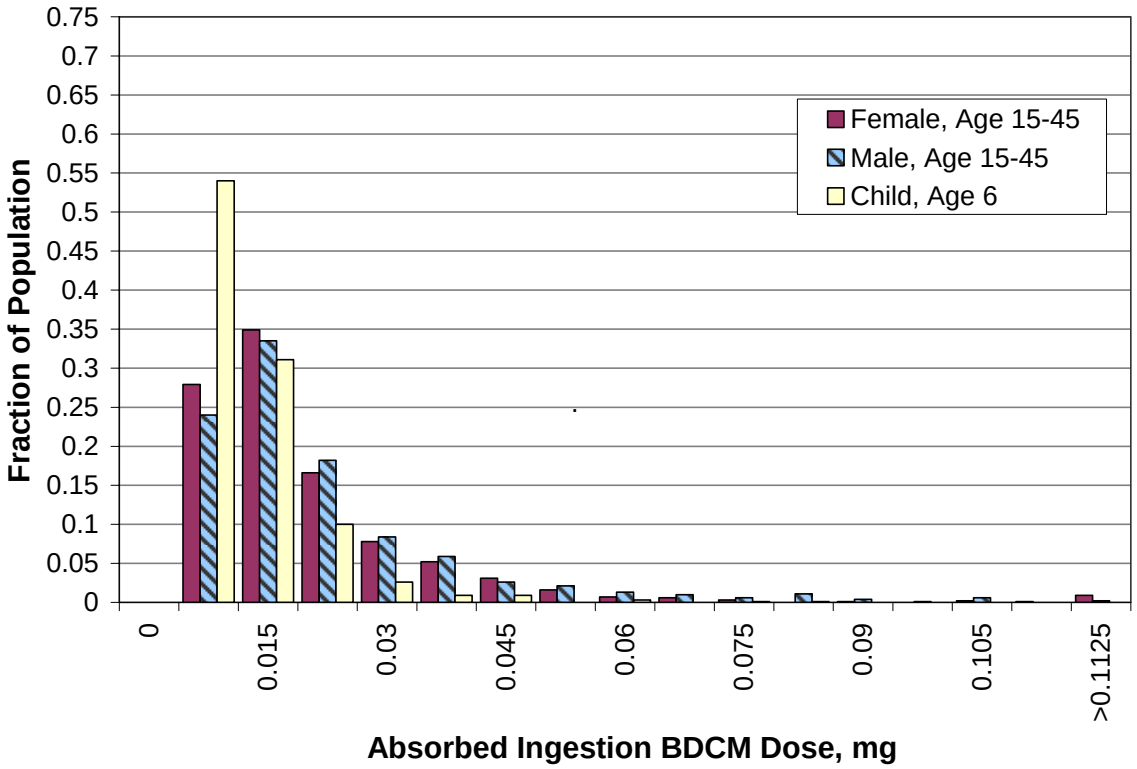


Figure 29. Histogram of Absorbed BDCM Ingestion Dose for Females, Males, and Children

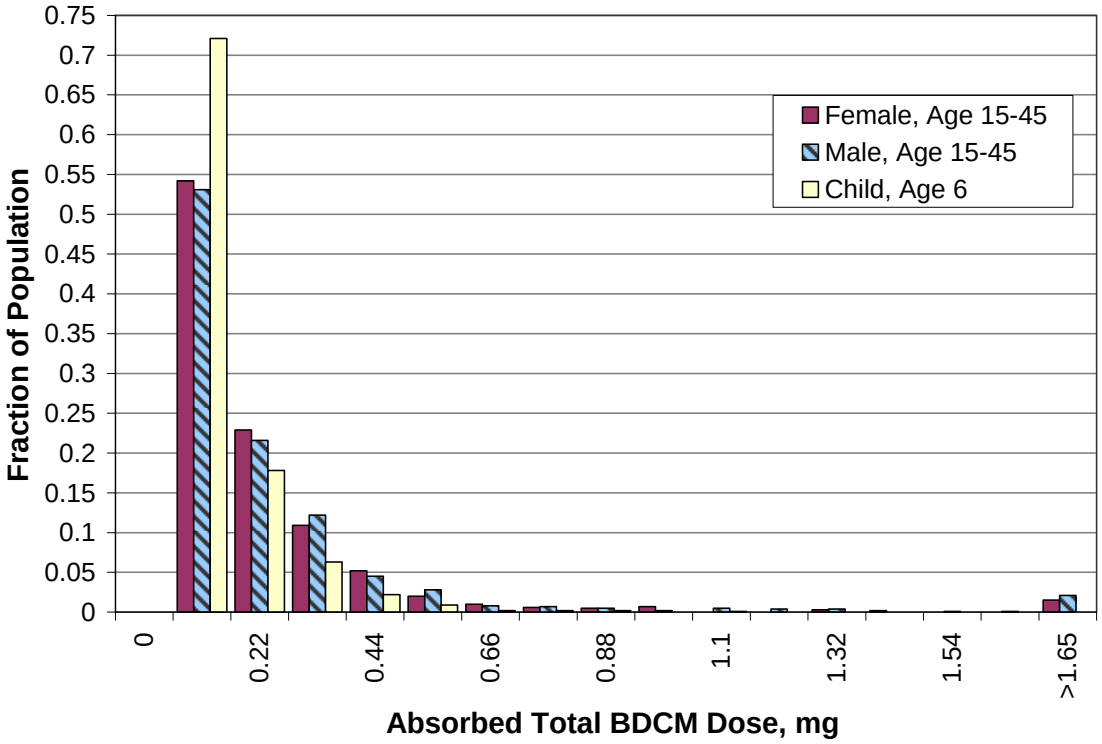


Figure 30. Histogram of Total Absorbed BDCM Dose for Females, Males, and Children

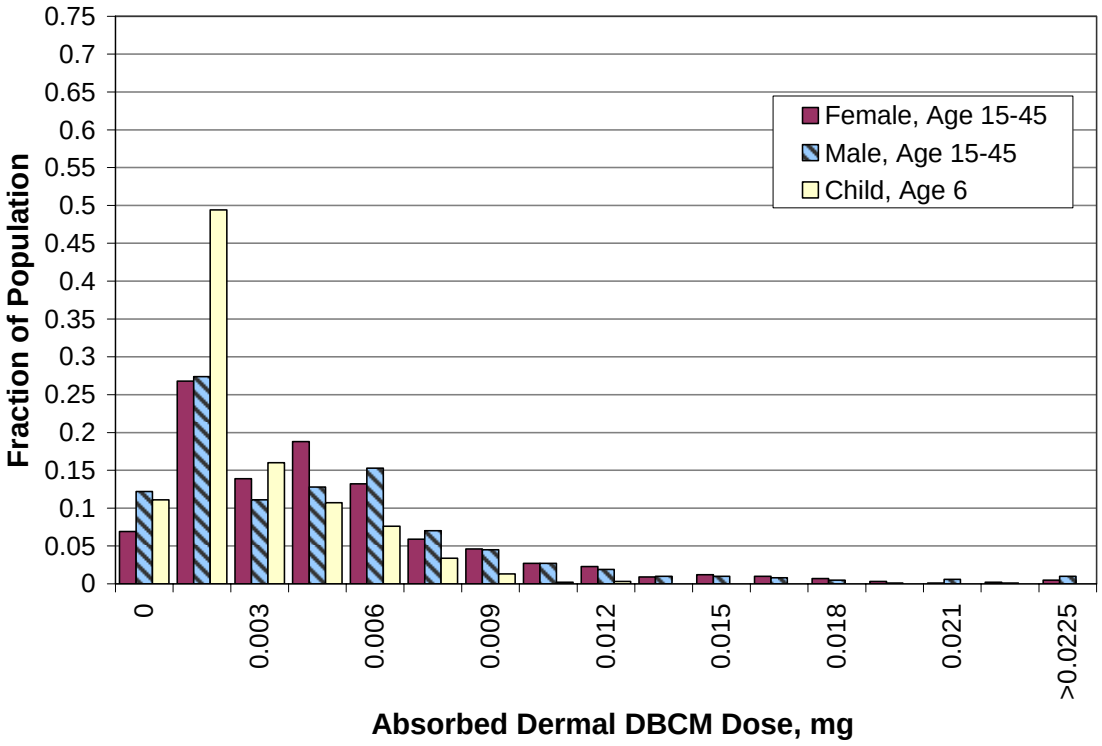


Figure 31. Histogram of Absorbed DBCM Dermal Dose for Females, Males, and Children

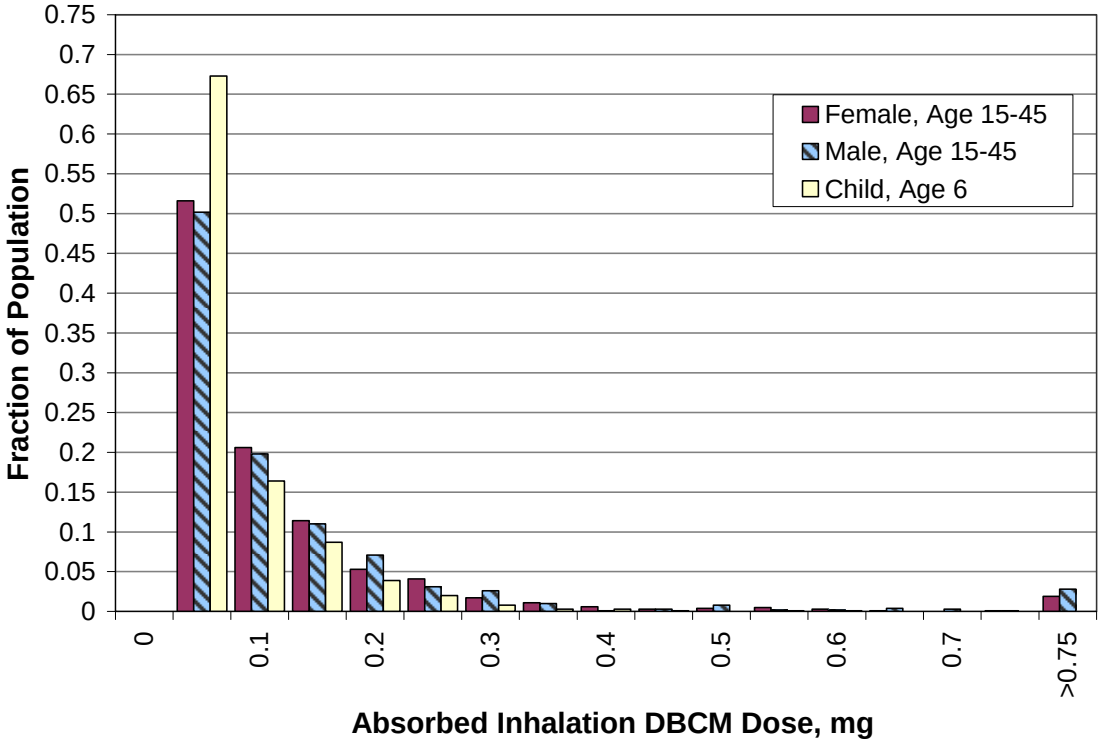


Figure 32. Histogram of Absorbed DBCM Inhalation Dose for Females, Males, and Children

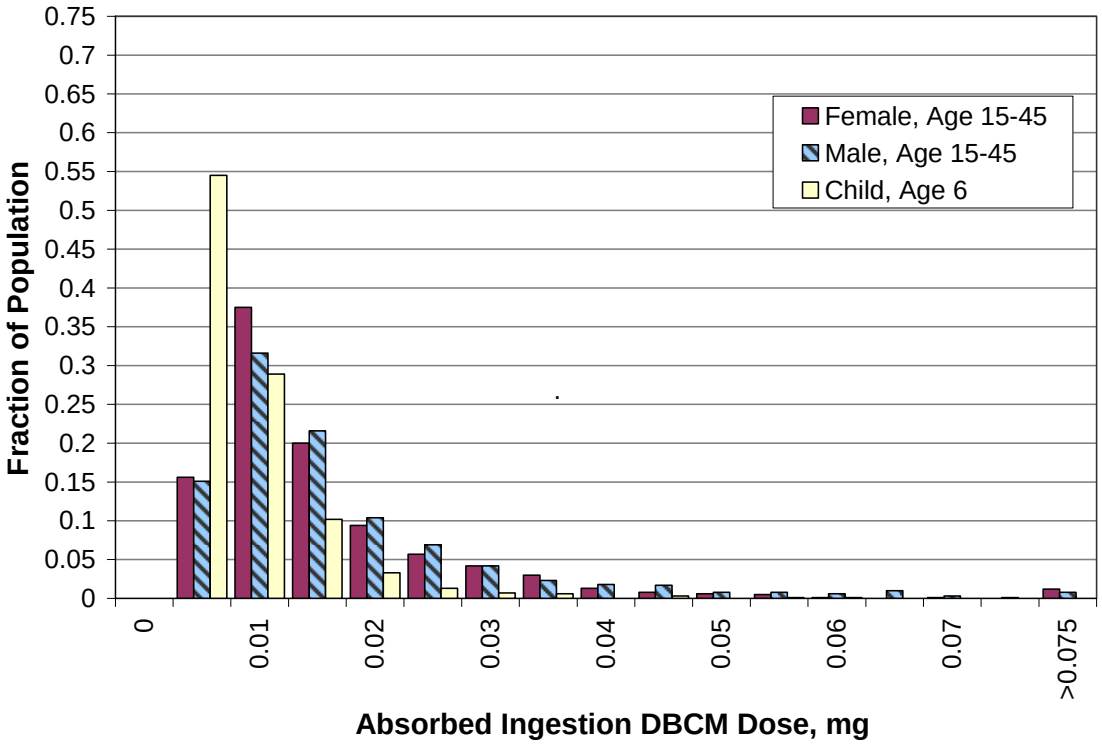


Figure 33. Histogram of Absorbed DBCM Inhalation Dose for Females, Males, and Children

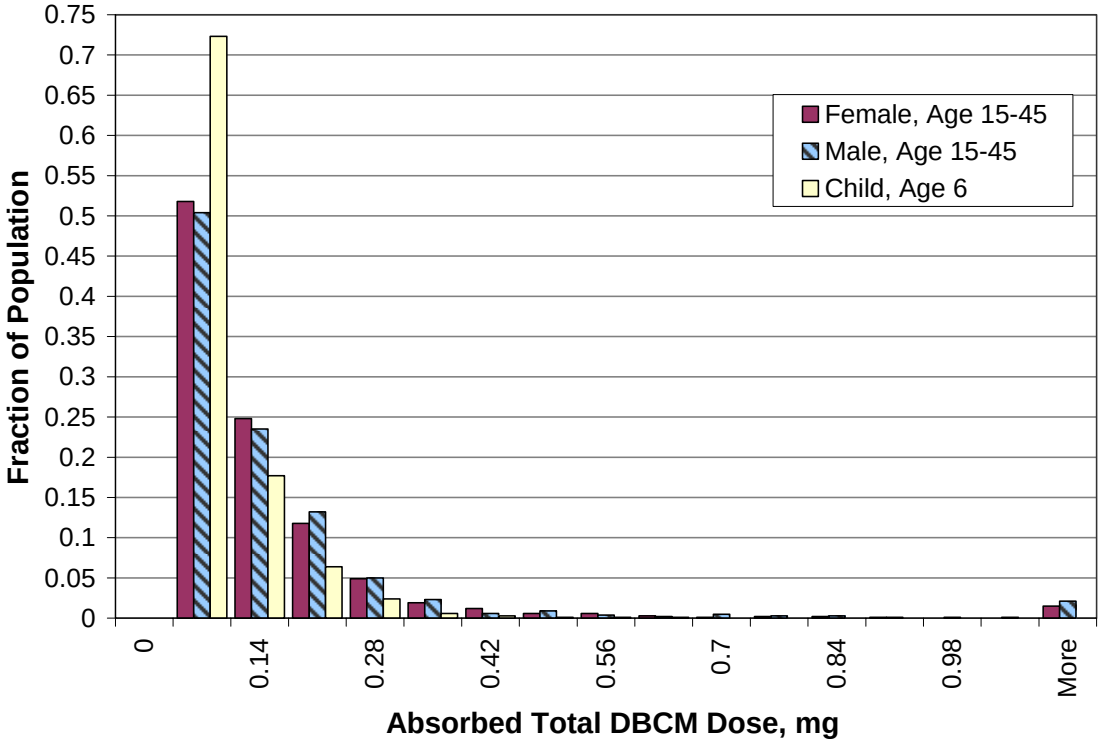


Figure 34. Histogram of Total Absorbed DBCM Dose for Females, Males, and Children

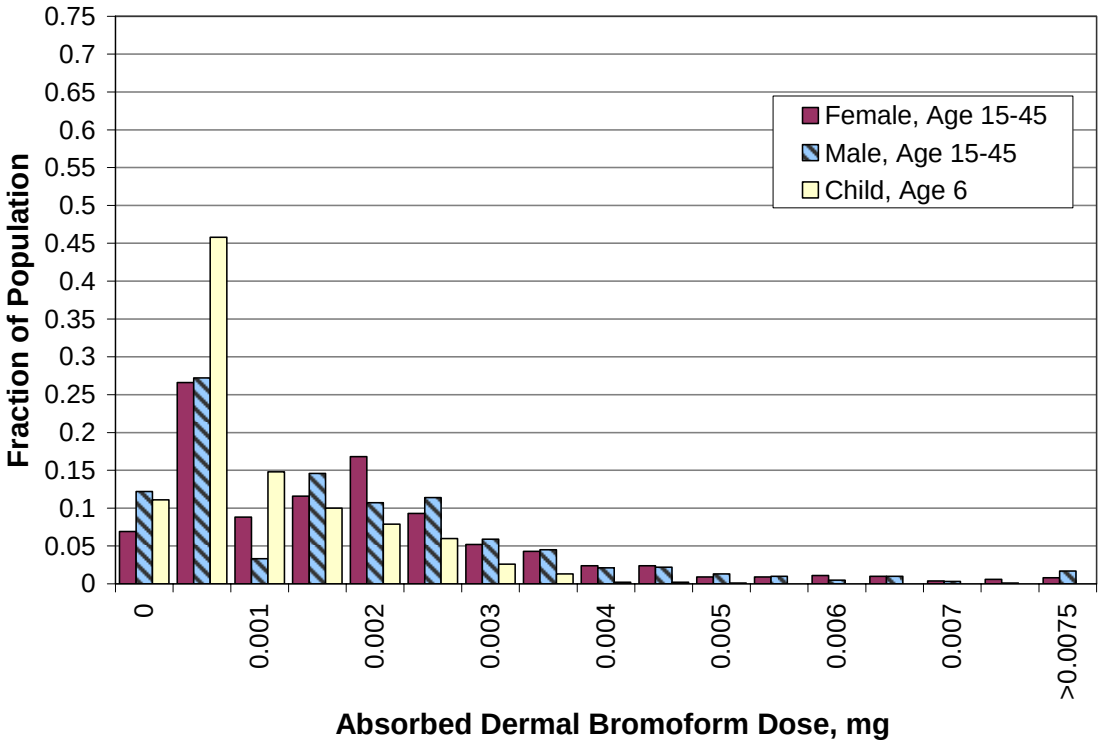


Figure 35. Histogram of Absorbed Bromoform Dermal Dose for Females, Males, and Children

