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AMBIENT WATER QUALITY CRITERIA DERIVATION METHODOLOGY HUMAN HEALTH

TECHNICAL SUPPORT DOCUMENT

FINAL DRAFT

Office of Science and Technology
U.S. Environmental Protection Agency
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AMBIENT WATER QUALITY CRITERIA DERIVATION METHODOLOGY FOR THE PROTECTION OF HUMAN HEALTH - TECHNICAL SUPPORT DOCUMENT

1. INTRODUCTION

1.1 Background

EPA published the availability of ambient water quality criteria (AWQC) documents for 64 toxic pollutants and pollutant categories identified in Section 307(a) of the Clean Water Act (CWA or the Act) in the *Federal Register* on November 28, 1980 (45 FR 79318). The November 1980 *Federal Register* notice also summarized the criteria documents and discussed in detail the methods used to derive the AWQC for those pollutants. The AWQC for those 64 pollutants and pollutant categories were published pursuant to Section 304(a)(1) of the CWA:

> "The Administrator, . . . shall develop and publish, . . . , (and from time to time thereafter revise) criteria for water quality accurately reflecting the latest scientific knowledge (A) on the kind and extent of all identifiable effects on health and welfare including, but not limited to, plankton, fish, shellfish, wildlife, plant life, shorelines, beaches, esthetics, and recreation which may be expected from the presence of pollutants in any body of water, including ground water; (B) on the concentration and dispersal of pollutants, or their byproducts, through biological, physical, and chemical processes; and (C) on the effects of pollutants on the biological community diversity, productivity, and stability, including information on the factors affecting rates of eutrophication and rates of organic and inorganic sedimentation for varying types of receiving waters."

The AWQC published in November 1980 provided two essential types of information: (1) discussions of available scientific data on the effects of the pollutants on public health and welfare, aquatic life, and recreation; and (2) quantitative concentrations or qualitative assessments of the levels of pollutants in water which, if not exceeded, will generally ensure adequate water quality for a specified water use. Water quality criteria developed under Section 304(a) are based solely on data and scientific judgments on the relationship between pollutant concentrations and environmental and human health effects. The 304(a) criteria do not reflect consideration of economic impacts or the technological feasibility of meeting the chemical concentrations in ambient water. As discussed below, 304(a) criteria are used by States and Tribes to establish water quality standards, and ultimately provide a basis for controlling discharges or releases of pollutants.

The 1980 AWQC were derived using guidelines and methodologies developed by the Agency for calculating the impact of waterborne pollutants on aquatic organisms and on human health. Those guidelines and methodologies consisted of systematic procedures for assessing valid and appropriate data concerning a pollutant's acute and chronic adverse effects on aquatic organisms, nonhuman mammals, and humans. The guidelines and methodologies were fully described in Appendix B (for protection of aquatic life and its uses) and Appendix C (for protection of human health) of the November 1980 *Federal Register* notice.

The focus of the current *Federal Register* notice, which this document accompanies, is the draft revisions to the methodology for the development of AWQC to protect human health; a similar

process to revise the methodology for deriving AWQC for the protection of aquatic life is currently underway at the Agency. Once the draft revisions are finalized, the Agency will use the revised AWQC methodology to both develop new AWQC for additional chemicals and to revise existing AWQC. The notice includes summaries of three criteria developed using the draft revised methodology which are also included in this document (Appendix H). The full criteria documents for these three chemicals are available through the National Technical Information Service (NTIS) or on EPA's Internet web site. These AWQC were developed to demonstrate the different risk assessment and exposure approaches presented in the *Federal Register* notice. In addition, EPA intends to derive AWQC for the protection of human health for several chemicals of high priority, including but not limited to, PCBs, lead, mercury, arsenic, and dioxin, within the next several years. EPA anticipates that the focus of 304(a) criteria development will be criteria for bioaccumulative chemicals and chemicals considered highest priority by the Agency. EPA's prioritization process for developing and revising AWQC is discussed in Appendix II of the *Federal Register* notice. It is important to emphasize that the Draft AWQC Methodology Revisions presented here are also intended to provide States and Tribes flexibility in setting water quality standards by providing scientifically valid options for developing their own water quality criteria that consider local conditions. States and Tribes are encouraged to use the methodology once it is finalized to derive their own AWQC. However, the draft methodology in the *Federal Register* also defines the default factors EPA will use in evaluating and determining consistency of State water quality standards with the requirements of the CWA. These default factors will also be used by the Agency to calculate 304(a) criteria values when promulgating water quality standards for a State or Tribe under Section 303(c) of the Act.

1.2 Need for Revision of the 1980 AWQC National Guidelines

l.2.1 Scientific Advances Since 1980

Since 1980, EPA risk assessment practices have evolved significantly, particularly in the areas of cancer and noncancer risk assessments, exposure assessments, and bioaccumulation.

In cancer risk assessment, there have been advances with respect to the use of mode of action information to support both the identification of carcinogens and the selection of procedures to characterize risk at low, environmentally relevant exposure levels. Related to this is the development of new procedures for quantifying cancer risk at low doses to replace the current default linear multistage model (LMS).

In noncancer risk assessment, the Agency is moving toward the use of statistical models, such as the benchmark dose approach and categorical regression, to derive reference doses (RfDs) in place of the traditional NOAEL- (no observed adverse effect level) based method.

In exposure analysis, several new studies have addressed water consumption and fish-tissue consumption. These exposure studies provide a more current and comprehensive description of national, regional, and special-population consumption patterns; these are reflected in the Draft AWQC Methodology Revisions presented in the *Federal Register* notice accompanying this technical

support document. In addition, more formalized procedures are now available to account for human exposure from multiple sources when setting health goals that address only one exposure source.

With respect to bioaccumulation, the Agency has moved toward the use of a bioaccumulation factor (BAF) to reflect the uptake of a contaminant by fish from all sources rather than just from the water column as reflected by the use of a bioconcentration factor (BCF) in the 1980 methodology. The Agency has also developed detailed procedures and guidelines for estimating BAF values.

1.2.2 EPA Risk Assessment Guidelines Development Since 1980

When the 1980 AWQC National Guidelines were developed, EPA had not yet developed formal cancer or noncancer risk assessment guidelines. Since then EPA has published several risk assessment guidelines documents. In 1996, the Agency published Proposed Guidelines for Carcinogen Risk Assessment (61 FR 17960), which, when finalized, will supersede the carcinogenic risk assessment guidelines published in 1986 (51 FR 33992). In addition, guidelines for mutagenicity assessment were also published in 1986 (51 FR 34006). With respect to noncancer risk assessment, the Agency published guidelines in 1988 for assessing male and female reproductive risk (53 FR 24834) and in 1991 for assessing developmental toxicity (56 FR 63798). In 1991, the Agency also developed an external review draft of revised risk assessment guidelines for noncancer health effects.

In addition to these risk assessment guidelines, EPA also published the Exposure Factors Handbook in 1990, which presents commonly used Agency exposure assumptions and the surveys from which they are derived. In 1992 EPA published the Guidelines for Exposure Assessment (57 FR 22888), which describes general concepts of exposure assessment, including definitions and associated units, and provides guidance on planning and conducting an exposure assessment. Also, in the 1980's the Agency published the Total Exposure Assessment Methodology (TEAM), which presents a process for conducting comprehensive evaluation of human exposures. Finally, the Agency has recently developed the Relative Source Contribution Policy, which is currently undergoing Agency review, for assessing total human exposure to a contaminant and allocating the RfD among the media of concern.

Additionally, since 1980 work groups have been established at EPA, specifically, CRAVE and the RfD/RfC Work Group, to support the consistent evaluation of the carcinogenic and non-carcinogenic effects of chemicals.

1.2.3 Differing Risk Assessment and Risk Management Approaches for AWQC and MCLGs

There are some differences that have arisen in the risk assessment and risk management approaches used by EPA's Office of Water for the derivation of AWQC under the authority of the Clean Water Act and MCLGs (Maximum Contaminant Level Goals) under the Safe Drinking Water Act. Two notable differences are with respect to the treatment of chemicals designated as Group C carcinogens and the consideration of non-water sources of exposure when setting an AWQC or MCLG for a noncarcinogen.

1.2.3.1 Group C Chemicals

Chemicals are typically classified as Group C—i.e., possible human carcinogens—under the existing EPA cancer classification scheme for any of the following reasons:

- Carcinogenicity has been documented in only one test species and/or only one cancer bioassay, and the results do not meet the requirements of "sufficient evidence."
- Tumor response is of marginal significance due to inadequate design or reporting.
- Benign, but not malignant, tumors occur with an agent showing no response in a variety of short-term tests for mutagenicity.
- There are responses of marginal statistical significance in a tissue known to have a high or variable background rate.

The 1986 Guidelines for Carcinogenic Risk Assessment specifically recognized the need for flexibility with respect to quantifying the risk of Group C carcinogens. The guidelines noted that agents judged to be in Group C may generally be regarded as suitable for quantitative risk assessment, but that case-by-case judgments may be made in this regard.