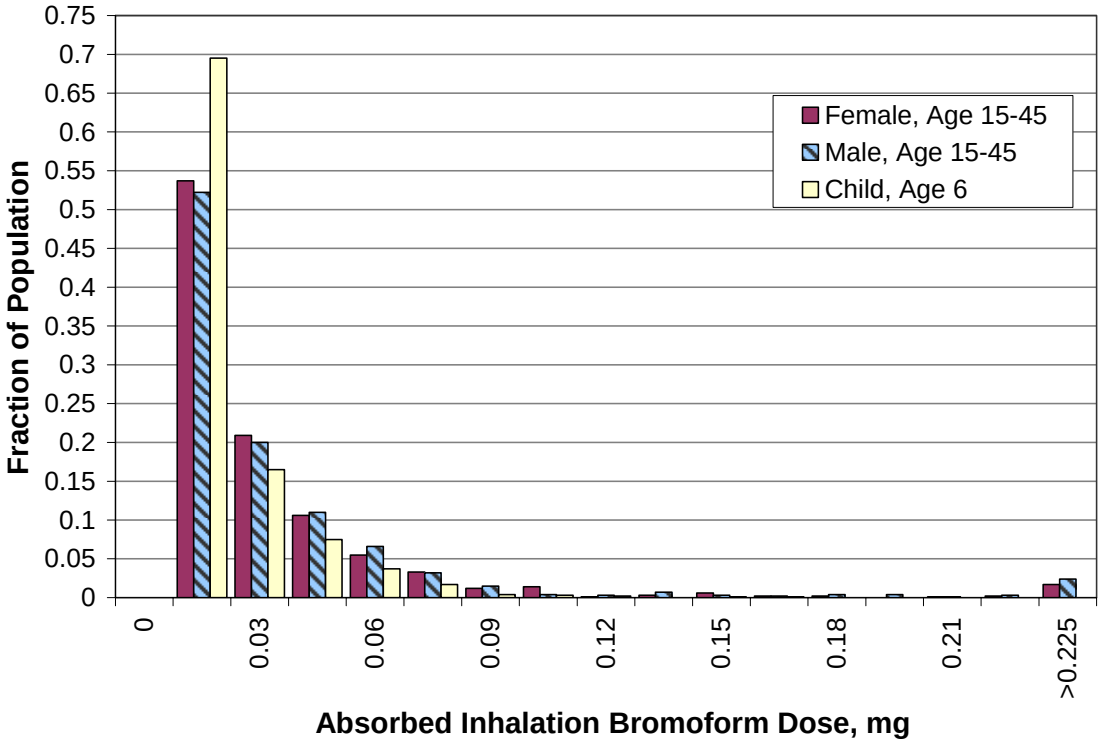


Figure 36. Histogram of Absorbed Bromoform Inhalation Dose for Females, Males, and Children

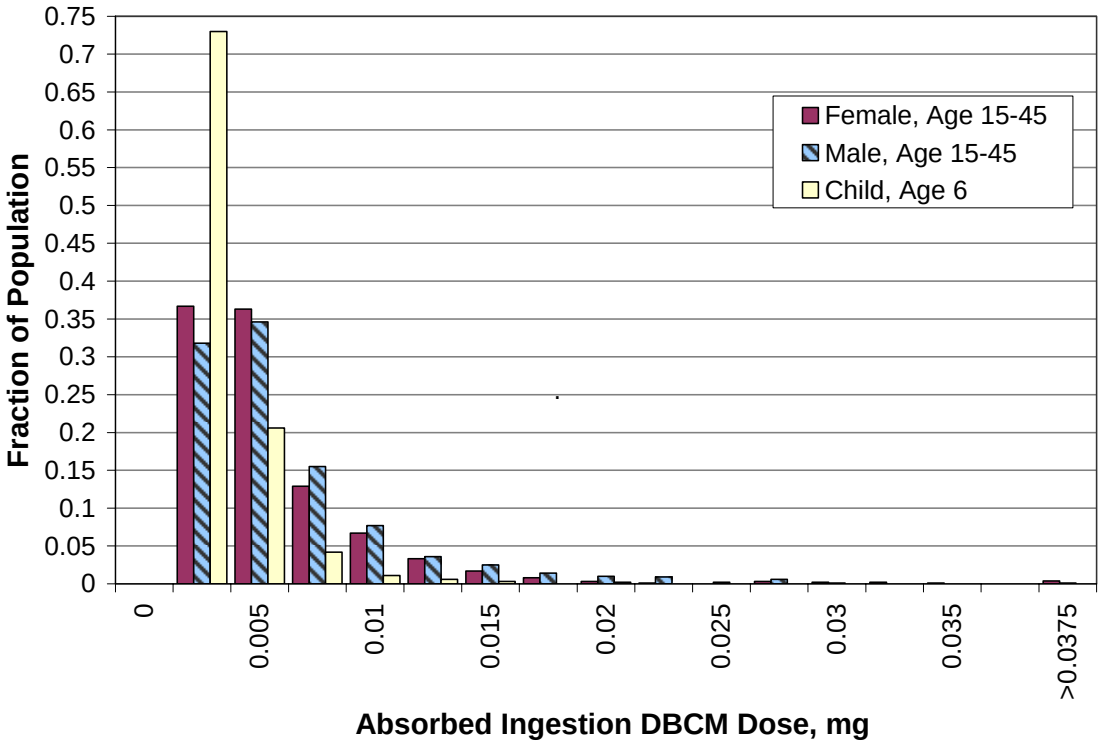


Figure 37. Histogram of Absorbed Bromoform Inhalation Dose for Females, Males, and Children

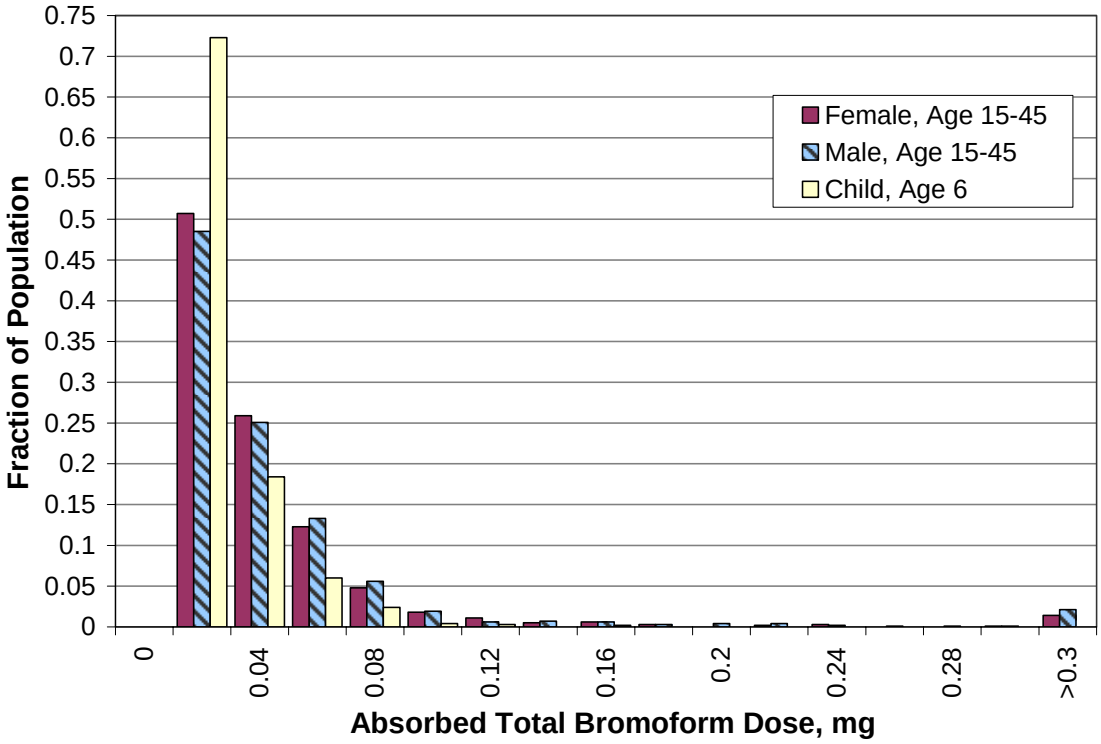


Figure 38. Histogram of Total Absorbed Bromoform Dose for Females, Males, and Children

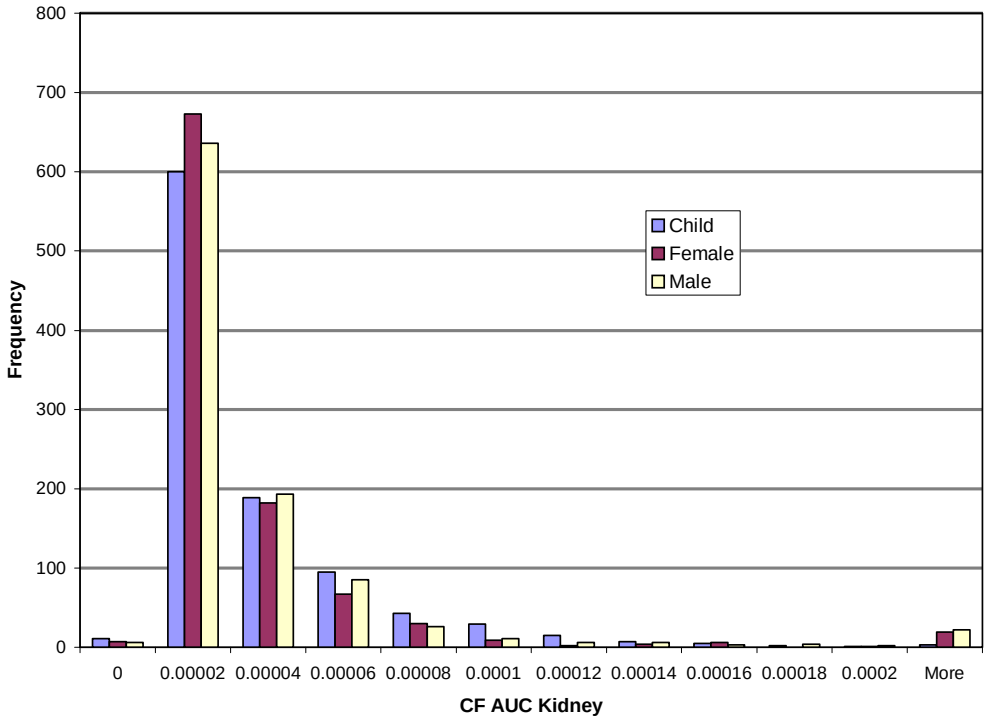


Figure 39. Histogram of the distribution of the AUC for chloroform in the kidneys of exposed subjects from 1000 different water-use patterns.

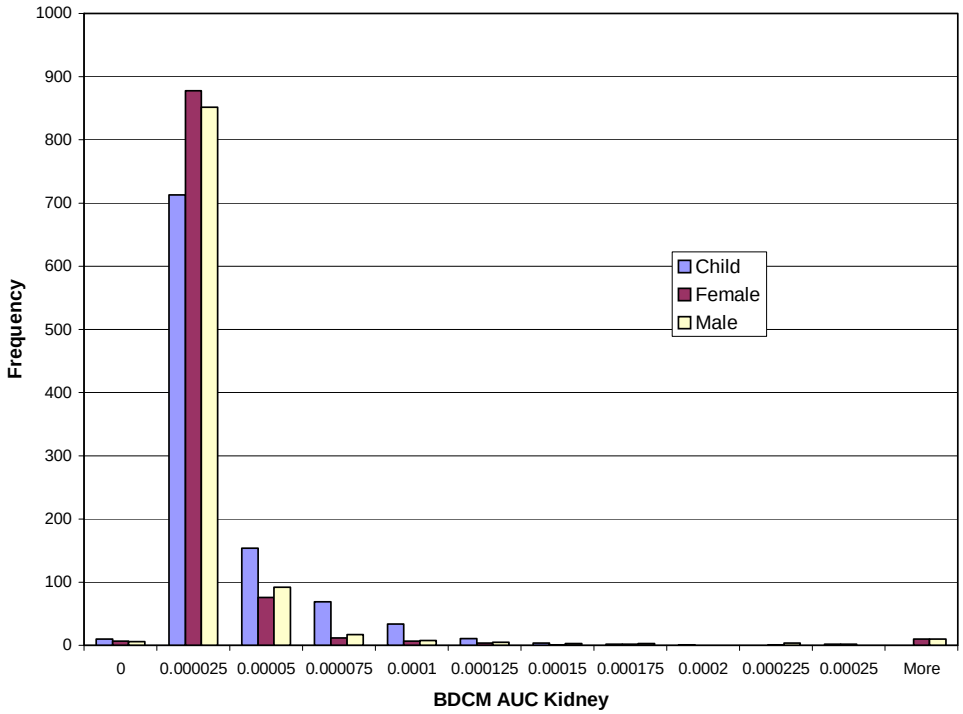


Figure 40. Histogram of the distribution of the AUC for BDCM in the kidneys of exposed subjects from 1000 different water-use patterns.

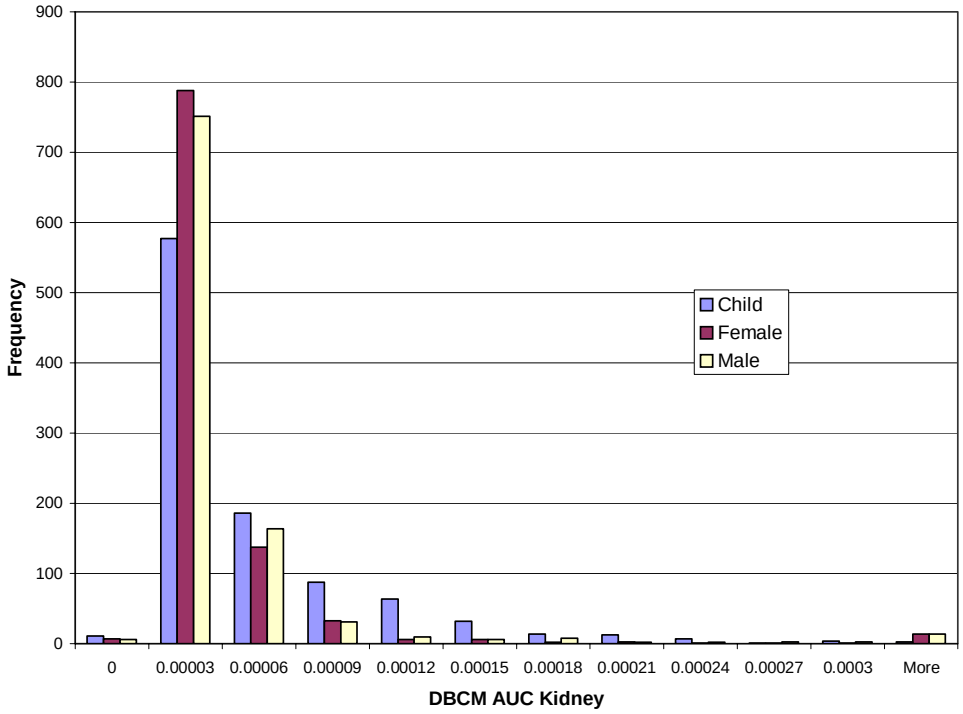


Figure 41. Histogram of the distribution of the AUC for DBCM in the kidneys of exposed subjects from 1000 different water-use patterns.

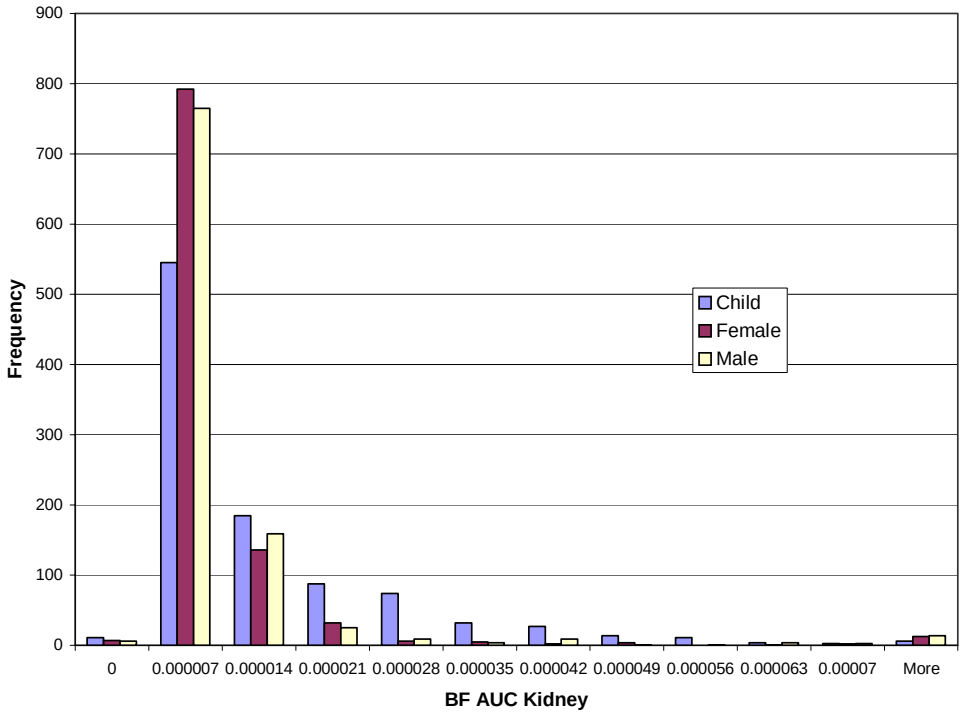


Figure 42. Histogram of the distribution of the AUC for bromoform in the kidneys of exposed subjects from 1000 different water-use patterns.

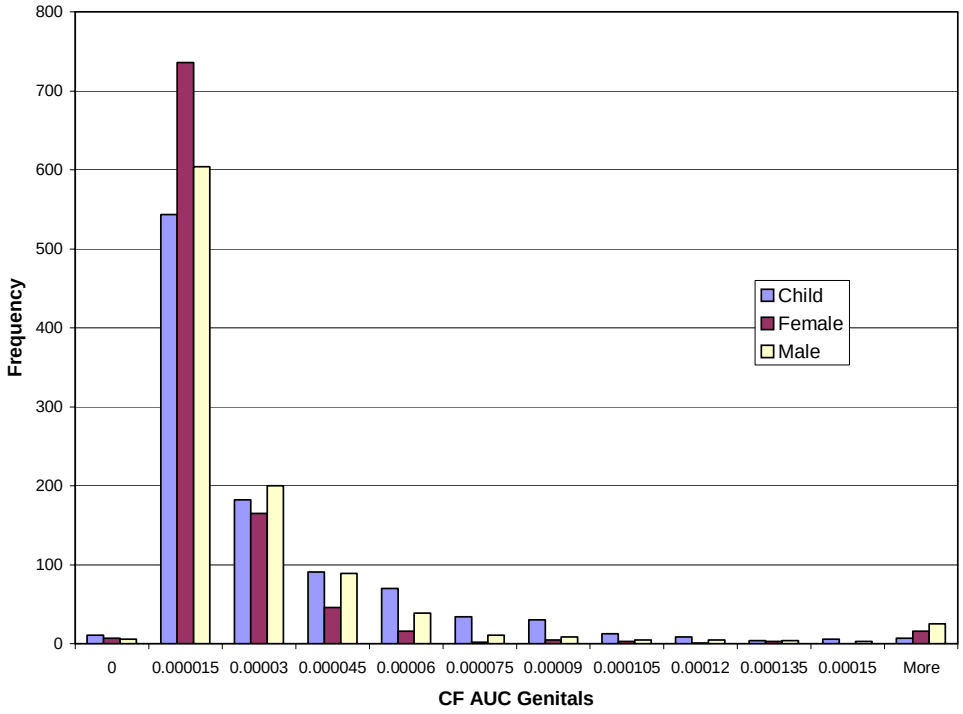


Figure 43. Histogram of the distribution of the AUC for chloroform in the genitals of exposed subjects from 1000 different water-use patterns.