The EPA Office of Water has historically treated Group C chemicals differently under the CWA and the SDWA. It is important to note that the 1980 AWQC National Guidelines for setting AWQC under the CWA predated EPA's carcinogen classification system, which was proposed in 1984 (49 FR 46294) and finalized in 1986 (51 FR 33992). The 1980 AWQC National Guidelines did not explicitly differentiate among carcinogens with respect to the weight-of-evidence for characterizing them. For all pollutants judged as having adequate data for quantifying carcinogenic risk— including those now classified as Group C—AWQC were derived based on carcinogenic risk data. In the November 1980 *Federal Register* notice, EPA emphasized that the AWQC for carcinogens should state that the recommended concentration for maximum protection of human health is zero. At the same time, the criteria published for specific carcinogens presented water concentrations for these pollutants corresponding to individual lifetime cancer risk levels in the range of 10^{-7} to 10^{-5}.

In the development of national primary drinking-water regulations under the SDWA, EPA is required to promulgate a health-based MCLG for each contaminant. The Agency policy has been to set the MCLG at zero for chemicals with strong evidence of carcinogenicity associated with exposure from water. For chemicals with limited evidence of carcinogenicity, including many Group C carcinogens, the MCLG is usually obtained using the RfD for that chemical based on its noncancer effects with the application of an additional uncertainty factor (UF) of 1 to 10 to account for its possible carcinogenicity. If valid noncancer data for a Group C carcinogen are not available to establish an RfD but adequate data are available to quantify the cancer risk, then the MCLG is based upon a nominal lifetime excess cancer risk calculation in the range of 10^{-5} to 10^{-6} (ranging from one case in a population of 100,000 to one case in a population of one million). Even in those cases

where the RfD approach has been used for the derivation of the MCLG for a Group C carcinogen, the drinking water concentrations associated with excess cancer risks in the range of 10^{-5} to 10^{-6} are also provided for comparison.

It should also be noted that EPA's pesticides program has applied both of the previously described methods for addressing Group C chemicals in actions taken under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and finds both methods applicable on a case-by-case basis. Unlike the drinking water program, however, the pesticides program does not add an extra UF to account for potential carcinogenicity when using the RfD approach.

1.2.3.2 Consideration of Non-Water Sources of Exposure

The 1980 AWQC National Guidelines for setting AWQC recommended the use of the following equation to derive the criterion:

$$C = [ADI - (DT + IN)] \div [2 + 0.0065R]$$

(Equation 1.2.1)

where C is the criterion value; ADI is the acceptable daily intake (mg/kg-day); DT is the non-fish dietary intake (mg/kg-day); IN is the inhalation intake (mg/kg-day); 2 is the assumed daily water intake (L/day); 0.0065 is the assumed daily fish consumption (kg); and R is the bioconcentration factor (L/kg). As implied by this equation, the contributions from non-water sources, namely air and non-fish dietary intake, were to be subtracted from the ADI, thus reducing the amount of the ADI "available" for water-related sources of intake. In practice, however, when calculating human health criteria, these other exposures were generally not considered because reliable data on these exposure pathways were not available. Consequently, the AWQC were usually derived such that drinking water and fish ingestion accounted for the entire ADI (now called RfD).

In the drinking water program, a similar "subtraction" method was typically used in the derivation of MCLGs proposed and promulgated in drinking water regulations through the mid-1980s. More recently, the drinking water program has consistently used a "percentage" method in the derivation of MCLGs for noncarcinogens. In this approach, the percentage of total exposure typically accounted for by drinking water, referred to as the relative source contribution (RSC), is applied to the RfD to determine the maximum amount of the RfD "allocated" to drinking water. In using this percentage procedure, the drinking water program also applies a ceiling level of 80 percent of the RfD and a floor level of 20 percent of the RfD. That is, the MCLG cannot account for more than 80 percent of the RfD, nor less than 20 percent of the RfD.

The drinking water program usually takes a conservative approach of applying an RSC factor of 20 percent to the RfD when adequate exposure data do not exist, assuming that the major portion (80 percent) of the total exposure comes from other sources, such as diet.

1.2.3.3 Cancer Risk Ranges

In addition to the different risk assessment approaches discussed above for deriving AWQC and MCLGs for Group C carcinogens, different risk management approaches have arisen between the drinking water and ambient surface water programs for using upper bound lifetime excess risk values when setting health-based criteria for carcinogens.[1] As indicated previously, the surface water program derives AWQC for carcinogens that generally correspond to lifetime excess cancer risk levels of 10^{-7} to 10^{-5}. The drinking water program has set MCLGs for Group C carcinogens based on a slightly less stringent risk range of 10^{-6} to 10^{-5}, while MCLGs for chemicals with strong evidence of carcinogenicity are set at zero.

It is also important to note that under the drinking water program, for those substances having an MCLG of zero, enforceable Maximum Contaminant Levels (MCLs) have generally been promulgated to correspond with cancer risk levels ranging from 10^{-6} to 10^{-4}. Unlike AWQC and MCLGs, which are strictly health-based criteria, MCLs are developed with consideration given to the costs and technological feasibility of reducing contaminant levels in water to meet those standards.

1.3 Purpose of this Document

This document is meant to add technical detail to the principles and recommendations presented in the *Federal Register* notice for the Proposed Revisions to the Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health. This document includes detailed examples of many of the ideas presented in the *Federal Register* in an effort to explain the thought process behind many of the new risk assessment directions being taken by the Agency. For instance, there is an example of how to apply the new cancer guidelines to a chemical which causes cancer but may not be genotoxic or mutagenic. In addition, three sample criteria have been derived applying the new cancer guidelines; these are included in Appendix H and should be read together with this document and the *Federal Register* notice. On the noncancer side, an example is included on how to use the benchmark dose approach. To supplement the discussion in the *Federal Register* on exposure, many datasets on fish consumption rates (both nationally and regionally) have been incorporated into this document. In addition, a detailed discussion on deriving relative source contributions is presented. To support the understanding of bioaccumulation, the data used to calculate the percent lipid by fish species has been added.

As noted above, three sample criteria (actual 307(a) list toxic chemicals) have been updated using the revised methodology to (1) illustrate the changes that can be expected (numerically) when applying the revised methodology; and (2) to demonstrate the logic behind the revised methodology and the judgments required to fulfill the recommendations of the guidance. As noted on the criteria documents themselves, the Agency is proposing to develop streamlined criteria with a focus on critical toxicological and exposure studies only. Due to limited resources and a need to update criteria as quickly as possible, EPA has decided to develop more abbreviated versions of criteria documents with an emphasis on existing risk assessments (IRIS or other EPA health assessment documents) where available and still relevant, focusing to a greater degree on pertinent exposure and

[1] Throughout this document, the term "risk level" regarding a cancer assessment endpoint specifically refers to an upper bound estimate of excess lifetime cancer risk.

toxicological studies which may influence the development of a criterion. EPA will continue to conduct comprehensive reviews of the literature for the latest studies but will not provide a summary or evaluation of those studies which are deemed less significant in the criterion development process.

1.4 Criteria Equations

The following equations for deriving AWQC include toxicological and exposure assessment parameters which are derived from scientific analysis, science policy, and risk management decisions. For example, parameters such as a field-measured BAF or a point of departure from an animal study (in the form of a LOAEL/NOAEL/LED_{10}) are scientific values which are empirically measured, whereas the decision to use animal effects as a surrogate for human effects involves judgment on the part of the EPA (and other agencies) as to the best practice to follow when human data are lacking. Such a decision is, therefore, a matter of science policy. On the other hand, the choice of default fish consumption rates for protection of a certain percentage (in this case, 90 percent and 95 percent respectively) of the general population, is clearly a risk management decision. In many cases, the Agency has selected parameters using its best judgment of the overall protection afforded by the resulting AWQC when all parameters are combined. For a longer discussion of the differences between science, science policy, and risk management, please refer to Appendix I, Section E of the *Federal Register* notice. Section E also provides further details with regard to risk characterization as related to this methodology, with emphasis placed on explaining the uncertainties in the overall risk assessment.

The generalized equations for deriving AWQC based on noncancer and cancer effects are:

Noncancer Effects

$$AWQC = RfD \cdot RSC \cdot \left(\frac{BW}{DI + (FI \cdot BAF)} \right)$$

(Equation 1.4.1)

Nonlinear Cancer Effects

$$AWQC = \frac{Pdp}{SF} \cdot RSC \cdot \left(\frac{BW}{DI + (FI \cdot BAF)} \right)$$

(Equation 1.4.2)

Linear Cancer Effects

$$AWQC = RSD \cdot \left(\frac{BW}{DI + (FI \cdot BAF)} \right)$$

(Equation 1.4.3)

where:

AWQC	=	Ambient Water Quality Criterion (mg/L)
RfD	=	Reference dose for noncancer effects (mg/kg-day)
Pdp	=	Point of departure for nonlinear carcinogens (mg/kg-day), usually a LOAEL, NOAEL, or LED_{10}
SF	=	Safety Factor for nonlinear carcinogens (unitless)
RSD	=	Risk-specific dose for linear carcinogens (mg/kg-day) (Dose associated with a target risk, such as 10^{-5})
RSC	=	Relative source contribution factor to account for non-water sources of exposure. (Not used for linear carcinogens.) May be either a percentage (multiplied) or amount subtracted, depending on whether multiple criteria are relevant to the chemical.
BW	=	Human body weight (proposed default = 70 kg for adults)
DI	=	Drinking water intake (proposed default = 2 L/day for adults)
FI	=	Fish intake (proposed defaults = 0.0178 kg/day for general population and sport anglers, and 0.039 kg/day for subsistence fishers)
BAF	=	Bioaccumulation factor, lipid normalized (L/kg)

1.5 Glossary/Acronyms

List of Acronyms Used

ADI	Acceptable Daily Intake
ASTM	American Society of Testing and Materials
AWQC	Ambient Water Quality Criteria
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
BMD	Benchmark Dose
BMR	Benchmark Response
BSAF	Biota-Sediment Accumulation Factors
BW	Body Weight
C_{18}	Carbon-18
CDC	U.S. Centers for Disease Control and Prevention
CR	Consumption Rate
CSFII	Continuing Survey of Food Intake by Individuals

CWA	Clean Water Act
DI	Drinking Water Intake
DNA	Deoxyribonucleic Acid
DOC	Dissolved Organic Carbon
DT	Non-Fish Dietary Intake
ED_{10}	Dose Associated with a 10 Percent Extra Risk
EMAP	Environmental Modeling and Assessment Program
EPA	Environmental Protection Agency
FCM	Food Chain Multiplier
FDA	Food and Drug Administration
FEL	Frank Effect Level
FI	Fish Intake
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FR	Federal Register
FSTRAC	Federal State Toxicology and Risk Analysis Committee
GI	Gastrointestinal
GLI	Great Lakes Water Quality Initiative
IARC	International Agency for Research on Cancer
II	Incidental Intake
ILSI	International Life Sciences Institute
IN	Inhalation Intake
IRIS	Integration Risk Information System
kg	kilogram
K_{ow}	Octanol-Water Partition Coefficient
L	Liter
LED_{10}	The Lower 95 Percent Confidence Limit on a Dose Associated with a 10 Percent Extra Risk
LMS	Linear Multistage Model
LOAEL	Lowest Observed Adverse Effect Level
LR	Lifetime Risk
MCL	Maximum Contaminant Level
MCLG	Maximum Contaminant Level Goal
MF	Modifying Factor
mg	Milligrams
ml	Milliliters
MLE	Maximum Likelihood Estimate
MoA	Mode of Action
MoE	Margin of Exposure
MoS	Margin of Safety
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
NIEHS	National Institute of Environmental Health Sciences
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level

NPDES	National Pollutant Discharge Elimination System
NTIS	National Technical Information Service
NTR	National Toxics Rule
ODES	Ocean Data Evaluation System
PAH	Polycyclic Aromatic Hydrocarbon
PBPK	Physiologically Based Pharmacokinetic
PCB	Polychlorinated Biphenyl
PCS	Permits Compliance System
Pdp	Point of Departure
POC	Particulate Organic Carbon
q_1*	Cancer Potency Factors
RDA	Recommended Daily Allowance
RfC	Reference Concentration
RfD	Reference Dose
RPF	Relative Potency Factor
RSC	Relative Source Contribution
RSD	Risk Specific Dose
SAR	Structure-Activity Relationship
SAB	Science Advisory Board
SDWA	Safe Drinking Water Act
SF	Safety Factor
STORET	STOrage and RETrieval U.S. Waterways Parametric Data Base
TCDD-dioxin	Tetrachlorodibenzo-*p*-dioxin
TEAM	Total Exposure Assessment Methodology
TEF	Toxicity Equivalency Factor
TSD	Technical Support Document
USDA	United States Department of Agriculture
UF	Uncertainty Factor

2. ELEMENTS OF METHODOLOGY REVISIONS AND ISSUES BY TECHNICAL AREA

2.1 Cancer Effects

This section provides a discussion of the current status of the cancer risk assessment methodology employed by EPA and modifications in that methodology, which are based on recent scientific developments and the Agency's experience in this field.[2] A discussion is provided of:

- Background information on the origins of current cancer risk assessment methods and limitations associated with those methods.

[2]See also: Notice of Draft Revisions to the Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health, in the *Federal Register*. Herein after referred to as EPA, 1998).

- New approaches recommended in the *Proposed Guidelines for Carcinogen Risk Assessment* (61 FR 17960, April 23, 1996), which revises the 1986 Cancer Guidelines.

- Modifications in the AWQC methodology for carcinogens proposed by EPA's Office of Water.

- An example showing the application of the new methodology to an organo-phosphonate pesticide.

2.1.1 Background on EPA Cancer Assessment Guidelines

2.1.1.1 1980 AWQC National Guidelines

When EPA published the 1980 AWQC National Guidelines,[3] formal Agency guidelines for assessing carcinogenic risk from exposure to chemicals had not yet been adopted. The methodology for assessing carcinogenic risk used by EPA in the 1980 AWQC National Guidelines is based primarily on the *Interim Procedures and Guidelines for Health Risks and Economic Impact Assessment of Suspected Carcinogens* published by EPA in 1976 (41 FR 21402). Although the 1980 AWQC National Guidelines recommended the use of both human epidemiological and animal studies to identify carcinogens, potential human carcinogens were primarily identified as those substances causing a statistically significant carcinogenic response in animals. It was also assumed, for risk assessment purposes, that chemical carcinogenesis was a non-threshold phenomenon.

Two types of data are used for quantitative cancer risk estimates:

- Lifetime animal studies.

- Human studies where excess cancer risk is associated with exposure to the agent. (Human data with sufficient quantification to carry out risk assessment are not available for MoE agents.)

The scaling of doses from animals to humans uses a conversion factor of body weight raised to the 2/3 power ($BW^{2/3}$). The specific equation for converting an animal dose to a human equivalent dose using the $BW^{2/3}$ scaling factor is:

[3]The term "1980 AWQC National Guidelines" refers to material presented in Appendix C of the November 1980 FR notice describing EPA's method for deriving AWQC for the protection of human health.

$$\text{Human Equivalent Dose (mg/kg-day)} = \text{Animal Dose (mg/kg-day)} \times \left(\frac{\text{Animal BW}}{\text{Animal BW}^{2/3}} \right) \times \left(\frac{\text{Human BW}^{2/3}}{\text{Human BW}} \right)$$

(Equation 2.1.1)

This approach is based on the assumption that doses between species are related to surface area. Exposure is defined in mg of contaminant/(body weight)$^{2/3}$/day (Mantel and Schneiderman, 1975). This assumption is more appropriate at low concentrations, where sources of non-linearity, such as saturation or induction of enzyme activity, are less likely to occur.

The estimation of cancer responses typically uses animal bioassay data extrapolated to low doses approximating human exposure. Extrapolation is usually carried out using the linearized multi-stage model (LMS). The LMS model is used to fit the tumor data with computer programs (e.g., GLOBAL 86) that calculate the 95th percentile upper confidence limit on the linear slope in the low dose range. The slope which is obtained is referred to as the q_1*, or cancer potency.

When animal data are used for these calculations, the body weights are scaled using $BW^{2/3}$, as discussed above. The q_1* values obtained using the LMS model are expressed in the form of the upper bound estimate of lifetime risk per (mg/kg-day). These values are often used to estimate the upper bound of the lifetime cancer risk for long-term low level exposure to agents.

The risk assessments carried out with this model are generally considered conservative, representing the most plausible 95th percentile upper bound for risk. The "true risk" is considered unlikely to exceed the risk estimate derived by this procedure, and could be as low as zero. The LMS approach was endorsed by four agencies in the Interagency Regulatory Liaison Group and was characterized as less likely to under-estimate risk at the low doses typical of environmental exposure than other models and approaches that were available.

Because of the uncertainties associated with dose-response evaluations, EPA believed that it was prudent to use the LMS to estimate cancer risk for the AWQC. These uncertainties include:

- The need for animal-to-human extrapolation;
- The use of average exposure assumptions; and
- The serious public health consequences that could result if risk were underestimated.

In deriving water quality criteria, the slope factors are currently estimated using the LMS model under most circumstances. When human (epidemiological) data are available, other approaches have been used.

Basic assumptions which are used to calculate the AWQC include:

- An "average" daily consumption rate of 2 liters of water per person per day (from all sources).
- An average daily fish consumption rate of 6.5 grams per day.
- An average body weight of 70 kilograms (kg) (154 pounds).

The maximum lifetime cancer risk generated by waterborne exposure to the agent is targeted in the range of one in one hundred thousand to one in ten million (10^{-5} to 10^{-7}). The formula for deriving the AWQC in milligrams per liter (mg/L) for carcinogens presented in the 1980 AWQC National Guidelines is:

$$\text{AWQC (mg/L)} = \frac{(10^{-5})\ (70)}{(q_1^*)(2+0.0065R)}$$

(Equation 2.1.2)

where:

10^{-5}	=	Target cancer risk level; the 1980 AWQC National Guidelines recommended risk levels in the range of 10^{-5} to 10^{-7}
70	=	Assumed body weight of an adult human being (kg)
q_1*	=	Carcinogenic potency factor for humans derived from LMS model (mg/kg-day)$^{-1}$
2	=	Assumed daily water consumption of an adult human (L/day)
.0065	=	Assumed daily consumption of fish (kg)
R	=	Bioconcentration factor (L/kg) from water to food (e.g., fish, birds)

2.1.1.2 1986 EPA Guidelines for Carcinogenic Risk Assessment

Since 1980, EPA risk assessment practices have evolved significantly. In September 1986, EPA published its *Cancer Risk Assessment Guidelines* (referred to subsequently in this document as the 1986 Cancer Guidelines) in the *Federal Register* (51 FR 33992, EPA, 1986). The 1986 Cancer Guidelines were based on the publication by the Office of Science and Technology Policy (OSTP, 1985) that provided a summary of the state of knowledge in the field of carcinogenesis and a

statement of broad scientific principles of carcinogen risk assessment on behalf of the federal government.