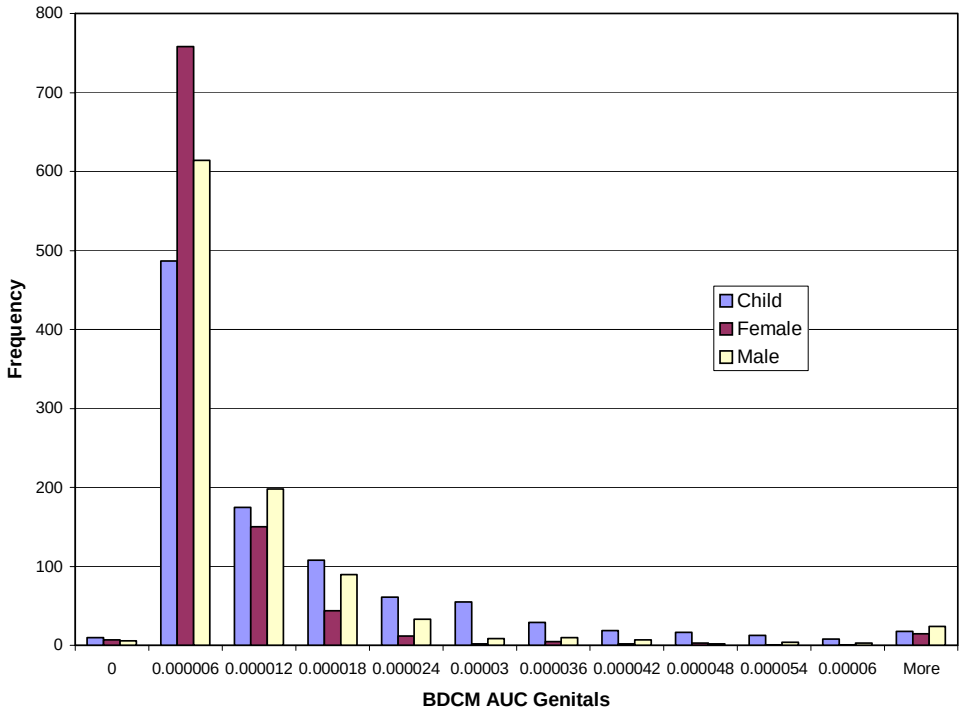


Figure 44. Histogram of the distribution of the AUC for BDCM in the genitals of exposed subjects from 1000 different water-use patterns.

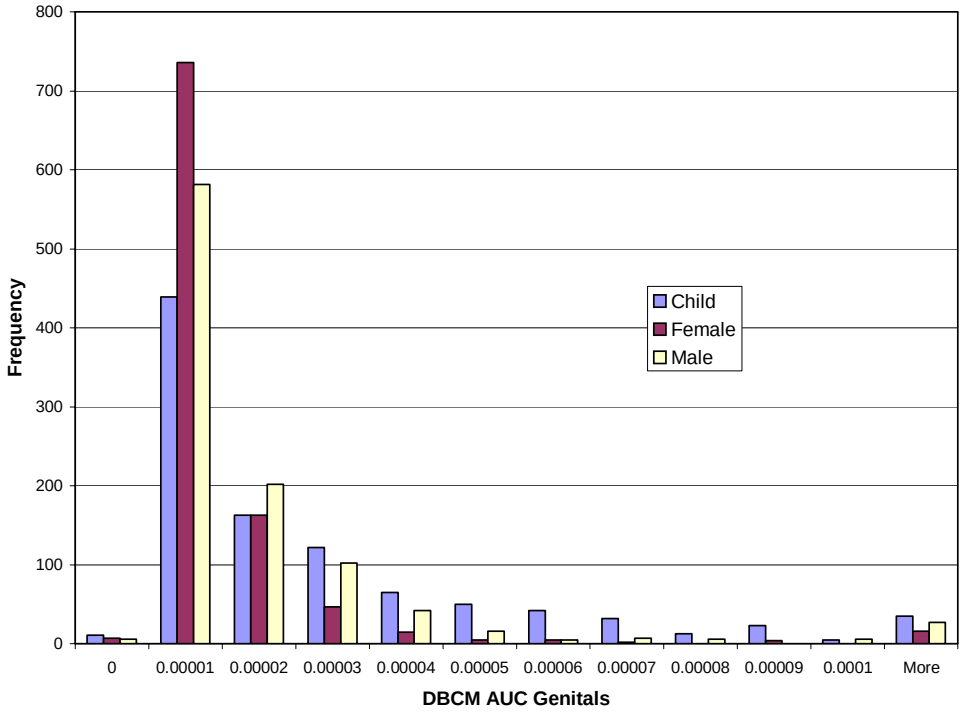


Figure 45. Histogram of the distribution of the AUC for DBCM in the genitals of exposed subjects from 1000 different water-use patterns.

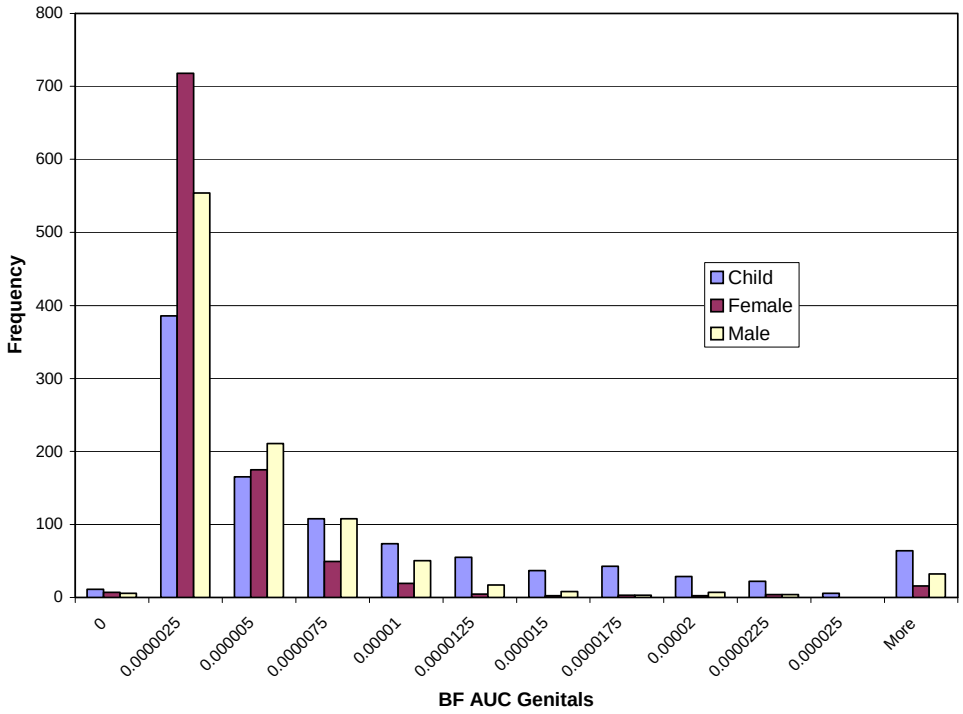


Figure 46. Histogram of the distribution of the AUC for bromoform in the genitals of exposed subjects from 1000 different water-use patterns.

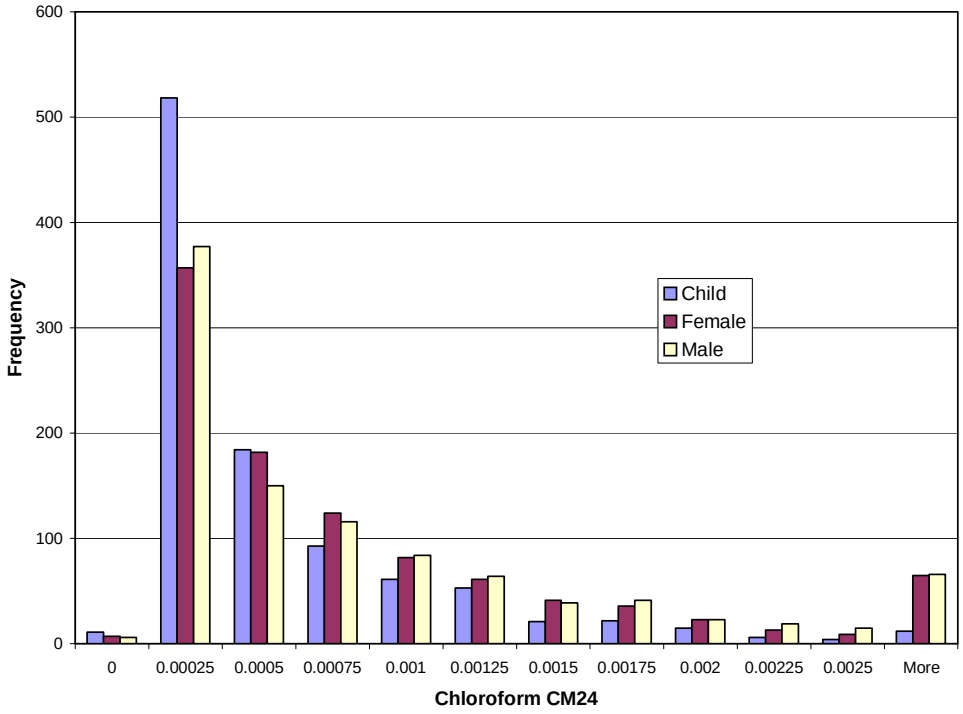


Figure 47. Histogram of the distribution of the concentration of chloroform metabolites (CM_{24}) formed in the liver over 24 hr in exposed subjects from 1000 different water-use patterns.

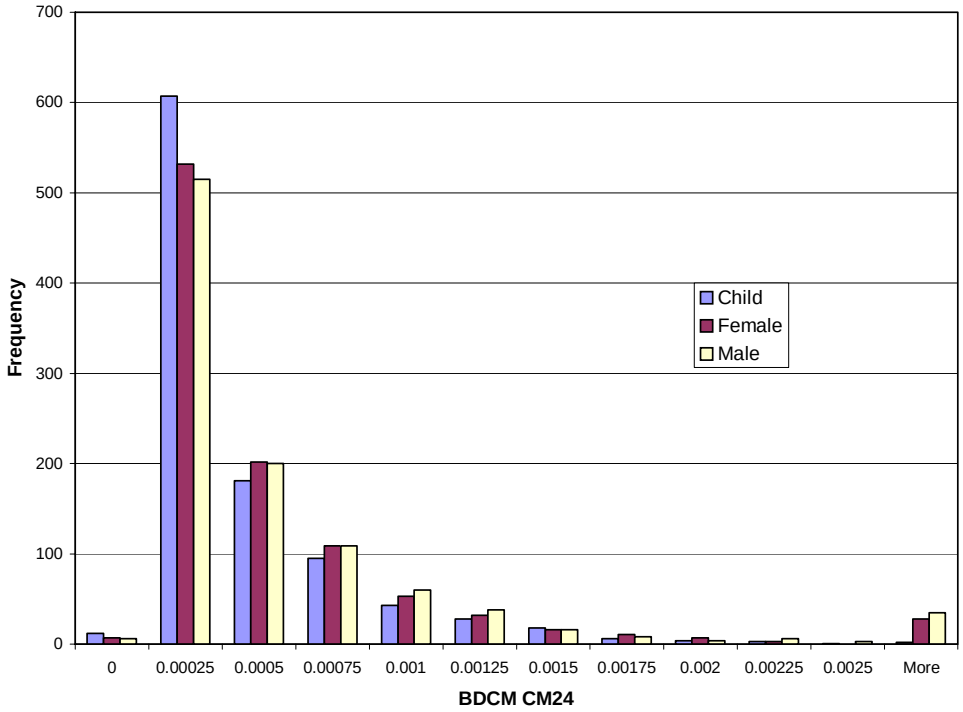


Figure 48. Histogram of the distribution of the concentration of BDCM metabolites (CM_{24}) formed in the liver over 24 hr in exposed subjects from 1000 different water-use patterns.

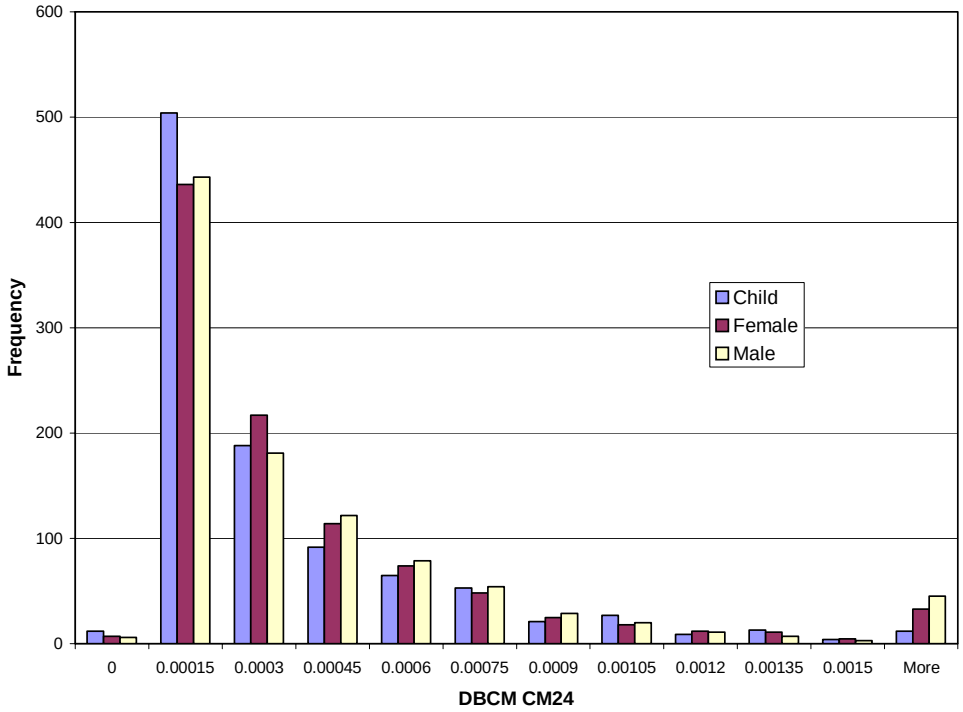


Figure 49. Histogram of the distribution of the concentration of DBCM metabolites (CM_{24}) formed in the liver over 24 hr in exposed subjects from 1000 different water-use patterns.

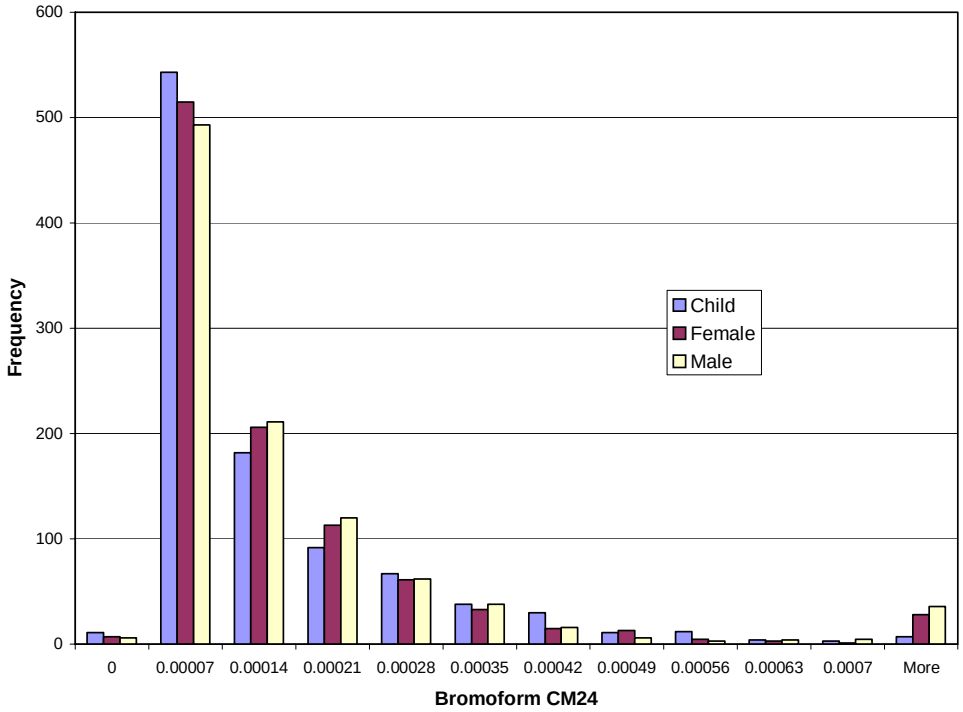


Figure 50. Histogram of the distribution of the concentration of bromoform metabolites (CM_{24}) formed in the liver over 24 hr in exposed subjects from 1000 different water-use patterns

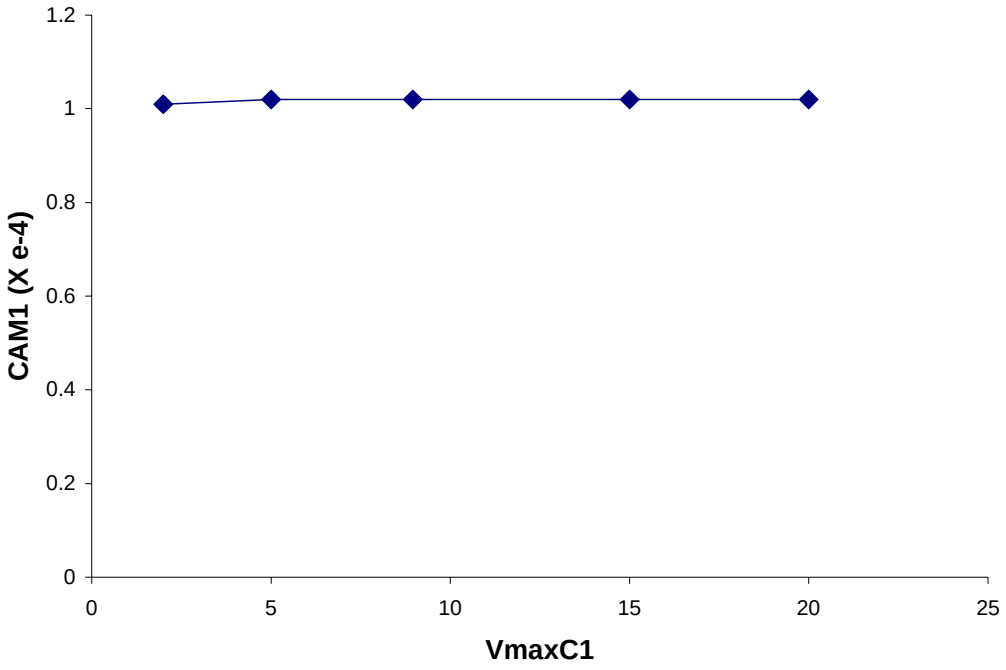


Figure 51. Effect of varying the maximal rate of metabolism (VmaxC) on the liver concentration of metabolites (CAM) for chloroform.

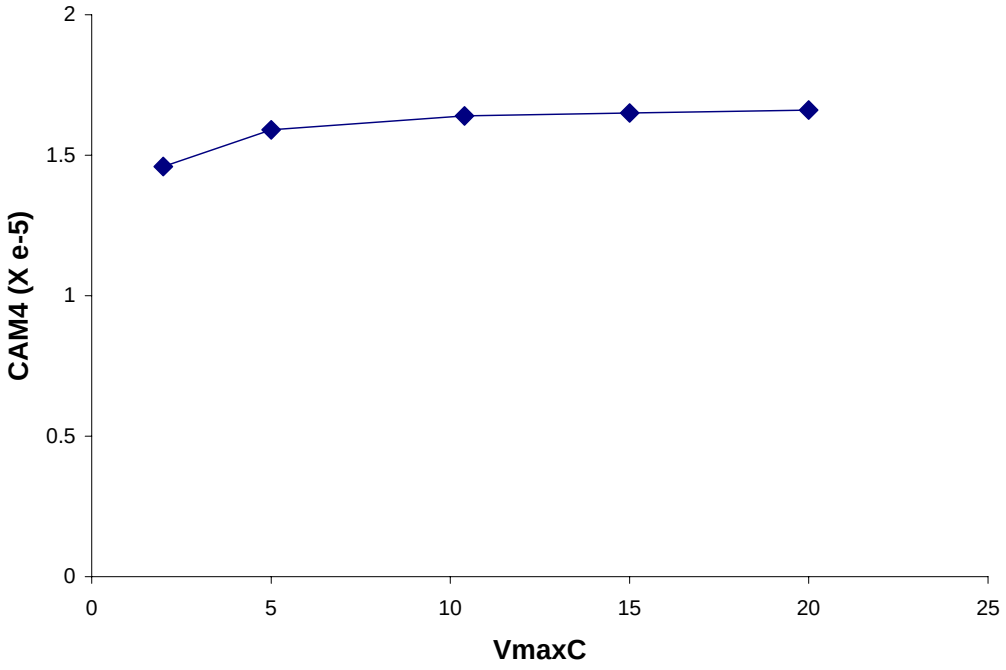


Figure 52. Effect of varying the maximal rate of metabolism (VmaxC) on the liver concentration of metabolites (CAM) for bromoform.

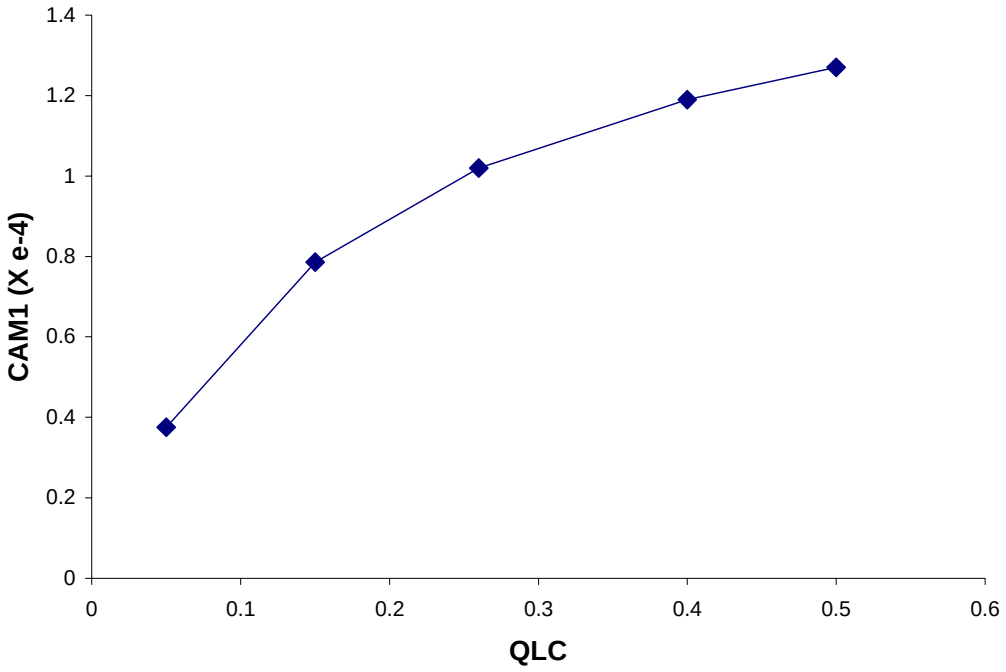


Figure 53. Effect of varying liver blood flow (QLC) on the liver concentration of metabolites (CAM) for chloroform.

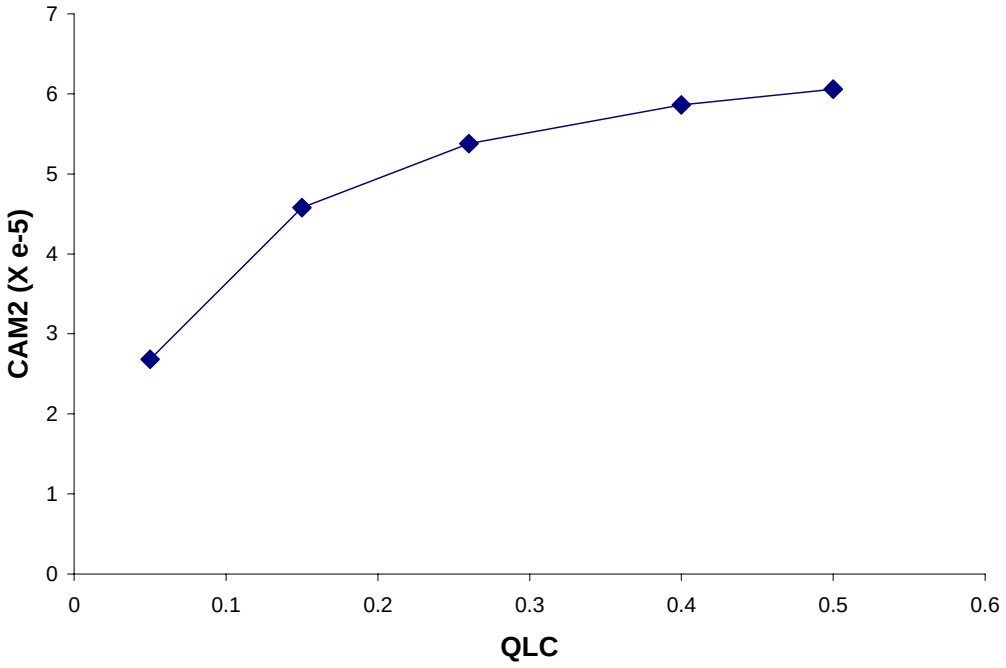


Figure 54. Effect of varying liver blood flow (QLC) on the liver concentration of metabolites (CAM) for bromodichloromethane.

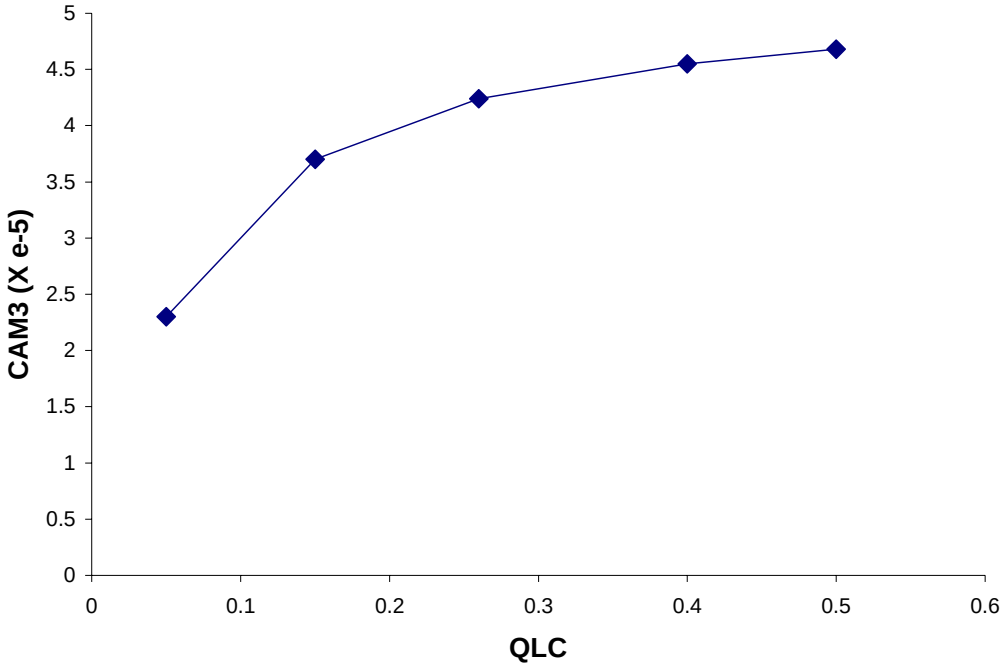


Figure 55. Effect of varying liver blood flow (QLC) on the liver concentration of metabolites (CAM) for dibromochloromethane.

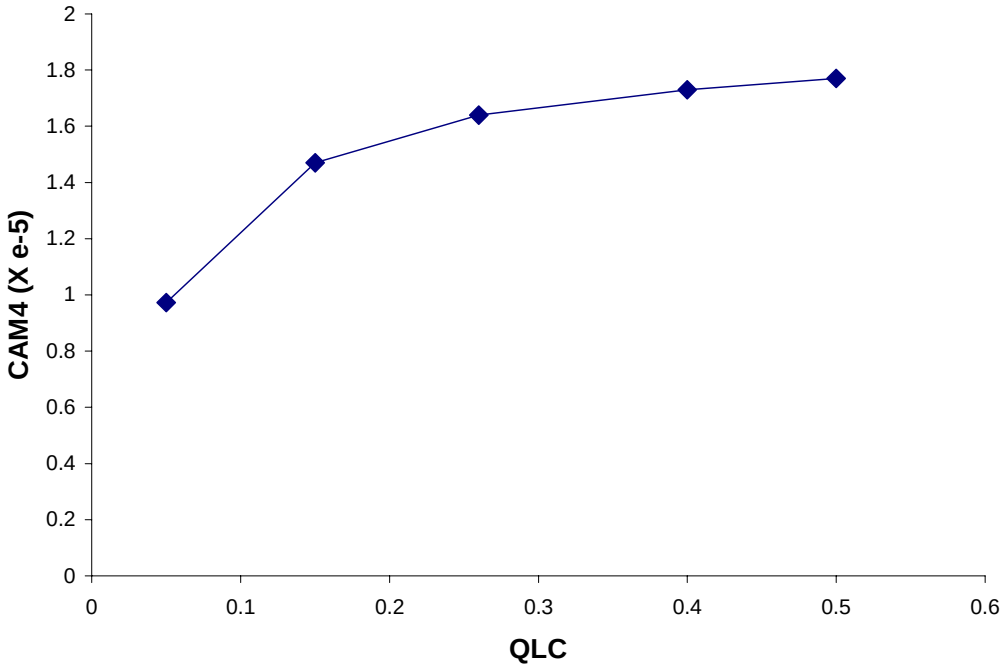


Figure 56. Effect of varying liver blood flow (QLC) on the liver concentration of metabolites (CAM) for bromoform.

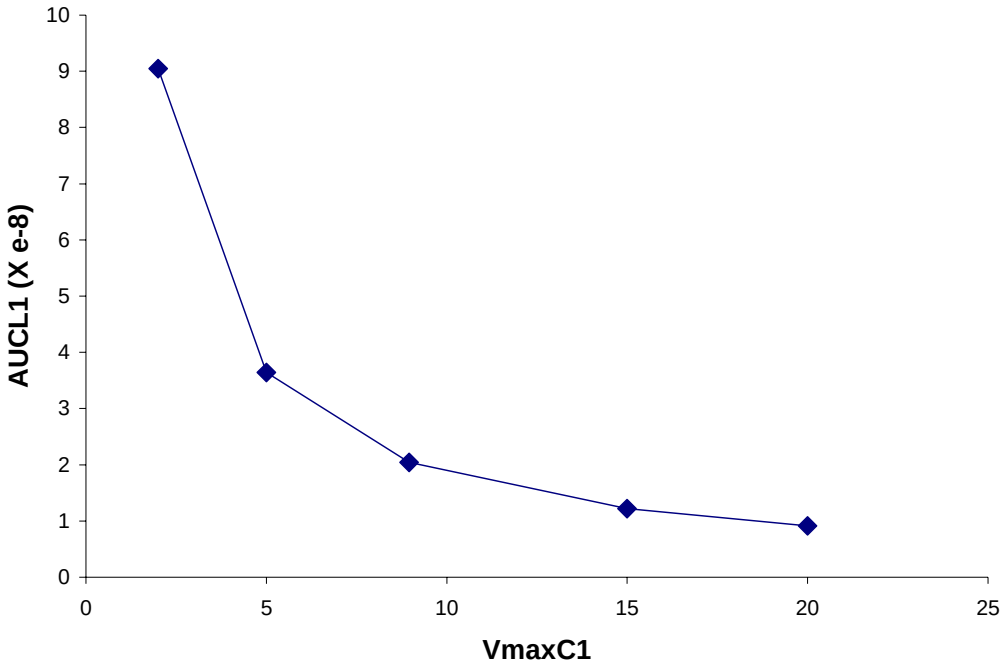


Figure 57. Effect of varying the maximal rate of metabolism (VmaxC) on the liver area under the curve (AUCL) for chloroform.

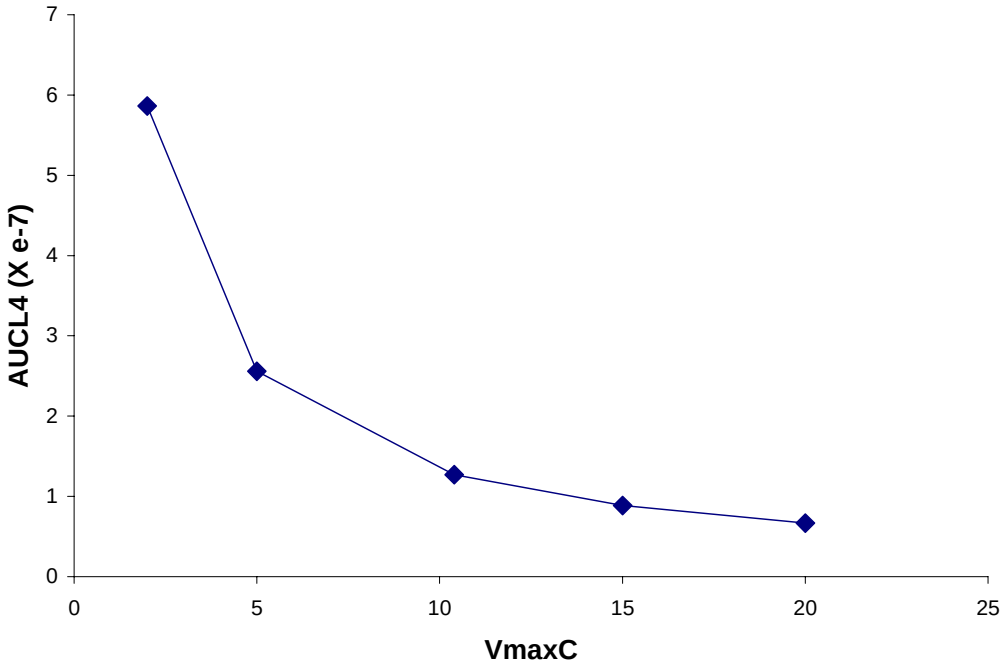


Figure 58. Effect of varying the maximal rate of metabolism (VmaxC) on the liver area under the curve (AUCL) for bromoform.

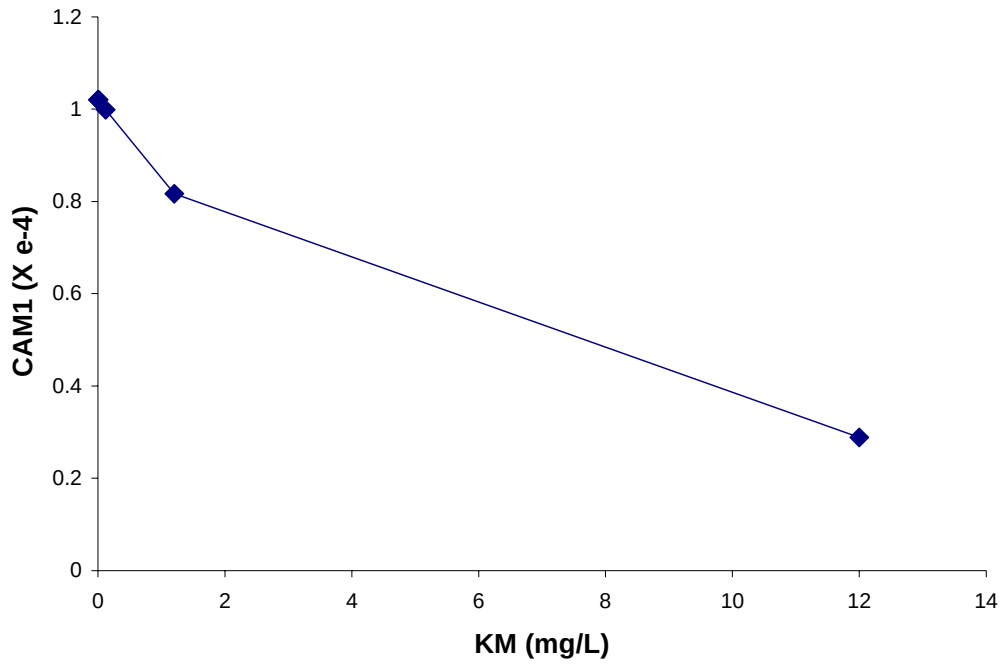


Figure 59. Effect of varying KM (mg/L) on the liver concentration of metabolites (CAM) for chloroform.

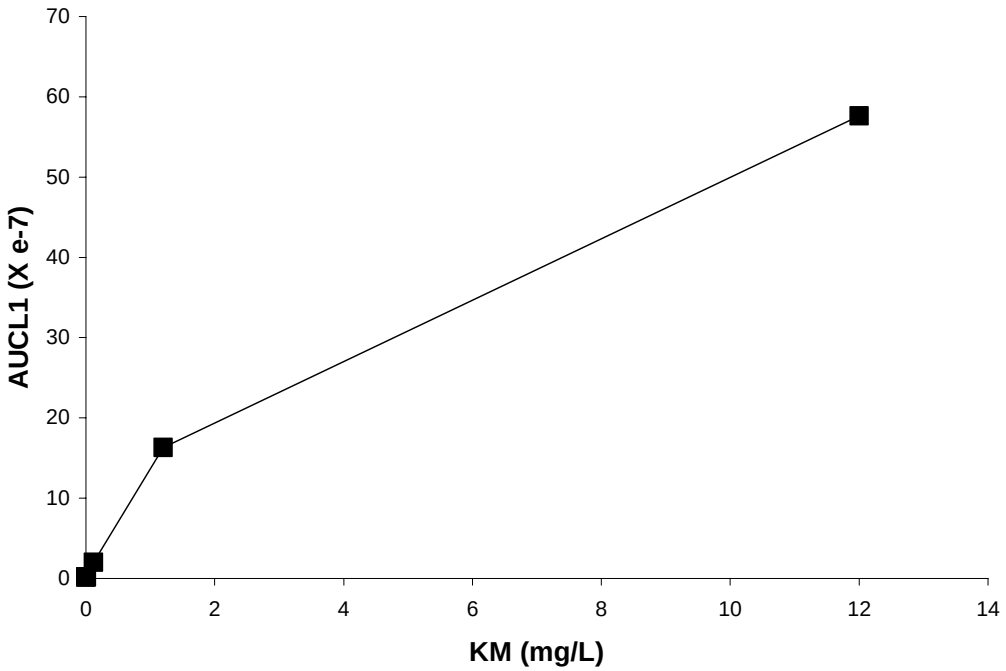


Figure 60. Effect of varying KM (mg/L) on the liver area under the curve (AUCL) for chloroform.