The 1986 Cancer Guidelines established a classification scheme to describe the nature of the cancer data base and evidence supporting the carcinogenicity of an agent. This classification system is based on a similar scheme developed by the International Agency for Research on Cancer (IARC). This scheme is described briefly below. More detailed information can be obtained from the 1986 Cancer Guidelines (EPA, 1986).

The classification scheme utilizes several alpha-numerical groups for classifying chemicals with respect to the evidence available regarding their carcinogenic potential for humans:

Group A: Human carcinogen; sufficient evidence from epidemiological studies.

Group B: Probable human carcinogen; sufficient evidence in animals or limited evidence in humans.

Group C: Possible human carcinogen; limited evidence of carcinogenicity in animals in the absence of adequate human data.

Group D: Not classifiable; inadequate data or no data.

Group E: No evidence of carcinogenicity in adequate studies in at least two species or in both epidemiological and animal studies.

Within Group B there are two subgroups: B1 and B2. According to the 1986 Cancer Guidelines: "Usually Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiologic studies. It is reasonable, for practical purposes, to regard an agent for which there is 'sufficient' evidence of carcinogenicity in animals as if it presented a carcinogenic risk to humans. Therefore, agents for which there is 'sufficient' evidence from animal studies and for which there is 'inadequate evidence' or 'no data' from epidemiologic studies would usually be categorized under Group B2." (USEPA, 1986)

The 1986 Cancer Guidelines also include guidance on the definition of sufficient or limited evidence. The weight-of-evidence for human studies is evaluated as sufficient when a causal relationship is indicated by the study. When animal studies are used in the evaluation of carcinogenicity, sufficient evidence includes agents which have been demonstrated to cause:

- an increased incidence of malignant tumors; or
- an increased incidence of combined malignant and benign tumors:
    1) in multiple species or strains; or

2) in multiple experiments (e.g., with different routes of administration or using different dose levels); or

3) to an unusual degree in a single experiment with regard to high incidence, unusual site or type of tumor.

- an early age at onset.

Additional evidence may be provided by data on dose-response, from short-term tests, or on chemical structure.

Evidence is considered limited when a causal interpretation is credible but alternative explanations are not sufficiently excluded. Limited evidence indicates that the data base for an agent can be placed into one of three categories:

- Studies involve a single species, strain, or experiment and do not meet criteria for sufficient evidence;

- Experiments are restricted by inadequate dosage levels, inadequate duration of exposure, inadequate period of follow-up, poor survival, too few animals, or inadequate reporting; or

- An increase in benign but not in malignant tumors.

Subsequent refinements of this designation have included agents which do not demonstrate positive responses in a variety of short-term tests for mutagenicity and those with responses of marginal statistical significance in a tissue known to have a high or variable background rate.

For cancer risk quantification, the 1986 Cancer Guidelines continued the recommended use of the linearized multistage model (LMS) as the only default approach. The 1986 Cancer Guidelines also state that low-dose extrapolation models and approaches other than the LMS model might be considered more appropriate based on biological grounds. However, no guidance was given in choosing other approaches; thus, departures from the LMS procedure have been rare in practice. The 1986 Guidelines continued to recommend the use of $BW^{2/3}$ as a dose scaling factor between species.

2.1.1.3 Scientific Issues Associated with the Current Cancer Risk Assessment Methodology for the Development of AWQC

In reviewing the current approach for the development of Water Quality Criteria for Human Health, EPA believes that there is not sufficient flexibility in the 1986 Cancer Guidelines. In addition, insufficient attention is given to critical information including:

- The mode of action.

- Relevance of animal bioassay data to humans.
- Route of exposure.
- The duration and magnitude of exposure.
- Additional difficulties are associated with the following:
    - Many agents fall between groups (e.g., between B2 and C) and may be difficult to assign to a specific group;
    - Effects may be greatly modulated by the conditions of exposure.
    - The use of linear extrapolation may not be appropriate for all agents, including some which appear to induce tumors at high but not low doses and which do not interact directly with DNA.

All of these issues have been considered in the development of new guidelines.

After the 1992 National Workshop on Revision of the Methods for Deriving National Ambient Water Quality Criteria for the Protection of Human Health, EPA requested its Scientific Advisory Board (SAB) to review the Workshop report. The SAB recommended against the interim adoption of the 1986 Guidelines into the AWQC methodology, indicating that it might create considerable confusion in the future, once new Cancer Guidelines were formally proposed and implemented. EPA was encouraged by both groups to incorporate new approaches into the AWQC methodology. As recommended by these two groups, EPA is proposing revisions to the cancer risk assessment methodology for the development of AWQC by incorporating new approaches discussed in the EPA Proposed Cancer Risk Assessment Guidelines dated April 23, 1996 (61 FR 17960).

2.1.2 Proposed Revisions to EPA's Carcinogen Risk Assessment Guidelines

EPA has recently published *Proposed Guidelines for Carcinogen Risk Assessment* (EPA, 1996), which contain proposed revisions to the 1986 Cancer Guidelines. These revisions are designed to ensure that the Agency's cancer risk assessment methods reflect the most current scientific information.[4] Although many fundamental aspects of the 1986 Cancer Guidelines have been retained, there are a number of key changes proposed, some of which address the specific issues mentioned in the preceding section. Proposed changes to the Cancer Guidelines are discussed here because many of the agency-wide principles that are proposed are incorporated into the proposed revisions to the AWQC methodology.

The key changes in the Proposed Cancer Guidelines include:

[4]They are referred to hereafter as the Proposed Cancer Guidelines.

a) **Hazard assessment promotes the analysis of all biological information** rather than just tumor findings.

b) **An agent's mode of action** in causing tumors is emphasized to reduce the uncertainty in describing the likelihood of harm and in determining the dose-response approach(es).

c) **Increased emphasis on hazard characterization to integrate the data analysis** of all relevant studies into a weight-of-evidence conclusion of hazard, to develop a working conclusion regarding the agent's mode of action in leading to tumor development, and to describe the conditions under which the hazard may be expressed (e.g., route, pattern, duration and magnitude of exposure).

d) **A weight-of-evidence narrative with accompanying descriptors (listed in Section 2.1.3.2 below) replaces the current alphanumeric classification system**. The narrative is intended for the risk manager and lays out a summary of the key evidence, describes the agent's mode of action, characterizes the conditions of hazard expression, and recommends appropriate dose-response approach(es). Significant strengths, weaknesses, and uncertainties of contributing evidence are highlighted. The overall conclusion as to the likelihood of human carcinogenicity is given for each route of exposure.

e) **Biologically-based extrapolation models are the preferred approach** for quantifying risk. It is anticipated, however, that the necessary data for the parameters used in such models will not be available for most chemicals. The new guidelines allow for alternative quantitative methods, including several default approaches.

f) **Dose-response assessment is a two-step process**. In the first step, response data are modeled in the range of observation, and in the second step, a determination of the point of departure or range of extrapolation below the range of observation is made. In addition to modeling tumor data, the new guidelines call for the use and modeling of other kinds of responses if they are considered to be more informed measures of carcinogenic risk.

g) **Three default approaches are provided—linear, nonlinear, or both**. Curve fitting in the observed range would be used to determine a point of departure. A standard point of departure is proposed as the effective dose corresponding to the lower 95 percent limit on a dose associated with 10 percent extra risk (LED_{10}). The linear default is a straight line extrapolation from the response at the LED_{10} to the origin (zero dose, zero extra risk). The nonlinear default begins with the identified point of departure and provides an MoE analysis rather than estimating the probability of effects at low doses. The MoE analysis is used to compare the point of departure with the human exposure levels of interest (Pdp/exposure). The key objective of the

MoE analysis is to describe for the risk manager how rapidly responses may decline with dose. Other factors are also considered in the MoE analysis (nature of the response, human variation, species differences, biopersistence).

h) **The approach used to calculate oral human equivalent dose** when assessments are based on animal bioassays has been refined to include a change in the default assumption for interspecies dose scaling (using body weight raised to the 3/4 power).

With recent proposals to emphasize mode of action understanding in risk assessment and to model response data in the observable range to derive points of departure or BMDs for both cancer and noncancer endpoints, EPA health risk assessment practices are beginning to come together. The modeling of observed response data to identify points of departure in a standard way will help to harmonize cancer and noncancer dose-response approaches and permit comparisons of cancer and noncancer risk estimates.

It is important to note that the cancer risk assessment process outlined in the Proposed Cancer Guidelines is not limited just to the quantitative aspects. Extensive guidance is provided in the Proposed Cancer Guidelines regarding hazard assessment and risk characterization (EPA, 1996).

The Proposed Cancer Guidelines should be consulted for detailed information regarding the new methodology and the scientific basis for the proposed changes. All of the above listed changes, as well as other methodological issues discussed in the Proposed Cancer Guidelines, have a direct bearing on the proposed methods for deriving AWQC discussed in this TSD. Rather than including a summary in this document that would provide only limited detail, the reader is urged to review the guidelines, as provided in the *Federal Register* notice in their original form (USEPA, 1996).

2.1.3 Revised Carcinogen Risk Assessment Methodology for Deriving AWQC

The revised methodology for deriving numerical AWQC for carcinogens is consistent with the principles included in the Proposed Cancer Guidelines. This discussion of the Draft AWQC Methodology Revisions for carcinogens focuses primarily on the quantitative aspects of deriving numerical AWQC values. However, the Proposed Cancer Guidelines emphasize the importance of qualitative information as critical to the cancer risk evaluation process. Consequently, the proposed guidelines also recommend that a numerical AWQC value derived for a carcinogen is to be accompanied by appropriate hazard assessment and risk characterization information.[5]

This section contains a discussion of the weight-of-evidence narrative, describing information relevant to a cancer risk evaluation. This is followed by a discussion of the quantitative aspects of deriving numerical AWQC values for carcinogens. It is assumed that data from an appropriately conducted animal bioassay provide the underlying basis for deriving the AWQC value. The discussion focuses on the following topics:

[5] See also EPA, 1996.

- Dose estimation.
- Characterizing dose-response relationships in the range of observation and at low, environmentally relevant doses.
- Calculating the AWQC value.
- Risk characterization.
- Use of Toxicity Equivalent Factors (TEF) and Relative Potency Estimates.

The first three listed topics encompass the quantitative aspects of deriving AWQC for carcinogens.

2.1.3.1 Weight-of-Evidence Narrative

As stated in the EPA Proposed Cancer Guidelines, the new method for cancer risk assessment includes a weight-of-evidence narrative which is based on an overall weight-of-evidence of biological, chemical, and physical considerations. The weight-of-evidence narrative lays out key evidence and includes a discussion of tumor data, information on the mode of action, and its implications for human hazard and dose-response evaluation. Emphasis will also be focused on the route and level of exposure and relevance to humans. In addition, a discussion of the strengths and weaknesses of the data base is included. The hazard assessment emphasizes analysis of all biological information rather than just tumor findings.

The weight-of-evidence narrative is written for the risk manager, and thus explains in nontechnical language the key data and conclusions, as well as the conditions for hazard expression. Conclusions about potential human carcinogenicity are presented by route of exposure. Contained within this narrative are simple likelihood descriptors that essentially distinguish whether there is enough evidence to make a projection about human hazard (i.e., known human carcinogen, should be treated as if known, likely to be a human carcinogen, or not likely to be a human carcinogen) or whether there is insufficient evidence to make a projection (i.e., the cancer potential cannot be determined because evidence is lacking, conflicting, inadequate, or because there is some evidence but it is not sufficient to make a projection to humans). Because one encounters a variety of data sets on agents, these descriptors are not meant to stand alone; rather, the context of the weight-of-evidence narrative is intended to provide a transparent explanation of the biological evidence and how the conclusions were derived. Moreover, these descriptors should not be viewed as classification categories (like the alphameric system), which often obscure key scientific differences among chemicals. The new weight-of-evidence narrative also presents conclusions about how the agent induces tumors and the relevance of the mode of action to humans, and recommends a dose-response approach based on the mode-of-action understanding.

2.1.3.2 Dose Estimation (by the Oral Route)

Determining the Human Equivalent Dose

An important objective in the dose-response assessment is to use a measure of internal or delivered dose at the target site when sufficient data are available. This is particularly important in those cases where the carcinogenic response information is being extrapolated to humans from animal studies. Generally, the measure of dose provided in the underlying human studies and animal bioassays is the applied dose, typically given in terms of the unit mass per unit body weight per unit of time, (e.g., mg/kg-day). When animal bioassay data are used, it is necessary to make adjustments to the applied oral dose values to account for differences in pharmacokinetics between animals and humans that affect the relationship between applied dose and delivered dose at the target organ.

In the estimation of a human equivalent dose, the Proposed Cancer Guidelines recommend that when toxicokinetic data are available, they are used to convert the doses used in animal studies to equivalent human doses. However, in most cases, there are insufficient data available to compare dose between species. In these cases, the estimate of a human equivalent dose is based on science policy default assumptions. In the past, body weight raised to the 2/3 power was used (as discussed in Section 2.1.1.1). To derive an equivalent human dose from animal data, the new default procedure is to scale daily applied oral doses experienced over a lifetime in proportion to body weight raised to the 3/4 power.

The 3/4 adjustment factor is used because metabolic rates, as well as most rates of physiological processes that determine the disposition of a dose, scale this way. Thus, the rationale for this factor rests on the empirical observation that rates of physiological processes consistently tend to maintain proportionality with body weight raised to 3/4 power. Based on this assumption, the "human equivalent" of the applied oral dose in an animal study is obtained from the following algorithm where the doses are in mg/kg-day:

$$\text{Human Equivalent Dose} = \text{Animal Dose} \times \left(\frac{\text{Animal BW}}{\text{Animal BW}^{3/4}} \right) \times \left(\frac{\text{Human BW}^{3/4}}{\text{Human BW}} \right)$$

(Equation 2.1.3)

This equation can be simplified to:

$$\text{Human Equivalent Dose} = (\text{Animal Dose})[(\text{Animal BW})/(\text{Human BW})]^{1/4}$$

(Equation 2.1.4)

This procedure does not calculate the delivered dose, but rather adjusts the applied dose (e.g., exposure) to account for interspecies differences in delivered doses.

This change in approach yields an estimate of delivered dose which is larger than that obtained using body weight raised to the 2/3 power in cases where the animals used in the study have a lower body weight than humans (e.g. rodents, dogs, rabbits, and most animals used for toxicological testing). Since a larger dose is estimated using this approach, the cancer potency which is estimated using the 3/4 scaling approach is slightly lower than the potency which is calculated using body weight raised to the 2/3 power.

A more extensive discussion of the rationale and data supporting the Agency's change in scaling factors from 2/3 to 3/4 is in USEPA (1992b) and the Proposed Cancer Guidelines.

Dose Adjustments for Less-than-Lifetime Exposure Periods

In the 1980 AWQC National Guidelines, two other dose-related adjustments were discussed. The first addressed situations where the experimental dosing period (l_e) is less than the duration of the experiment (L_e). In these cases, the average daily dose is adjusted downward by multiplying by the ratio (l_e/L_e) to obtain an equivalent average daily dose for the full experimental period. This adjustment would also be used in situations where animals are dosed fewer than seven days per week. If, for example, "daily" dosing is done only five days each week, the lifetime daily dose would be calculated as 5/7 of the actual dose given on each of the five days.

The second dose adjustment addresses situations where the experimental duration (L_e) is substantially less than the natural lifespan (L) of the test animal. For example, for mice and rats the natural lifespans are defined as 90 weeks and 104 weeks respectively. If the study duration is less than 78 weeks for mice, or less than 90 weeks for rats, applied doses are adjusted by dividing by a factor of $(L/L_e)^3$. (Alternatively, the cancer potency factor obtained from the study could be adjusted upward by multiplying by the factor of $(L/L_e)^3$.)

This adjustment is considered necessary because a shortened experimental duration does not permit the full expression of cancer incidence that would be expressed during a lifetime study. In addition, most carcinogenic responses are manifest in humans and animals at higher rates later in life. Age-specific rates of cancer increase as a constant function of the background cancer rate (Anderson, 1983) by the 2nd or higher power of age (Doll, 1971). In the adjustment recommended here, it is assumed that the cumulative tumor rate will increase by at least the 3rd power of age. It is important to note that although both dose adjustments discussed in this section were included in the 1980 AWQC National Guidelines, the second adjustment has not been commonly used in practice.

2.1.3.3 Dose-Response Analysis

Dose-response analysis addresses the relationship of dose to the degree of response observed in an animal or human study. Extrapolations are necessary when environmental exposures are outside of the range of study observations. Past observations of response have focused on the observation of tumors. The Proposed Cancer Guidelines suggest that responses may include tumors or other effects related to carcinogenicity. Non-tumor effects may include changes in DNA, chromosomes, or other key macromolecules; effects on growth signal transduction, induction of physiological or

hormonal changes, effects on cell proliferation, or other effects that play a role in the carcinogenic process. Non-tumor effects are referred to as "precursor data" in the following discussion.

Specific guidance regarding the use of animal data, presentation of study results, and selection of the optimal data for use in a dose-response analysis is discussed in detail in the Proposed Cancer Guidelines. It includes recommendations that multiple data arrays be presented including: combined data from different experiments, ranges of results from more than one data set, tumors generated by different modes of action, and combined tumors at more than one site within a single experiment.

Characterizing Dose-Response Relationships in the Range of Observation

The first quantitative component in the derivation of AWQC for carcinogens is the dose-response assessment in the range of observation. Two options are available for the assessment in the observed range:

- Development of a biologically-based or case-specific model.
- Curve-fitting of the tumor or precursor data.

A biologically-based model is one whose parameters are calculated independently of curve-fitting of tumor data.[6] If data on the agent are sufficient to support the parameters of a biologically-based or case specific model and the purpose of the assessment is to justify investing resources supporting its use, this type of model is the first choice for both the observed tumor and related response data and for extrapolation below the range of observed data in either animal or human studies. Extensive data are required to both build the model and to estimate how well it conforms with observed tumor development specific to the agent. Case-specific models are based on general concepts of mode of action and data on the agent. The Proposed Cancer Guidelines contain more detail on these approaches. There is not sufficient data to utilize these types of models for most agents.

In the absence of adequate data to generate a biologically-based model or case-specific model, dose-response relationships in the observed range can be addressed through curve-fitting procedures for tumor or precursor data. The models should be appropriate to the type of response data in the observed range.