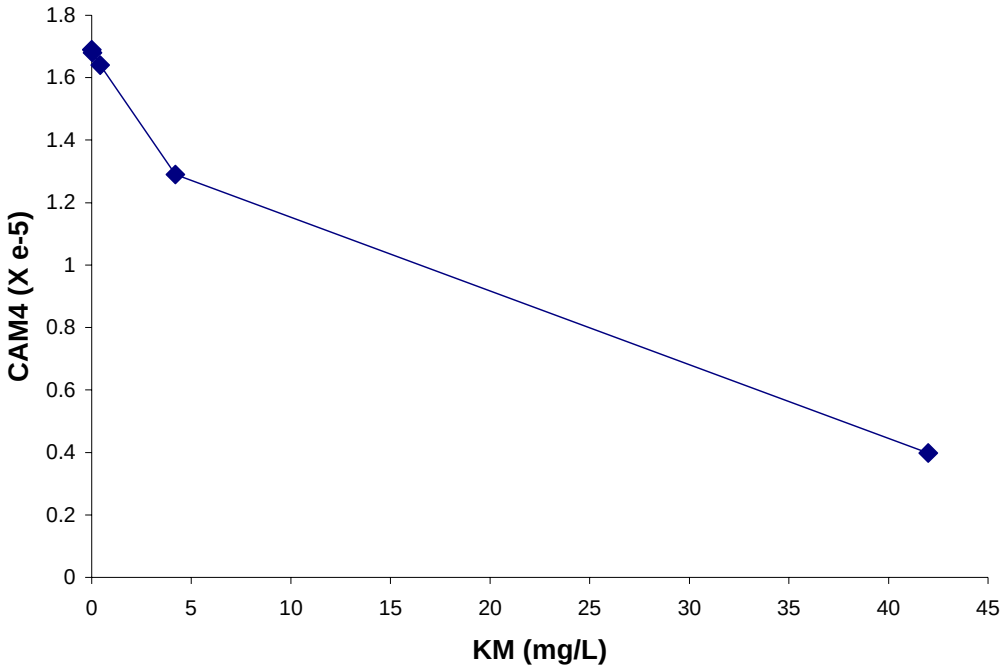


Figure 61. Effect of varying KM (mg/L) on the liver concentration of metabolites (CAM) for bromoform.

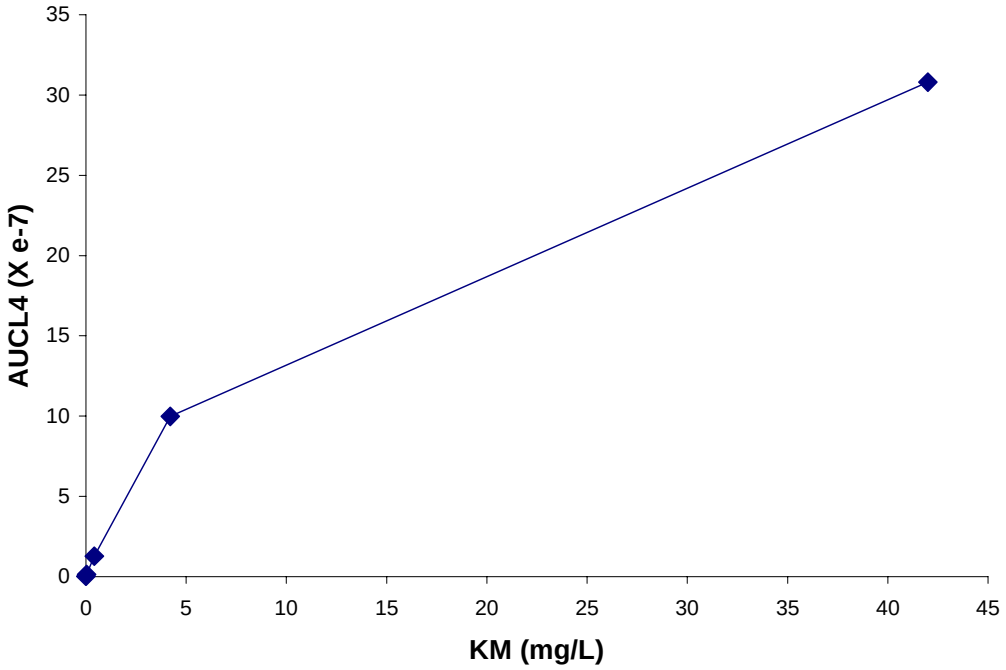


Figure 62. Effect of varying KM (mg/L) on the liver area under the curve (AUCL) for bromoform.

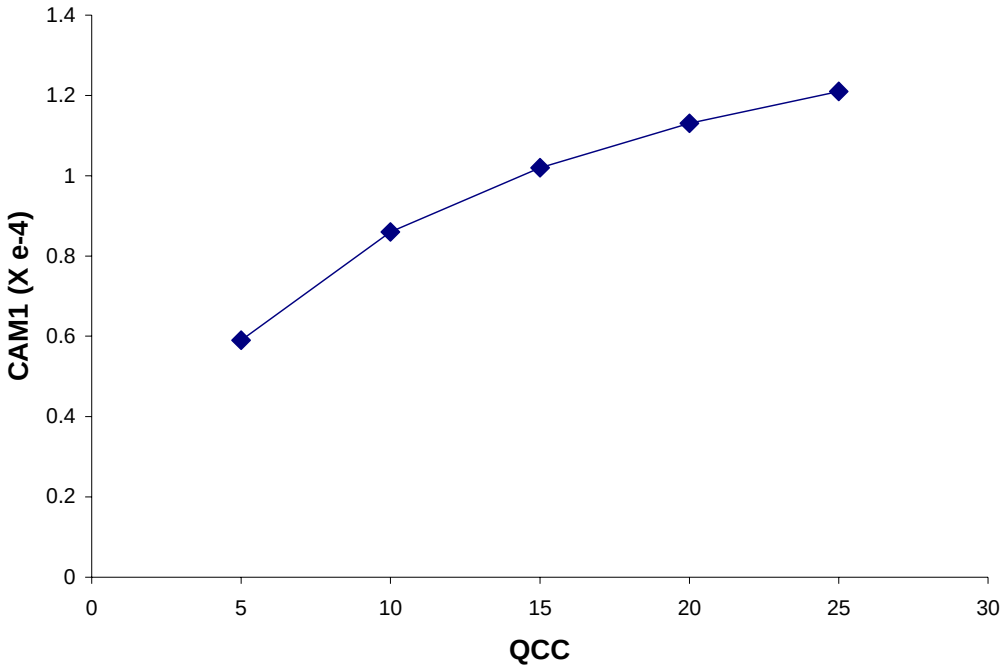


Figure 63. Effect of varying cardiac output (QQC) on the liver concentration of metabolites (CAM) for chloroform.

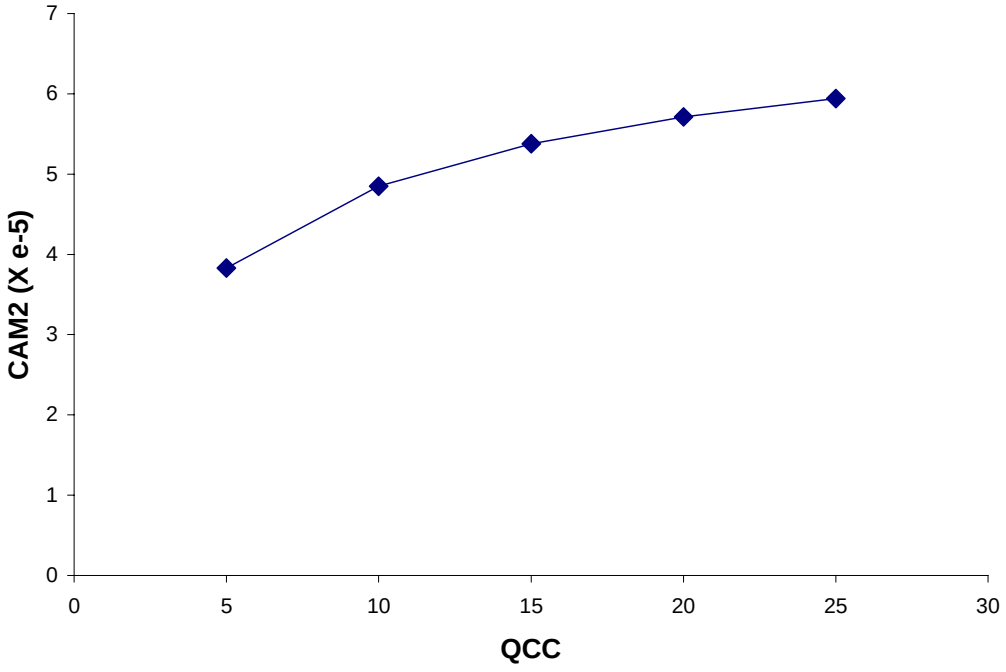


Figure 64. Effect of varying cardiac output (QCC) on the liver concentration of metabolites (CAM) for bromodichloromethane.

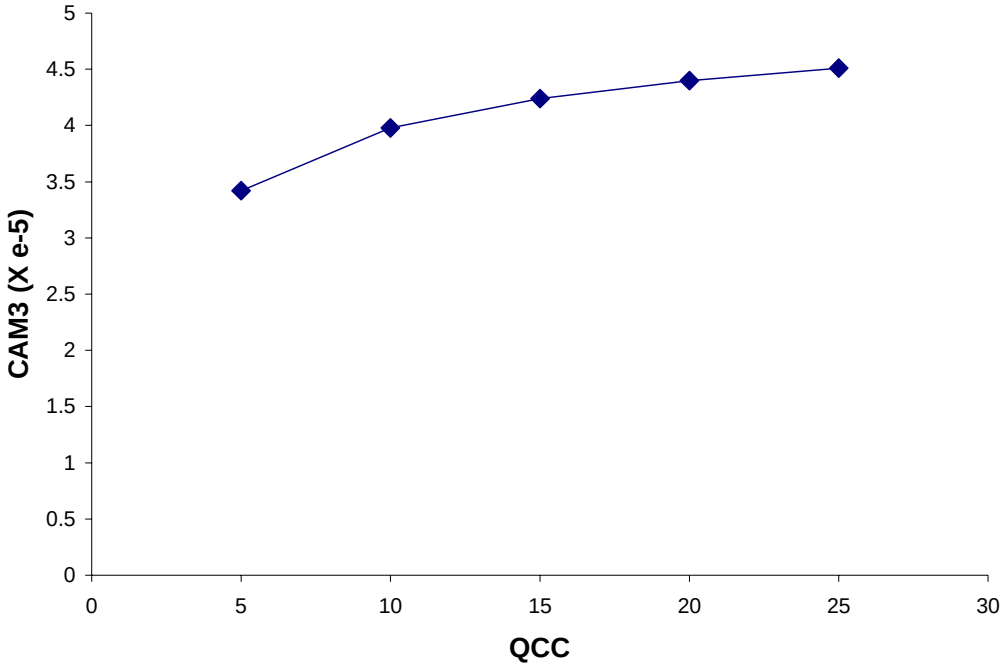


Figure 65. Effect of varying cardiac output (QCC) on the liver concentration of metabolites (CAM) for dibromochloromethane.

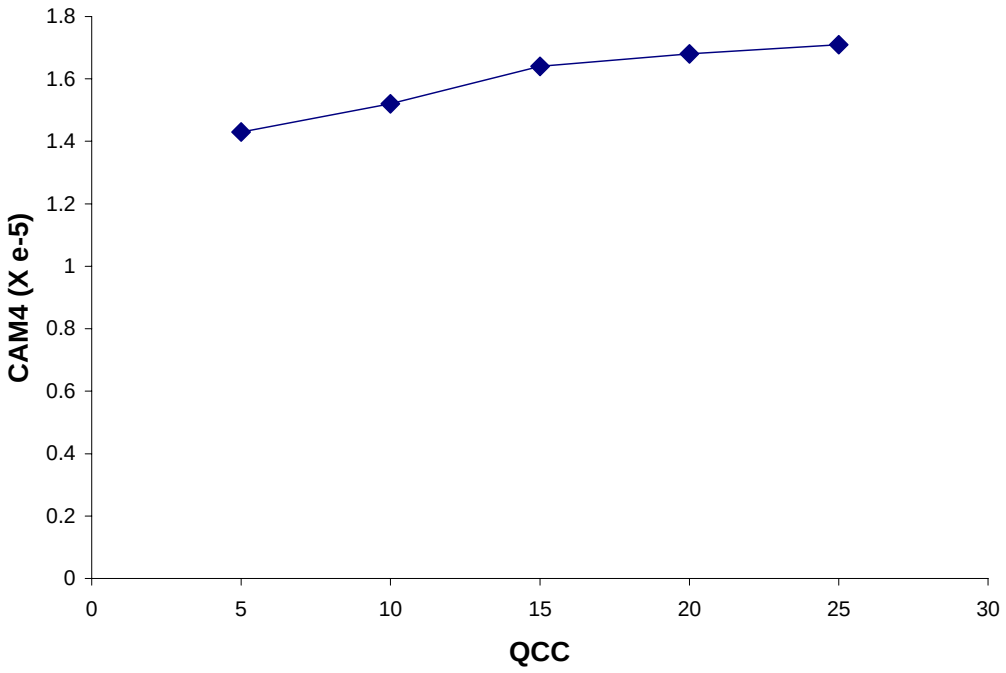


Figure 66. Effect of varying cardiac output (QCC) on the liver concentration of metabolites (CAM) for bromoform.

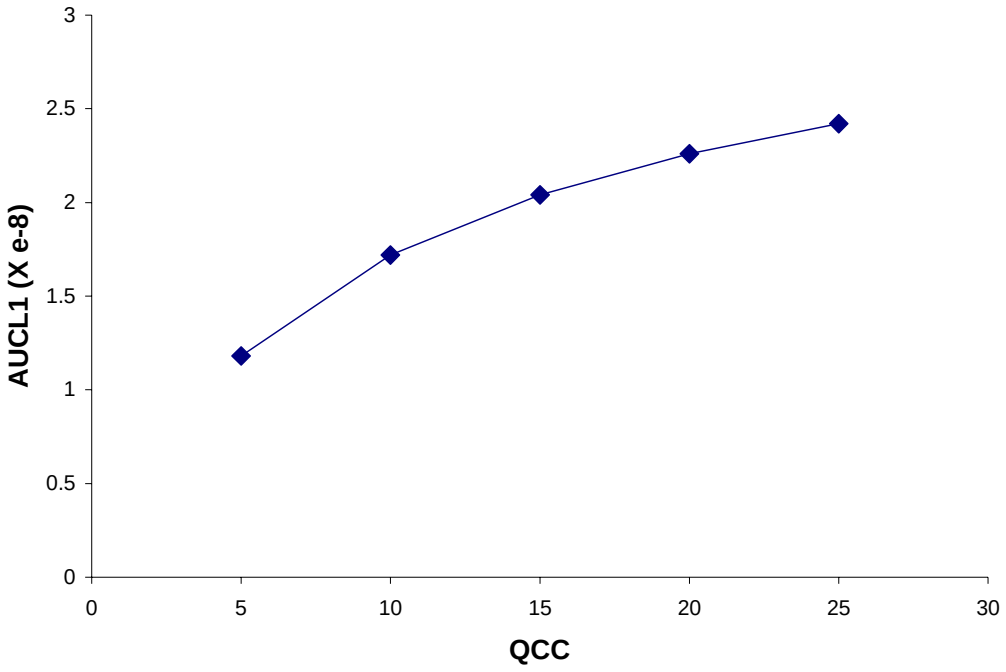


Figure 67. Effect of varying cardiac output (QCC) on the liver area under the curve (AUCL) for chloroform.

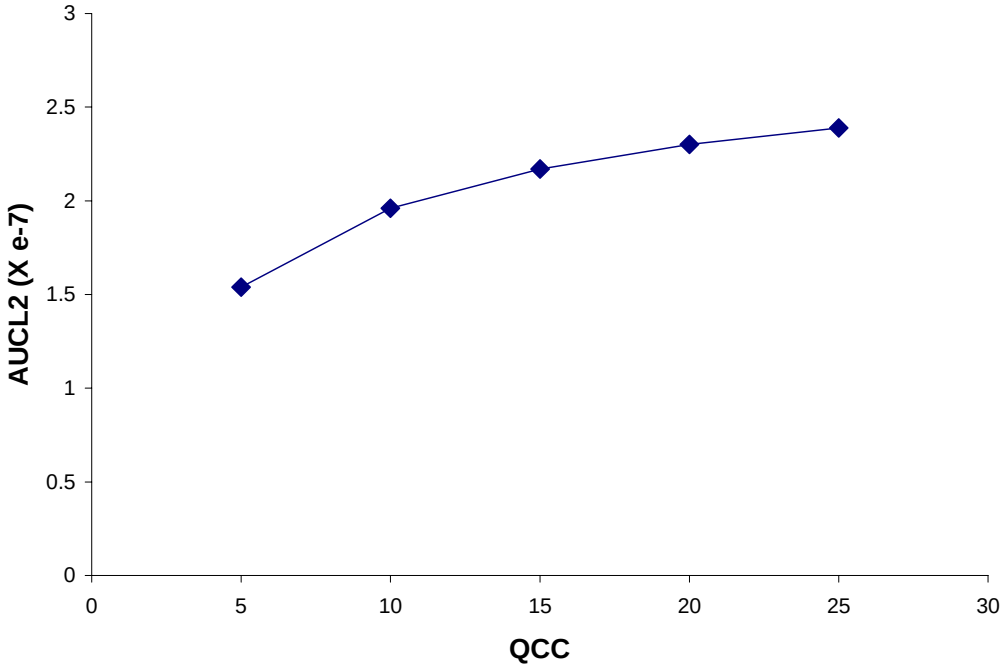


Figure 68. Effect of varying cardiac output (QCC) on the liver area under the curve (AUCL) for bromodichloromethane.

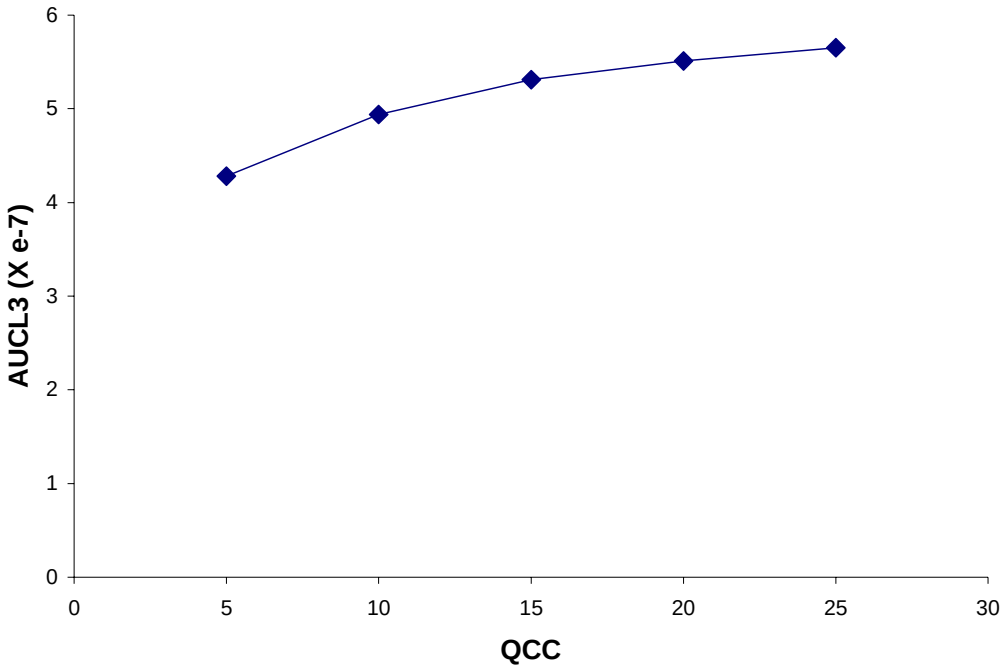


Figure 69. Effect of varying cardiac output (QCC) on the liver area under the curve (AUCL) for dibromochloromethane.