The Proposed Cancer Guidelines recommend employing the lower 95 percent confidence limit on a dose associated with an estimated 10 percent extra risk of tumor or relevant nontumor response (LED_{10}). The LED_{10} (the lower 95 percent confidence limit on a dose associated with 10 percent

[6]An example of a biologically-based model is applied in the case of diesel exhaust emission (See Chen, CW. and G. Oberdorster. 1996. Selection of Models for Assessing Dose-Response Relationship for Particle-Induced Lung Cancer. Inhalation Toxicol., 8: 259-278).

extra risk) is a standard point of departure,[7] adopted as a matter of science policy to remain as consistent and comparable from case to case as possible. It is also a comparison point for noncancer endpoints.

The rationale supporting its use is that a 10 percent response is at or just below the limit of sensitivity for discerning a significant difference in most long-term rodent studies. The lower confidence limit on dose is used to appropriately account for experimental uncertainty (Barnes et al., 1995); it does not provide information about human variability. Uncertainties include such factors as number and spacing of doses, sample sizes, the precision and accuracy of dose measurements, the accuracy of pathological findings, and the selection of low dose extrapolation (discussed below).

For some data sets, a choice of the point of departure other than the LED_{10} may be appropriate. The objective is to determine the lowest reliable part of the dose-response curve for the beginning of the second step of the dose-response assessment--determining the extrapolation range. Therefore, if the observed response is below the LED_{10}, then a lower data point may be a better choice. Moreover, some forms of data may not be amenable to curve-fitting estimation, but can be evaluated using an estimation of a LOAEL or NOAEL, e.g., certain continuous data.

Analysis of human studies in the observed range is designed on a case by case basis depending on the type of study and how dose and response are measured in the study. In some cases the analysis may incorporate consideration of an agent's interactive effects with other agents. The use of population risk rather than individual risk may be appropriate in some cases, depending on the nature of the data set (e.g., human epidemiological data).

Extrapolation to Low, Environmentally Relevant Doses

In most cases, the derivation of an AWQC will require an evaluation of carcinogenic risk at environmental exposure levels substantially lower than those used in the underlying bioassay. Various approaches are used to extrapolate risk outside the range of observed experimental data. In the Proposed Cancer Guidelines, the choice of extrapolation method is largely dependent on the mode of action. The Proposed Guidelines also indicate that the choice of extrapolation procedure follows the conclusions developed in the hazard assessment about the agent's carcinogenic mode of action, and it is this mode of action understanding that guides the selection of the most appropriate dose-response extrapolation procedure. It should be noted that the term "mode of action" is deliberately chosen in the new guidelines in lieu of the term "mechanism" to indicate the use of knowledge that is sufficient to draw a reasonable working conclusion without having to know the processes in detail as the term mechanism might imply. The proposed guidelines preferred the choice of a biologically-based model, if the parameters of such models can be calculated from data sources independent of tumor data. It is anticipated that the necessary data for such parameters will not be available for most

[7] Use of the LED_{10} as the point of departure is recommended with this methodology, as it is with the Proposed Cancer Guidelines. Public comments were requested on the use of the LED_{10}, ED_{10}, or other points. EPA is currently evaluating these comments, and any changes in the Cancer Guidelines will be reflected in the final AWQC methodology.

chemicals. Thus, the new guidelines allow for several default extrapolation approaches (low-dose linear, nonlinear, or both).

Biologically-Based Modeling Approaches. If a biologically-based or case-specific model has been used to characterize the dose-response relationships in the observed range, and the confidence in the model is high, it may be used to extrapolate the dose-response relationship outside the observed data range. Although biologically-based and case-specific approaches are appropriate both for characterizing observed dose-response relationships and extrapolating to environmentally relevant doses, it is not expected that adequate data will be available to support such approaches for most substances. In the absence of such data, the default linear approach, the non-linear (margin of exposure) approach, or both linear and non-linear approaches are used.

Default Linear Extrapolation Approach. The default linear approach proposed here is essentially a replacement of the linearized multistage (LMS) approach that has served as the default approach for EPA cancer risk assessments. This new approach is used in the derivation of AWQC for:

- Agents with a mode of action of gene mutation resulting from reactivity with DNA;
- Agents, with evidence that supports a mode of action other than DNA reactivity, that are better supported by the assumption of low dose linearity; and
- Carcinogenic agents lacking information on the mode of action.

As this suggests, the linear default is used for carcinogens which lack information supporting the use of a non-linear approach. The proposed default linear approach is considered generally health-conservative. Evidence of effects on cell growth control via direct interaction with DNA constitutes an expectation of a linear dose-response relationship in the low dose range, unless there is information to the contrary.

The procedures for implementing the default linear approach begin with the estimation of a point of departure (LED_{10}). The point of departure value incorporates the interspecies conversion to the human equivalent dose and the other adjustments for less-than-lifetime experimental duration. In most cases, the extrapolation for estimating response rates at low, environmentally relevant exposures is accomplished by drawing a straight line between the response at the "point of departure" (LED_{10}) and the origin (i.e., zero dose, zero response). This is mathematically represented as:

$$y = mx$$

(Equation 2.1.5)

where:

y = Response or incidence

m	=	Slope of the line (cancer potency factor)
x	=	Dose

The slope of the line, "m" (i.e., $\Delta y/\Delta x$, the estimated cancer potency factor at low doses), is computed as:

$$m = \frac{0.10}{LED_{10}}$$

(Equation 2.1.6)

When an LED_{10} isn't used, the standard equation for the slope of a line may be used:

$$m = \frac{y_2 - y_1}{x_2 - x_1}$$

(Equation 2.1.7)

where:

y_2	=	Response at the point of departure
y_1	=	Response at the origin (zero)
x_2	=	Dose at the point of departure
x_1	=	Dose at the origin (zero)

Due to the use of the origin for y_1 and x_1, the equation simplifies to:

$$\frac{y_2}{x_2}$$

(Equation 2.1.8)

The risk-specific dose (RSD) is then calculated for a specific incremental targeted lifetime cancer risk (in the range of 10^{-4} to 10^{-6}) as:

$$RSD = \frac{\text{Target Incremental Cancer Risk}}{m}$$

(Equation 2.1.9)

where:

RSD	=	Risk-specific dose (mg/kg-day)
Target Risk[8]	=	Value typically in the range of 10^{-4} to 10^{-6}
m	=	Cancer potency factor $(mg/kg\text{-}day)^{-1}$

The use of the RSD to compute the AWQC is described below in the section titled "AWQC Calculation."

Default Non-Linear Approach. As discussed in the Proposed Cancer Guidelines, the use of a non-linear approach for risk assessment is recommended where there is no evidence for linearity and there is sufficient evidence to support an assumption of non-linearity. As noted above, this would NOT be used for agents with:

- A mode of action of gene mutation resulting from reactivity with DNA;
- Evidence that supports another mode of action that is anticipated to be linear; or
- Carcinogenic agents lacking information on the mode of action.

A definitive determination regarding an agent's mutagenicity may not be possible, since many agents yield mixed results in mutagenicity assays. Mode of action data are used in a case study provided in Section 2.1.4 of this document. The chemical discussed is not mutagenic but causes stone formation in male rat bladders, leading to tumor formation at high doses. Stone and subsequent tumor formation are not expected to occur at doses lower than those that induced the physiologic change that leads to stones, based on the mode of action data.

The non-linear approach is indicated for agents having a mode of action that may lead to a dose-response relationship that is non-linear, with response falling much more quickly than linearly with dose, or those being most influenced by individual differences in sensitivity. Alternatively, the mode of action may theoretically have a threshold (e.g., the carcinogenic response may be a secondary effect of toxicity or of an induced physiological change (that is itself a threshold phenomenon). EPA does not generally try to distinguish between modes of action that might imply

[8] In 1980, the target lifetime cancer risk range was set at 10^{-7} to 10^{-5}. However, both the expert panel for the AWQC workshop (1992) and SAB recommended that EPA change the risk range to 10^{-6} to 10^{-4}, to be consistent with drinking water.

a "true threshold" from others with a non-linear dose-response relationship, because there is usually not sufficient information to determine empirically.

The Proposed Cancer Guidelines recommend that non-linear probability functions NOT be fitted to the response data to extrapolate quantitative low-dose risk estimates. Different models can lead to a very wide range of results. Also, there is currently no basis to choose among the different models. If there is sufficient information to choose a model, a biologically-based or case-specific model should be used.

The Proposed Cancer Guidelines recommend use of a margin of exposure (MoE) approach to evaluate concern for various levels of exposure. This entails the comparison of a minimum effect dose level such as the LED_{10}, NOAEL, or LOAEL environmental exposures of interest. In the context of deriving AWQC, the environmentally relevant exposures are targets rather than actual exposures. A Safety Factor (SF) is then applied to account for various types of uncertainty. This approach is similar to the benchmark dose approach described in the noncancer section of this TSD.

The MoE approach used here is similar to the analysis carried out by EPA to accompany estimates of RfD or concentrations for noncancer endpoints. However, a threshold of carcinogenic response is not necessarily assumed. If the evidence for an agent indicates a threshold, (e.g., when carcinogenicity is secondary to another toxicity that has a threshold) the MoE analysis is similar to what has been done for a noncancer endpoint, and an RfD for that toxicity may also be estimated and considered in the cancer assessment.

To support the use of the MoE approach, information is provided in the risk assessment about the current understanding of the phenomena that may be occurring as dose (exposure) decreases substantially below the observed data. This provides information about the risk reduction that is expected to accompany a lowering of exposure. Information regarding the various factors which influence the selection of a SF are also included in the discussion below.

There are two main steps in the MoE approach:

- The first step is the selection of a point of departure (Pdp) that is a "minimum effect dose level." As noted above, the Pdp may be the LED_{10} for tumor incidence, or in some cases, it may also be appropriate to use a NOAEL or LOAEL value from a precursor, such as a response that is a precursor to tumors. *When animal data are used, the Pdp is a human equivalent dose or concentration arrived at by interspecies dose adjustment* (as discussed above) or toxicokinetic analysis.

- The second step in using MoE analysis to establish an AWQC is to conduct an analysis to derive a SF to apply to the Pdp. (This is supported by analysis in the MoE discussion provided in the risk assessment). The following issues are to be considered when establishing the SF for the derivation of AWQC using the MoE approach (others may be found appropriate in specific cases):

- The slope of the observed dose-response relationship at the point of departure and its uncertainties and implications for risk reduction associated with exposure reduction (e.g., a steep slope implies an apparent greater reduction in risk as exposure decreases that may support a smaller margin).

- Variation in sensitivity to the phenomenon involved, among members of the human population.

- Variation in sensitivity between humans and the animal study population.

- The nature of the response used for the dose-response assessment, for instance, a precursor effect, or tumor response. The latter may support a greater margin.

- Persistence of the agent in the body. Greater persistence argues for a greater MoE. This persistence issue is particularly relevant when precursor data from less than lifetime studies are the response data being assessed.

As a default assumption for two of the factors listed above, the Proposed Cancer Guidelines recommend that a factor of no less than 10-fold each be employed to account for human variability and for interspecies differences in sensitivity when humans may be more sensitive than animals. When data indicate that humans are less sensitive than animals, a default factor of no smaller than 1/10 may be employed to account for this. If information about human variability or interspecies differences is available, it is used.

The size of the overall SF is a matter of policy. The rationale for selection of the SF should be fully explained and related to the toxicity and other data presented in the weight-of-evidence narrative discussed previously.

The SF is used to modify the Pdp in the final equation. This is shown below in the Section 2.1.3.4 on AWQC calculation.

Both Linear and Non-Linear Approaches. In some cases both linear and non-linear procedures may be used. When data indicate that there may be more than one operant mode of action for cancer induction at different tumor sites, an appropriate procedure is used for each site. The use of both the default linear approach and the non-linear approach may be appropriate to discuss implications of complex dose-response relationships, and may be decoupling analysis of regions of the overall dose response that reflect differing modes of action.

2.1.3.4 AWQC Calculation

Linear Approach

The following equation is used for the calculation of the AWQC for carcinogens where a RSD is obtained from the default linear approach:

$$AWQC = RSD \times \left(\frac{BW}{DI + (FI \times BAF)} \right)$$

(Equation 2.1.10)

The AWQC calculation shown above is appropriate for water bodies that are used as sources of drinking water (and for other uses). If the water bodies are not used as drinking water sources the approach is modified. The drinking water value (DI in the equation shown above) is substituted with an incidental ingestion value (II) of 0.01 L/day. The incidental intake is assumed to occur from swimming and other activities. The fish intake value is assumed to remain the same.

Non-Linear Approach

In those cases where the non-linear, MoE approach is used, a similar equation is used to calculate the AWQC:

$$AWQC = \frac{Pdp}{SF} \times \left(\frac{BW}{DI + (FI \times BAF)} \right) \times RSC\%$$

(Equation 2.1.11)

where:

AWQC	=	Ambient water quality criterion (mg/L)
RSD	=	Risk-specific dose (mg/kg-day)
Pdp	=	Point of departure (mg/kg-day)
SF	=	Safety factor (unitless)
BW	=	Human body weight (kg)
DI	=	Drinking water intake (L/day)
FI	=	Fish intake (kg/day)
BAF	=	Bioaccumulation factor (L/kg)
RSC%	=	Relative source contribution (%)

As noted above for the linear approach, the AWQC calculation shown above is appropriate for water bodies that are used as sources of drinking water (and for other uses). If the water bodies are not used as drinking water sources DI is substituted with an incidental ingestion value (II) of 0.01 L/day.

A difference between the AWQC values obtained using the linear and non-linear approaches is that the AWQC value obtained using the default linear approach corresponds to a specific estimated incremental lifetime cancer risk level in the range of 10^{-4} to 10^{-6}. In contrast, the AWQC value obtained using the non-linear approach does not describe or imply a specific cancer risk.

The actual AWQC chosen is based on a review of all relevant information, including cancer, noncancer, ecological, and other critical data. The AWQC may, or may not, utilize the value obtained from the cancer analysis, if it is less protective than that derived from the noncancer endpoint.

2.1.3.5 Risk Characterization

Risk characterization information is included with the numerical AWQC value and addresses the major strengths and weaknesses of the assessment arising from the availability of data and the current limits of understanding of the process of cancer causation. Key issues relating to the confidence in the hazard assessment and the dose-response analysis (including the low dose extrapolation procedure used) are discussed.

Whenever more than one interpretation of the weight-of-evidence for carcinogenicity or the dose-response characterization can be supported, and when choosing among them is difficult, the alternative views are provided along with the rationale for the interpretation chosen in the derivation of the AWQC value. Where possible, quantitative uncertainty analyses of the data are provided; at a minimum, a qualitative discussion of the important uncertainties is presented.

Important features of the risk characterization include significant scientific issues, significant science and science policy choices that were made when alternative interpretations of data exist, and the constraints of the data and the state of knowledge. The assessments of hazard, dose-response, and exposure are summarized to generate risk estimates for the exposure scenarios of interest.

The Proposed Cancer Guidelines contain more detailed guidance regarding the development of risk characterization summaries and analyses.

2.1.3.6 Use of Toxicity Equivalence Factors (TEF) and Relative Potency Estimates

The 1996 Proposed Guidelines for Carcinogen Risk Assessment (USEPA, 1991; 1996) state: "A Toxicity Equivalence Factor (TEF) procedure is one used to derive quantitative dose-response estimates for agents that are members of a category or class of agents. TEFs are based on shared characteristics that can be used to order the class members by carcinogenic potency when cancer bioassay data are inadequate for this purpose. The ordering is by reference to the characteristics and potency of a well-studied member or members of the class. Other class members are indexed to the reference agent(s) by one or more shared characteristics to generate their TEFs." In addition, the Proposed Cancer Guidelines (USEPA, 1996) state that TEFs are generated and used for the limited purpose of assessment of agents or mixtures of agents in environmental media when better data are not available. When better data become available for an agent, its TEF should be replaced or revised.

To date, adequate data to support use of TEFs has been found in only one class of compounds (dioxins) (USEPA, 1989).

The uncertainties associated with TEFs are explained when this approach is used. This is a default approach to be used when tumor data are not available for individual components in a mixture. Relative potency factors (RPFs) can be similarly derived and used for agents with carcinogenicity or other supporting data. These are conceptually similar to TEFs, but are less firmly based on science and do not have the same levels of data to support them. TEFs and relative potency factors are used only when there is no better alternative. When they are used, uncertainties associated with them are discussed. As of today, there are only three classes of compounds for which relative potency approaches have been examined by EPA: dioxins, polychlorinated biphenyls (PCBs), and polycyclic aromatic hydrocarbons (PAHs).

2.1.4 Case Study (Compound Y, a Rodent Bladder Carcinogen)

This section illustrates an application of the non-linear method (MoE) for a rodent bladder carcinogen (Compound Y). A brief summary of the data set is provided below with conclusions regarding the weight-of-evidence. The AWQC obtained using the default linear and LMS approaches are included for purposes of comparison only and would not be used for agents with the characteristics described for Compound Y. In addition, considerably more detail would be provided in a weight-of-evidence narrative.

2.1.4.1 Background and Evaluation for Compound Y

Compound Y is an organophosphonate which has been tested in subchronic, chronic, reproductive, and carcinogenic assays in multiple species. Tumors were observed only in rat studies. No human data are available. Based on a review of the toxicity, mechanistic, metabolic, and other data summarized below for this agent, it was concluded that a non-linear approach is most appropriate for establishing AWQC based on carcinogenicity.

Lifetime cancer bioassays of Compound Y identified bladder tumors and hyperplasia in male and female rats at doses of 1500 mg/kg-day and higher in the diet. These effects were not observed at 100 and 400 mg/kg-day. The rates of bladder cancer observed in females were lower than those observed in males. In a 90-day study designed to evaluate the mechanisms of tumor induction, the following sequence was identified as critical to bladder tumor formation in rats:

1) Large doses of Compound Y produce urinary calcium/potassium imbalance followed by

2) Diuresis, a sharp drop in urine pH, formation of urinary calculi, and

3) Appearance of transitional cell hyperplasia in the renal pelvis, ureter, and urinary bladder.

These effects occurred within two weeks of exposure onset, persisted to the end of exposure, and were reversible upon cessation of the 90-day exposure.