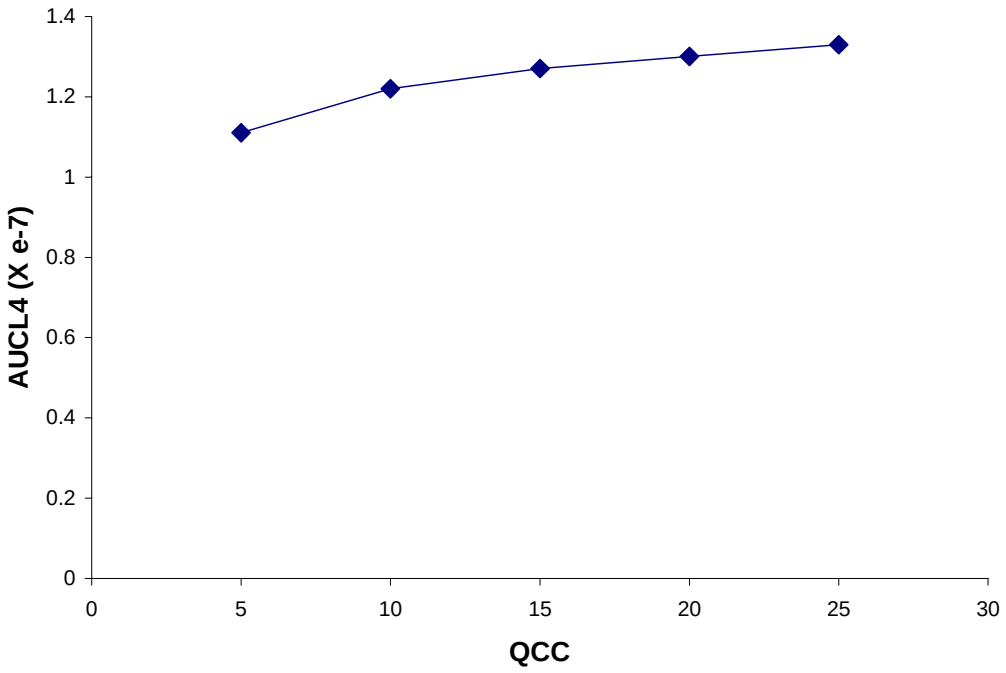


Figure 70. Effect of varying cardiac output (QCC) on the liver area under the curve (AUCL) for bromoform.

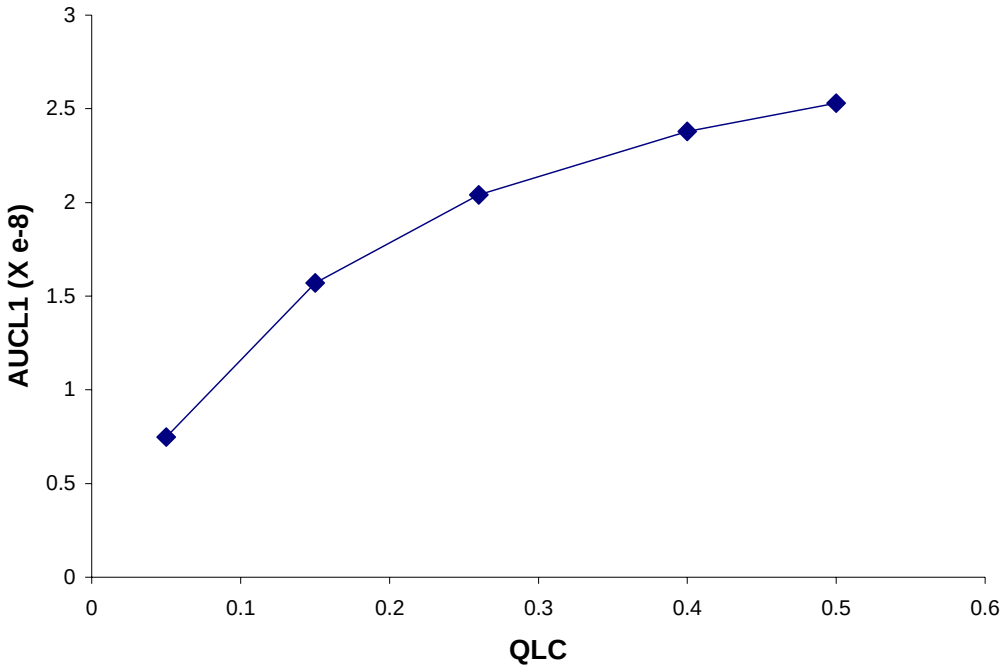


Figure 71. Effect of varying liver blood flow (QLC) on the liver area under the curve (AUCL) for chloroform.

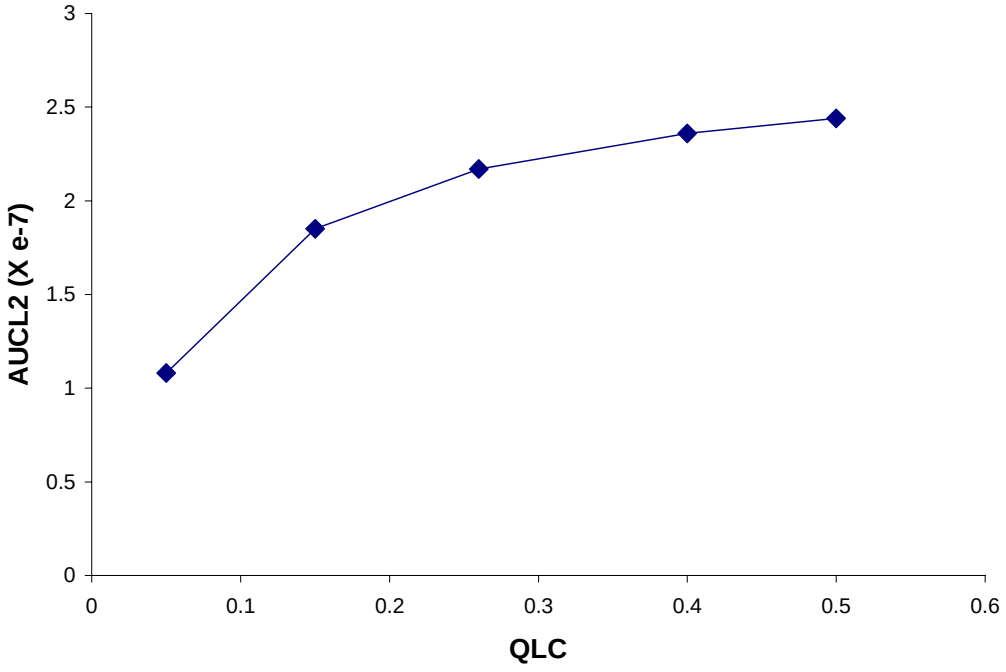


Figure 72. Effect of varying liver blood flow (QLC) on the liver area under the curve (AUCL) for bromodichloromethane.

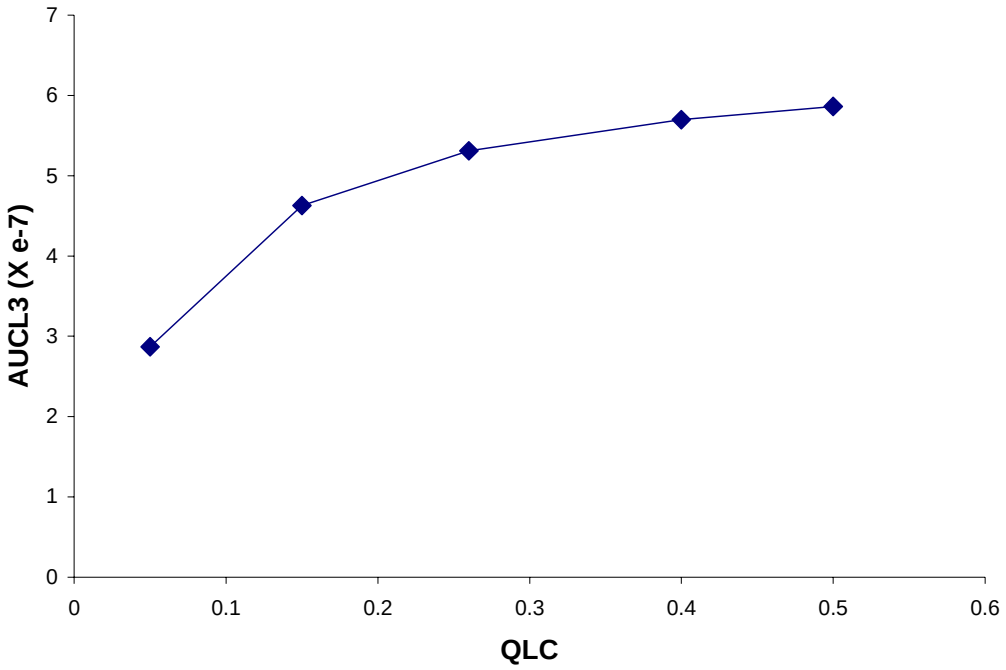


Figure 73. Effect of varying liver blood flow (QLC) on the liver area under the curve (AUCL) for dibromochloromethane.

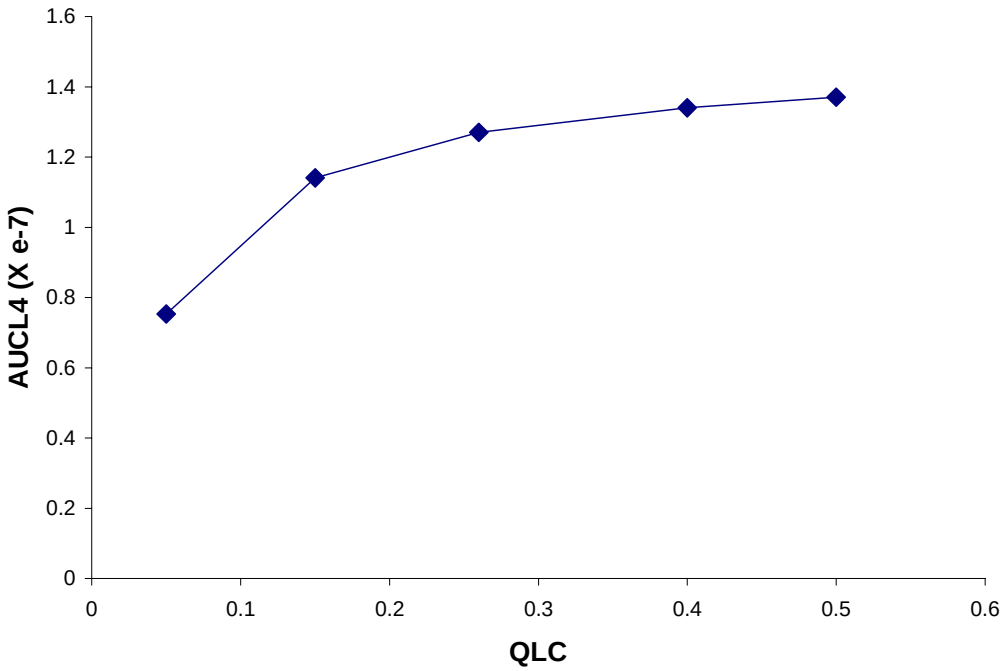


Figure 74. Effect of varying liver blood flow (QLC) on the liver area under the curve (AUCL) for bromoform.

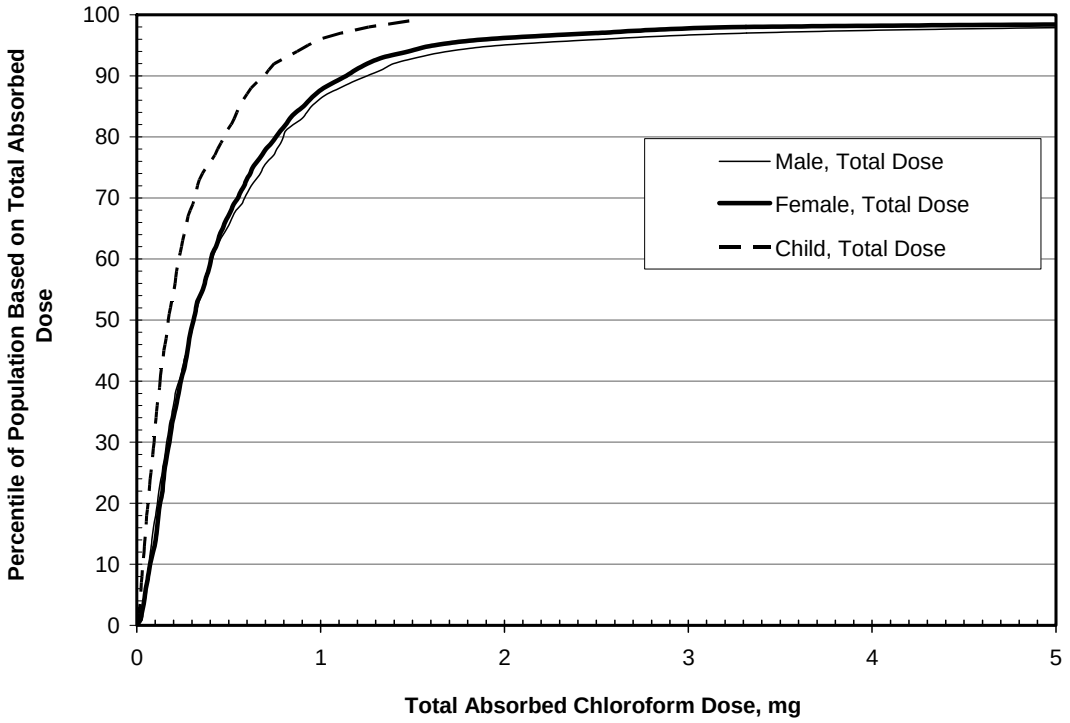


Figure 75A. Cumulative Total Absorbed Chloroform Dose.

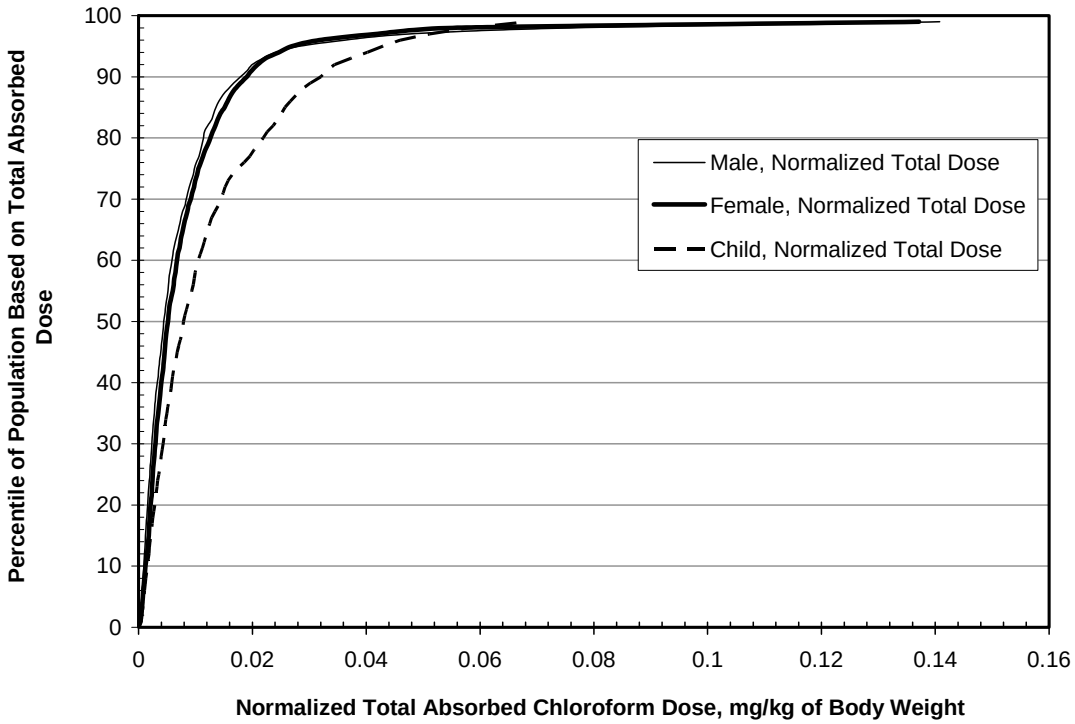


Figure 75B. Normalized Cumulative Total Absorbed Chloroform Dose.

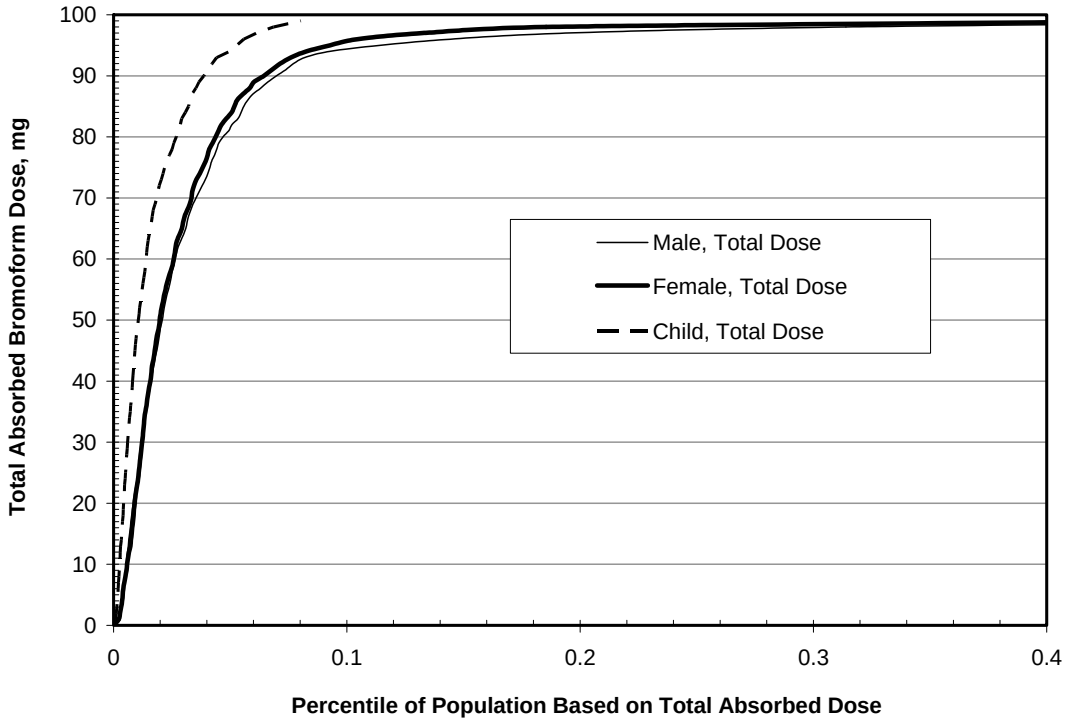


Figure 76A. Cumulative Total Absorbed Bromoform Dose.

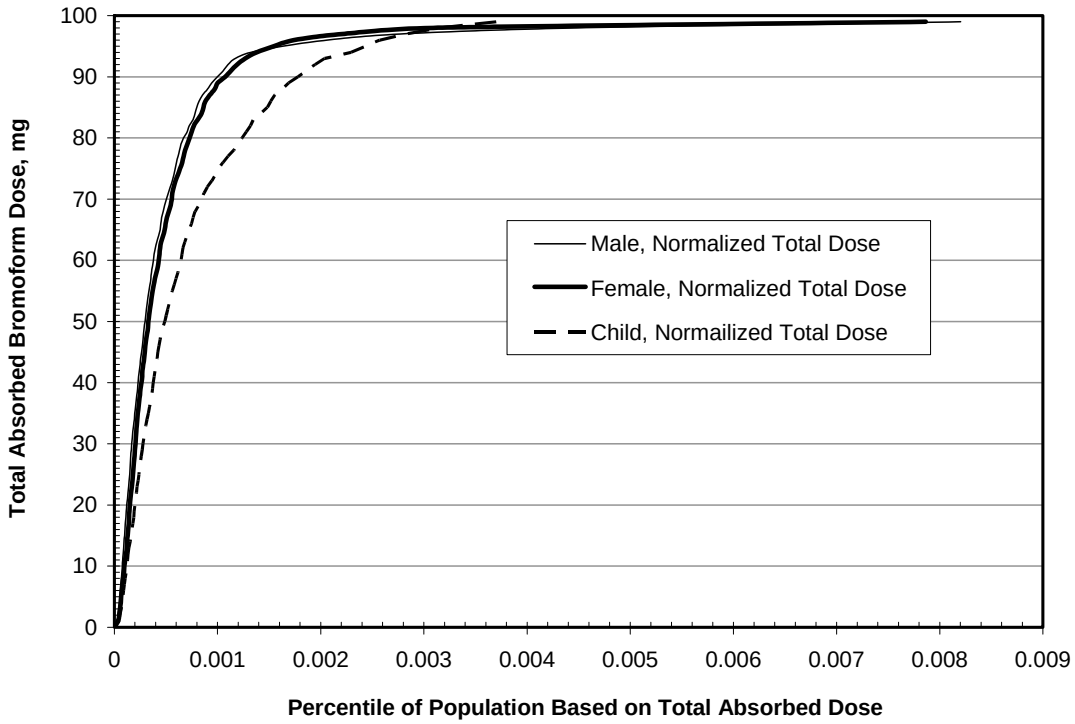


Figure 76B. Normalized Cumulative Total Absorbed Bromoform Dose.

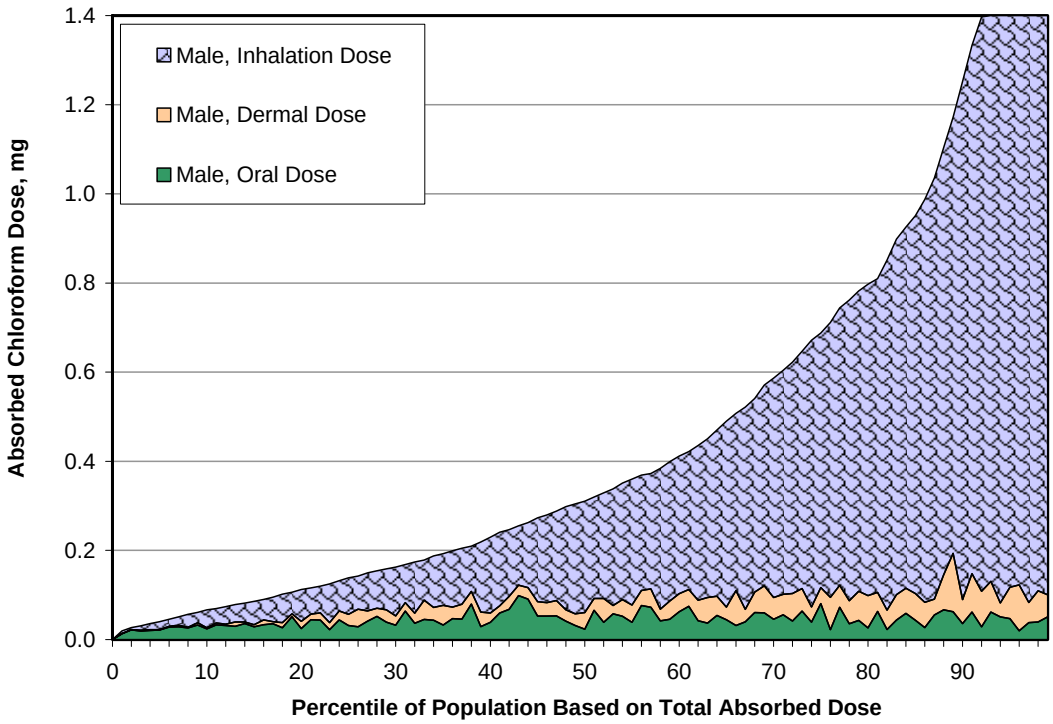


Figure 77A. Route-Specific Contributions to the Total Absorbed Chloroform Dose for the Male Population Group.

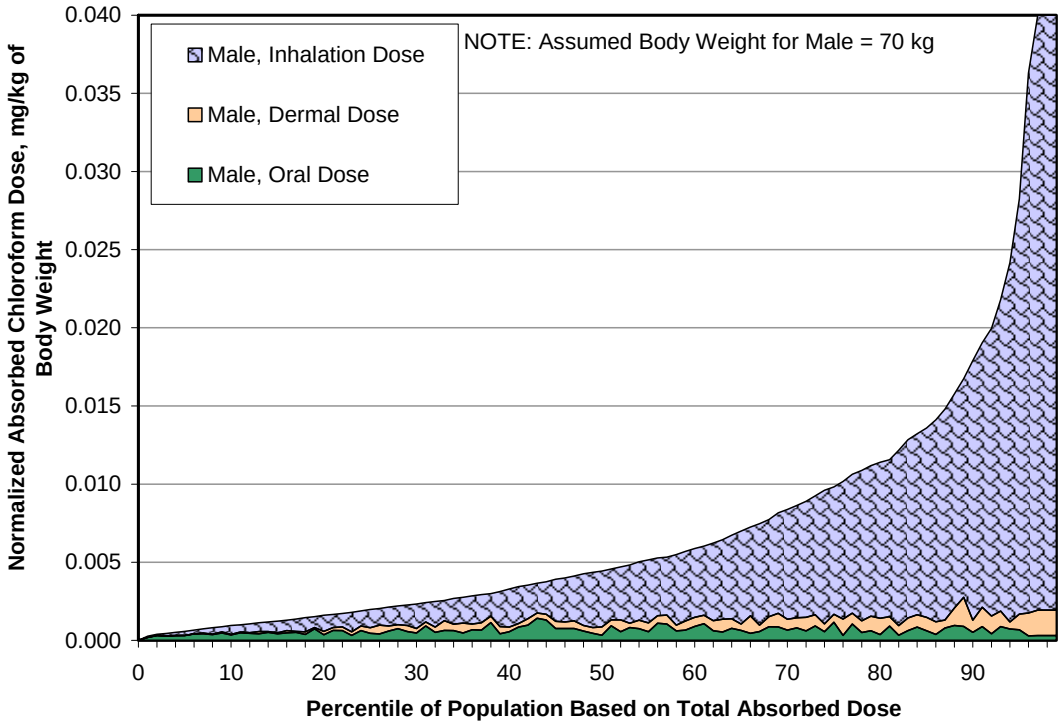


Figure 77B. Route-Specific Contributions to the Normalized Total Absorbed Chloroform Dose for the Male Population Group.

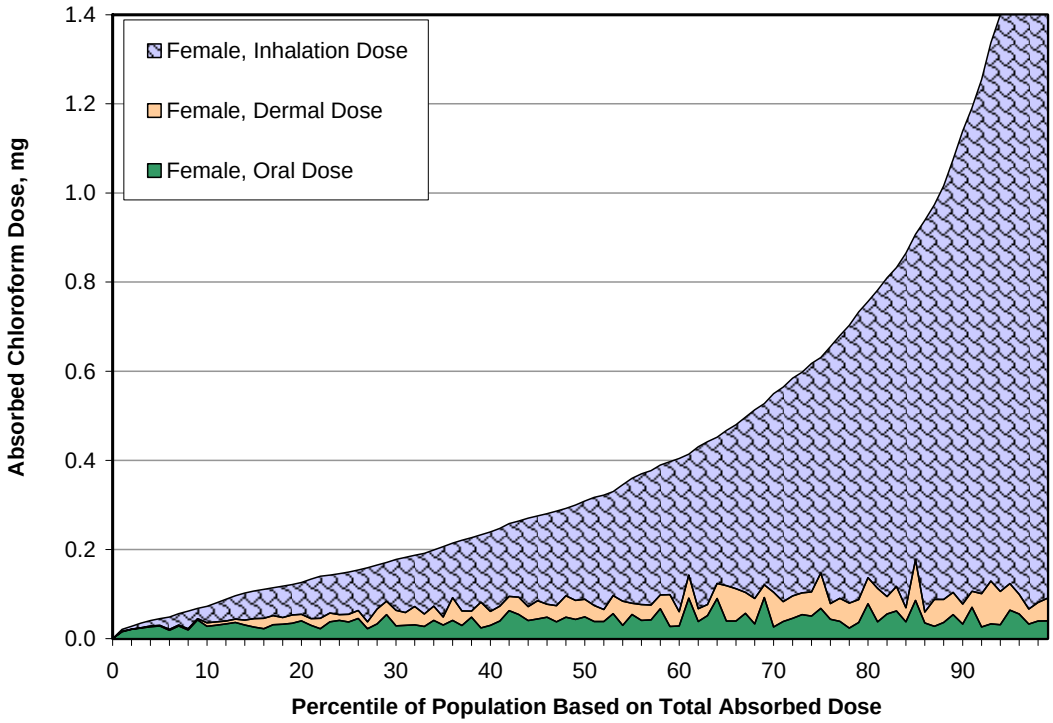


Figure 78A. Route-Specific Contributions to the Total Absorbed Chloroform Dose for the Female Population Group.

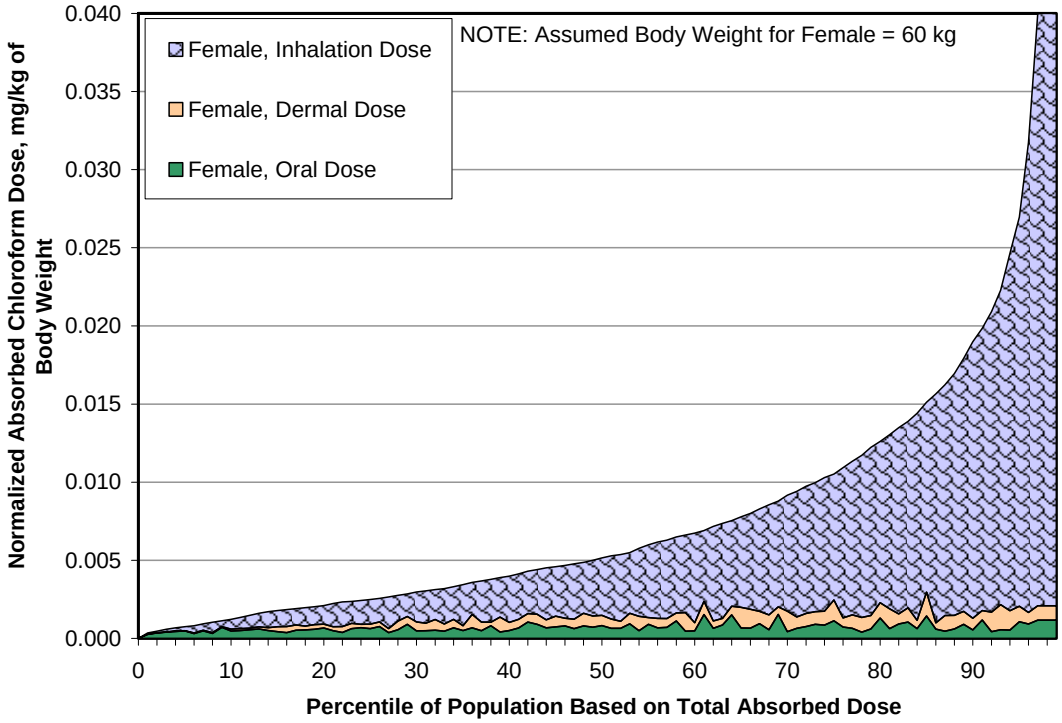


Figure 78B. Route-Specific Contributions to the Total Absorbed Chloroform Dose for the Female Population Group.

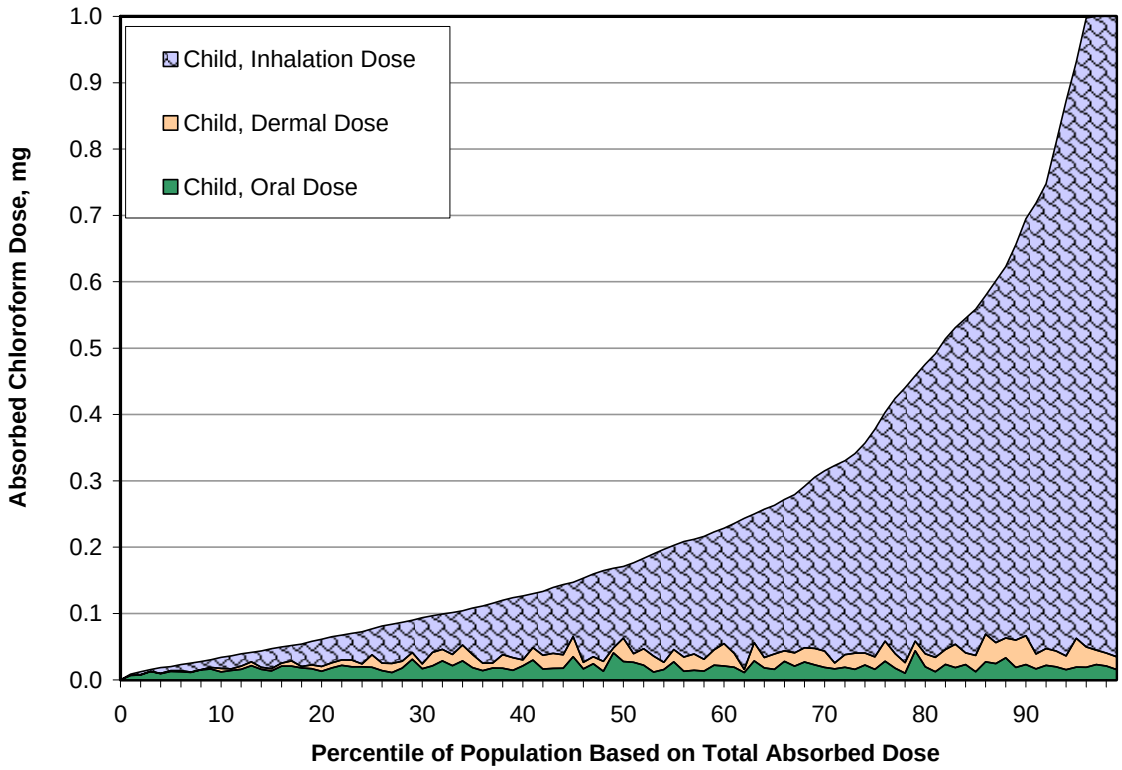


Figure 79A. Route-Specific Contributions to the Total Absorbed Chloroform Dose for the Child Population Group.

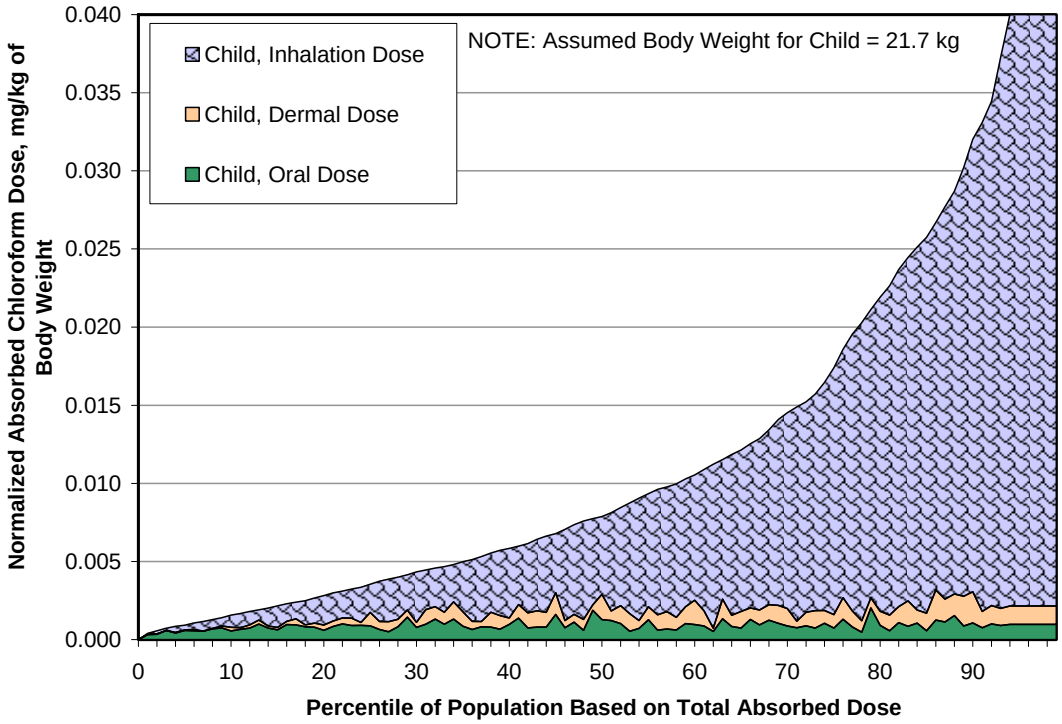


Figure 79B Route-Specific Contributions to the NormalizedTotal Absorbed Chloroform Dose for the Child Population Group.

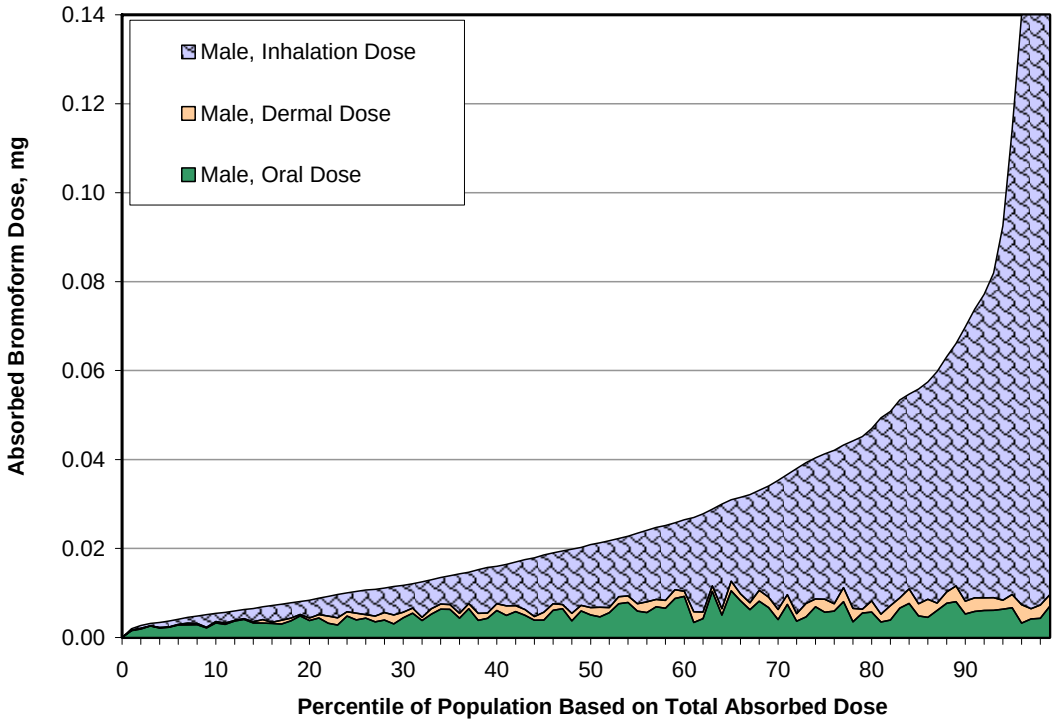


Figure 80A. Route-Specific Contributions to the Total Absorbed Bromoform Dose for the Male Population Group.

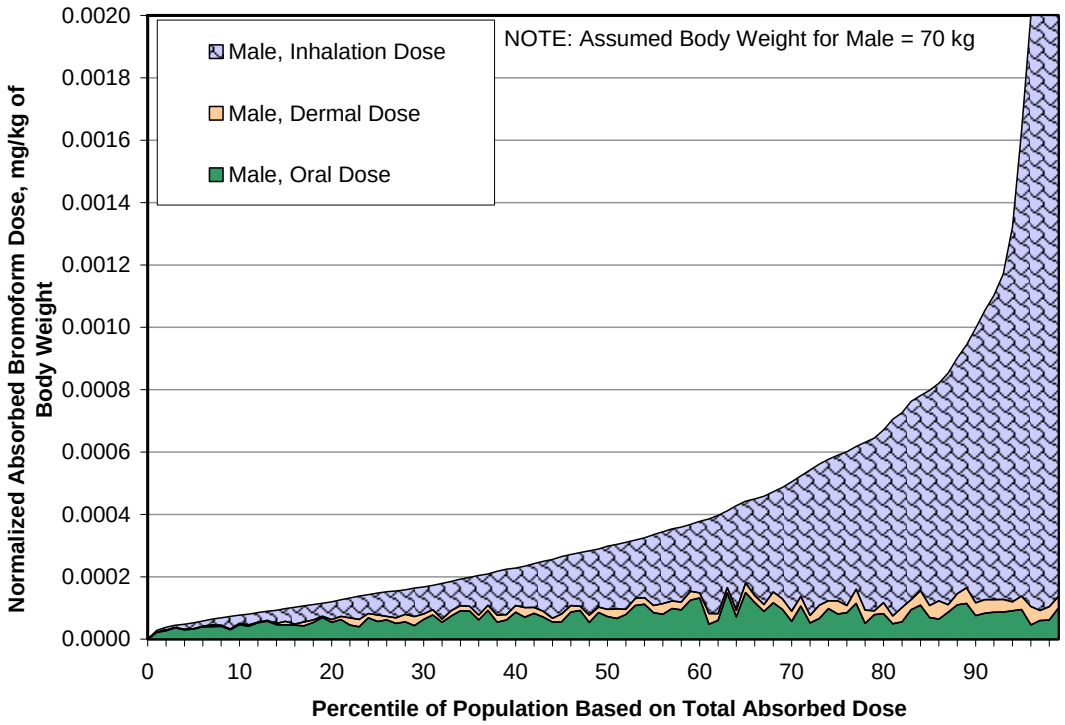


Figure 80B. Route-Specific Contributions to the Normalized Total Absorbed Bromoform Dose for the Male Population Group.

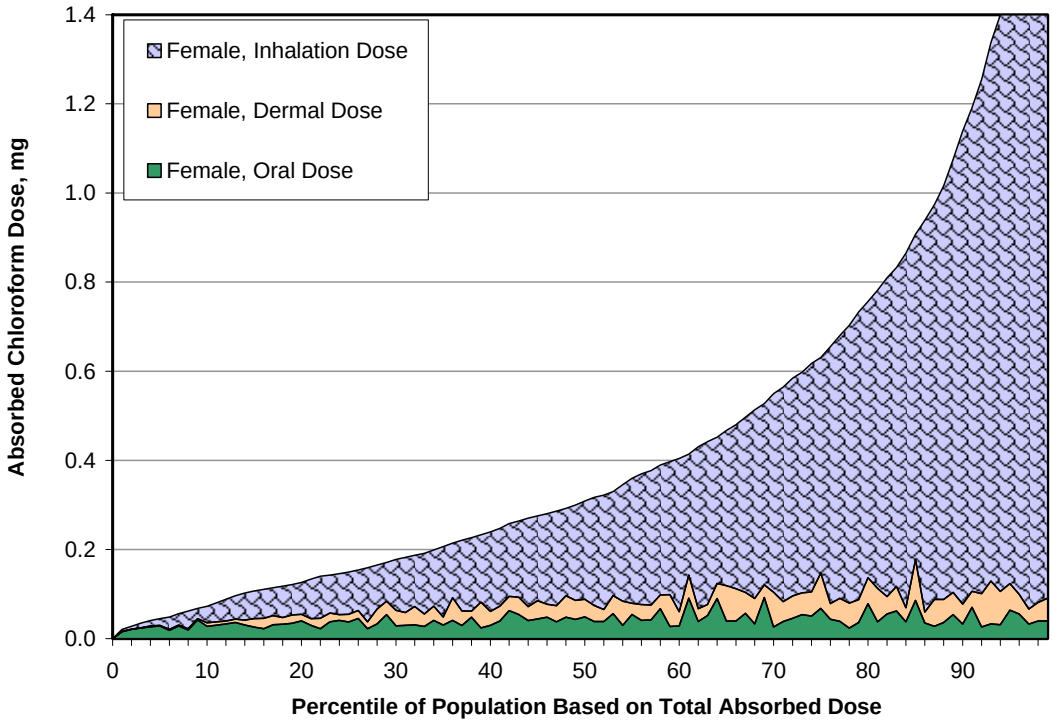


Figure 81A. Route-Specific Contributions to the Total Absorbed Bromoform Dose for the Female Population Group.

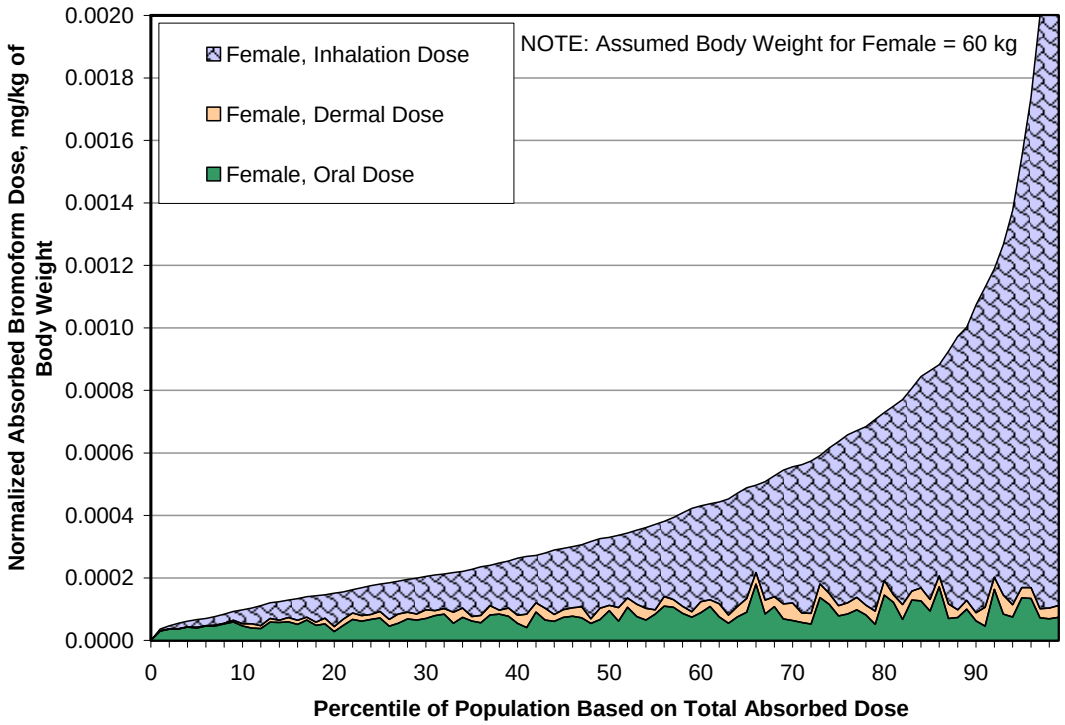


Figure 81B. Route-Specific Contributions to the Normalized Total Absorbed Bromoform Dose for the Female Population Group.

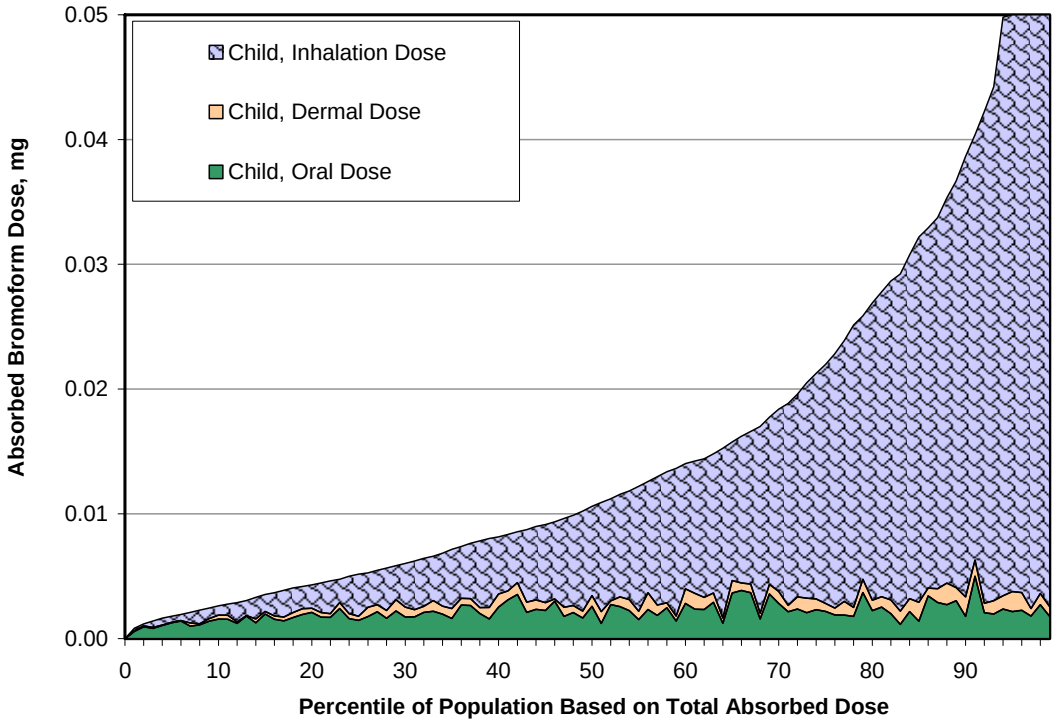


Figure 82A. Route-Specific Contributions to the Total Absorbed Bromoform Dose for the Child Population Group.

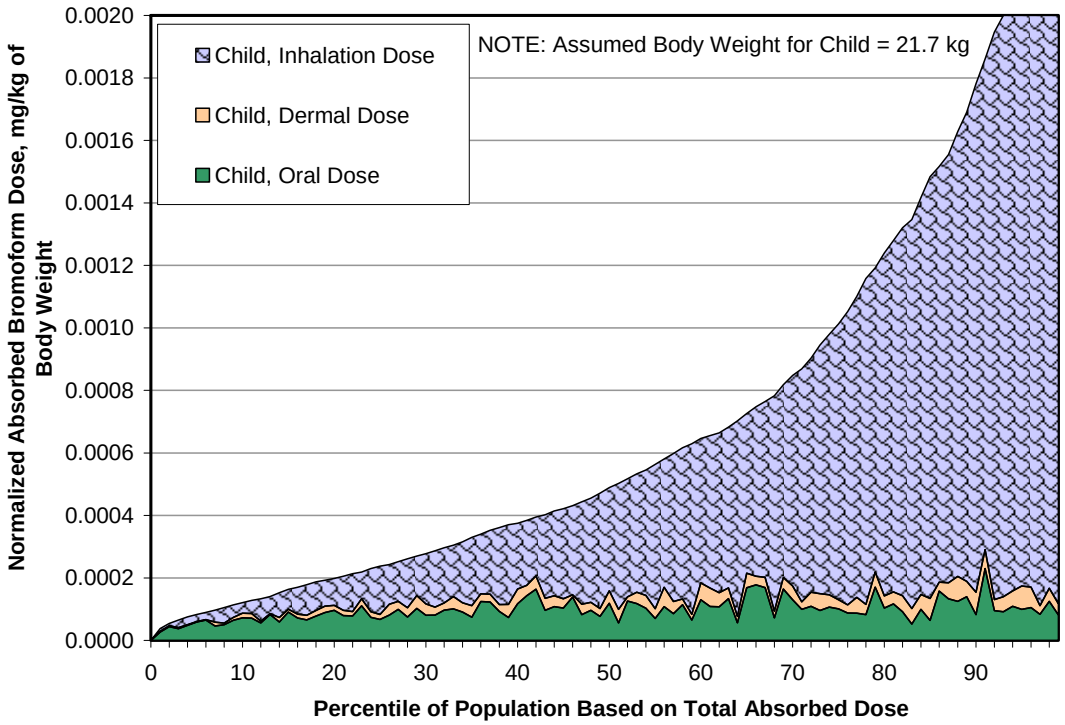


Figure 82B. Route-Specific Contributions to the Normalized Total Absorbed Bromoform Dose for the Child Population Group.

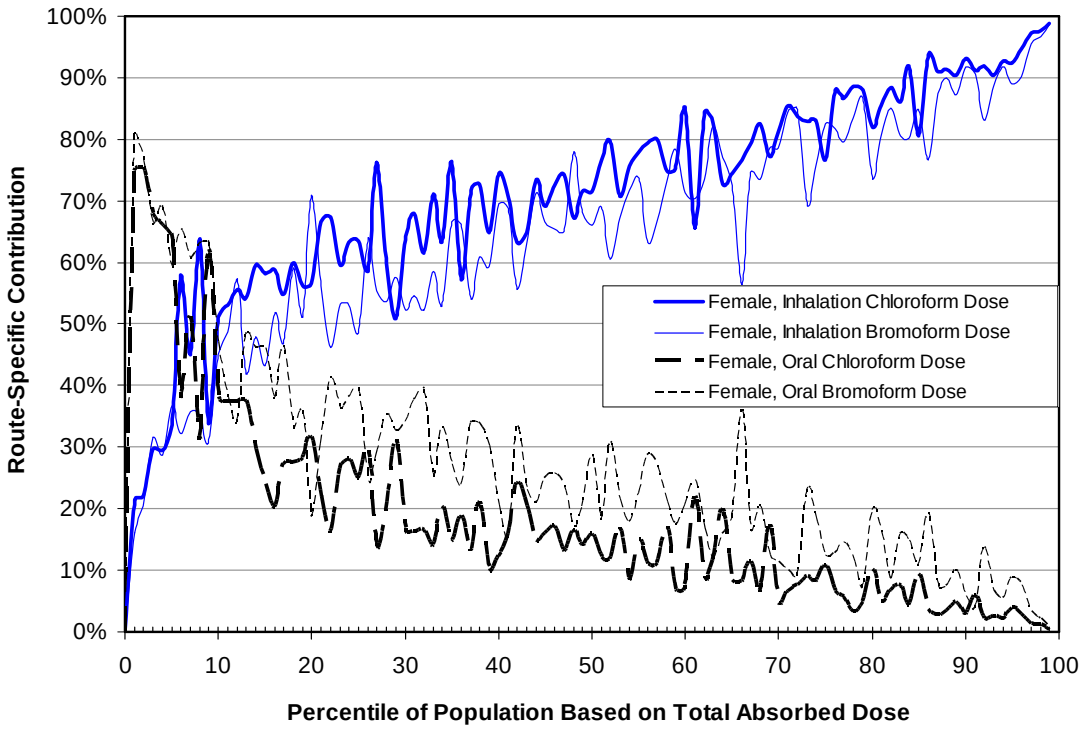


Figure 83. Comparison of Chloroform and Bromoform Route-Specific Contributions for the Female Population Group.

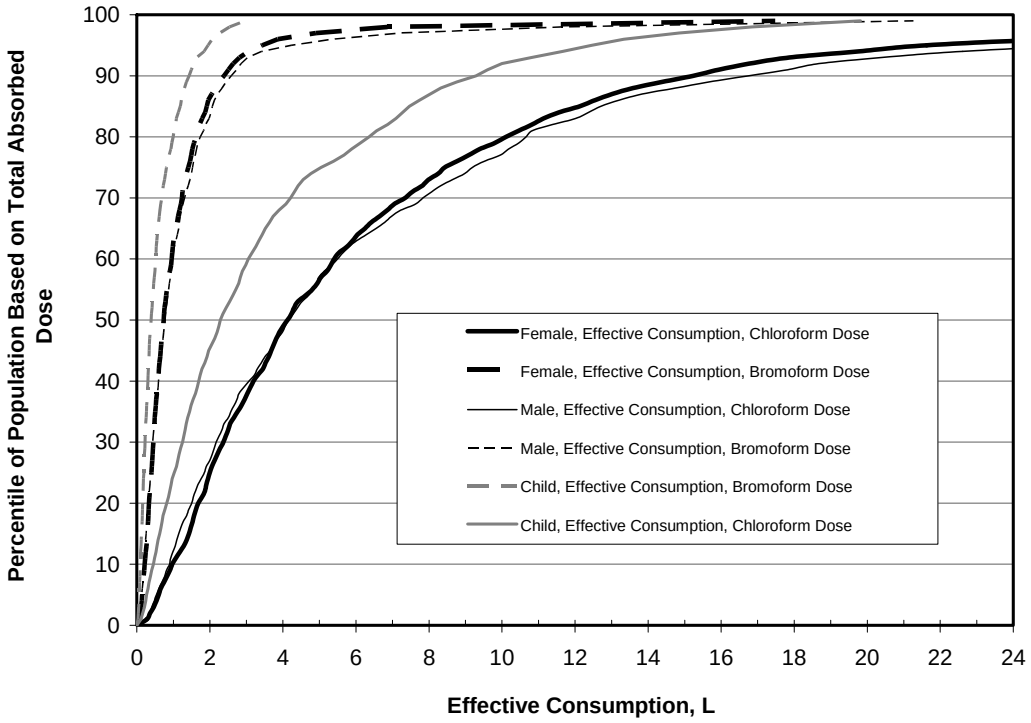


Figure 84. Effective Consumption Volume (Volume of Tap Water Consumed if all of the Absorbed Dose originated from the Ingestion Route).