The pathological events caused by Compound Y are believed to result from prolonged mechanical irritation by bladder calculi that developed in response to the exposure. At high but not lower subchronic doses in the male rat, Compound Y leads to elevated blood phosphorus levels; the body responds by releasing excess calcium into the urine. The calcium and phosphorus combine in the urine and precipitate into multiple stones in the bladder. The stones are very irritating to the bladder; the bladder lining is eroded, and cell proliferation occurs to compensate for the loss of the lining. This leads to development of hyperplasia, with subsequent tumor formation. A prolonged increase in the rate of proliferation of cells of the urinary bladder has been proposed to be an important step in the induction of urinary bladder tumors (Cohen and Ellwein, 1989; 1990). Thus, the association of cell proliferation, hyperplasia, and subsequent cancer induction as a result of urinary stone formations due to exposure to Compound Y is proposed as one mode of action which may justify, after a review of all relevant data, the use of a non-linear approach, such as the MoE approach.

Studies of the components of this agent yield no evidence of carcinogenicity in the bladder. In metabolic studies in animals, the metallic component in isolation from the parent molecule was not absorbed to a significant extent from the gastrointestinal tract.

Compound Y has been assessed via a battery of mutagenicity assays that have yielded negative results, and a review of the chemical structure does not suggest potential genotoxicity. The metabolites of Compound Y have also yielded negative results in mutagenicity assays and yielded no evidence of carcinogenicity. The negative genotoxicity results for Compound Y and structurally related agents provide further support for the use of a non-linear approach, such as the MoE approach, to establish AWQC.

2.1.4.2 Conclusion and Use of the MoE Approach for Compound Y

Compound Y, a metal aliphatic phosphonate, is likely to be carcinogenic to humans only under high-exposure conditions following oral and inhalation exposure that lead to bladder stone formation, but is not likely to be carcinogenic under low-exposure conditions. It is not likely to be a human carcinogen via the dermal route, given that the compound is a metal conjugate that is readily ionized and its dermal absorption is not anticipated. The weight-of-evidence is based on (1) bladder tumors only in male rats at high exposure; (2) the absence of tumors at any other site in rats or mice; (3) the formation of calcium-phosphorus-containing bladder stones in male rats at high, but not low, exposure. The bladder stones erode bladder epithelium and result in profound increases in cell proliferation and cancer; and (4) the absence of carcinogenic structural analogues or mutagenic activity.

There is a strong mode of action basis for the requirements of high doses of Compound Y, which leads to excess calcium and increased acidity in the urine, resulting in the precipitation of bladder stones and subsequent increase in cell proliferation and tumor hazard potential. Lower doses

fail to perturb urinary constituents, lead to stones, produce toxicity, or give rise to tumors. Therefore, dose-response assessment should assume non-linearity.

A major uncertainty is whether the profound effects of Compound Y may be unique to the rat. Even if Compound Y produced stones in humans, there is only limited evidence that humans with bladder stones develop cancer.

Based on the progression of pathology leading to tumors, in which hyperplasia is an early critical step, hyperplasia was selected as the sentinel precursor effect which was used as the basis for the calculation of AWQC using the MoE approach. Hyperplasia incidence data in a lifetime rat study are available for Compound Y. Tumor data from the same lifetime rat study were used to calculate AWQC using the default linear and LMS approaches for purposes of comparing methods and results. The data used for all three approaches are summarized in Table 2.1.1 below.

Table 2.1.1: Study Results from a Lifetime Exposure of Male Rats to Compound Y

Animal Dose in mg/kg-day (scaled human equivalent doses)	**Number in Group**	**Number Responding**	
		tumors (combined papilloma & carcinoma)	hyperplasia
0	73	3	5
400 $(BW^{3/4} = 106.4)^a$ $(BW^{2/3} = 68.4)^b$	78	2	5
1500 $(BW^{3/4} = 398.9)^a$ $(BW^{2/3} = 256.5)^b$	78	21*	29*

a. The 3/4 scaling factor is the new proposed method and is used with the new linear model in this case study for comparison purposes.

b. The 2/3 scaling factor is presently in use and is used with the LMS method later in this section for comparative purposes.

* There were statistically significant ($p<0.05$) increases in both tumor incidence and hyperplasia in the treated group compared to the control group.

Identification of the Point of Departure (Pdp) for Compound Y

The point of departure (Pdp) chosen for the MoE calculations was 400 mg/kg-day, which is the maximum animal dose yielding no observable hyperplastic effects (the NOAEL shown in Table 2.1.1).[9] The study found males to be more sensitive to tumor induction than females and the hyperplasia results in male rats were used for AWQC calculations. The human equivalent dose for the NOAEL of 106.4 mg/kg-day was calculated using the new scaling factor of body weight raised to the 3/4 power (as shown in Equation 2.1.3).

Discussion of the Points Affecting Selection of the SF for Compound Y

Intraspecies Variability. There is variability within the human population in responses to xenobiotic agents which may result from a variety of factors including health status, diet, age, and genetic composition. Research on Compound Y did not identify a common health or genetic condition which would yield a subpopulation who are particularly susceptible to the carcinogenic effects of Compound Y nor did it indicate an exceptionally high or low level of intraspecies variability.

Interspecies Variability. Animals and humans may vary widely in their responses to agents due to their differing physiologies and metabolism. A review of human case studies and epidemiological studies indicate that humans may be significantly less susceptible to the influence of bladder irritation, stone formation, and subsequent tumor formation than male rodents. This would suggest a smaller factor for interspecies variability.

Confidence in the Study (Dose Selection). There is a wide range in dose levels between the NOAEL and LOAEL in the selected study. The hyperplastic response rate at the LOAEL is 37 percent (i.e., 29/78), which is high for the initial response measurement. Additional data would help to refine the NOAEL and better describe the dose-response dynamic in the low response range.

Exposure Duration. This exposure scenario is chronic, so there is no need to apply an additional safety factor.

Persistence. This chemical is not persistent in the body, so there is no need to apply an additional safety factor.

Shape of the Dose-Response Curve. The data available indicate a steep slope at the point of departure (at 400 mg/kg-day animal dose). This would suggest a rapid reduction in risk with lower doses, or a smaller SF.

In summary, an overall SF of 30 is used in the MoE calculation. The selection of the SF is based on a consideration of all the factors discussed above, such as intraspecies variability (10), interspecies variability (3 is used here because animal dose has already been adjusted to a human equivalent dose), and the adequate data base on this chemical. This factor of 30 is sufficient for

[9]This is based on a dietary conversion factor for rats from ppm to mg/kg-day of .05.

human health protection. The risk may decline considerably with doses lower than the point of departure; the male rat is a very sensitive model (mice do not respond). Physiological phenomenon is likely to fall off sharply with dose as shown by the dose-response curve. Further, bladder stone and subsequent tumor formation is not a common phenomenon in humans.

AWQC Calculations for Compound Y

Equation 2.1.11 shown in Section 2.1.3 was used to calculate the AWQC for Compound Y:

$$AWQC = \frac{Pdp}{SF} \times \left(\frac{BW}{DI + (FI \times BAF)} \right) \times RSC\%$$

(Equation 2.1.11)

The following input parameters were used:

Pdp	=	Point of departure (106.4 mg/kg-day (NOAEL))
SF	=	Safety factor of 30
BW	=	Body weight for adult (70 kg)
DI	=	Drinking water intake (2 L/day)
FI	=	Fish intake (0.01780 kg/day)
BAF	=	Assumed bioaccumulation factor (BAF) (300 L/kg)
RSC	=	20% (assumed)

This calculation yields an AWQC of 6.7 mg/L. The body weight, water intake, fish intake, and RSC% values used in the above calculation are the currently proposed default values for adults (see the exposure section of this document). The BAF, which accounts for the accumulation of Compound Y from water through the food chain and into fish tissue, has been arbitrarily chosen for purposes of this case study.

The AWQC calculations shown above is appropriate for water bodies that are used as sources of drinking water (and for other uses). See Section 2.1.3.4 for additional information on modifications for non-drinking water sources.

2.1.4.3 Use of the Default Linear Approach for Compound Y

This section is provided for purposes of illustrating the use of the default linear approach for deriving AWQC based on carcinogenicity and to compare the resulting AWQC to that obtained above using the MoE approach. As discussed in Section 2.1.4.1 above, it is important to note that the default linear method would most likely not, in practice, be recommended as an approach for quantifying the risk and deriving the AWQC for Compound Y given the hazard characteristics described for this substance.

Computing the Human Equivalent Dose for Compound Y

The doses used in the study were adjusted to obtain a human equivalent dose, as shown in Table 2.1.1. In the absence of pharmacokinetic data, this was done using a scaling factor of $BW^{3/4}$, with a male rat weight of 0.35 kg and a human weight of 70 kg (as shown in Equation 2.1.3).

Calculation of AWQC for Compound Y

To describe the dose-response of tumor incidence data in the observed range, a curve-fitting model such as the multistage or other approach appropriate for the data can be used. In the case of Compound Y, three data points (at doses of 0, 400, and 1500 mg/kg-day) were used in the multistage model (GLOBAL 86) to calculate the LED_{10} (the 95 percent lower confidence limit on a dose associated with a 10 percent increase in response). The value obtained for the LED_{10} is 204 mg/kg-day.

The cancer slope factor (m) is calculated by dividing 0.1 by the LED_{10} using Equation 2.1.6:

$$m = \frac{0.10}{LED_{10}}$$

(Equation 2.1.6)

This yields an estimated cancer slope factor of 4.9×10^{-4} per mg/kg-day. The cancer slope factor is then used in Equation 2.1.9 with a specified risk level (in this case 10^{-6}) to calculate a RSD:

$$RSD = \frac{\text{Target Incremental Cancer Risk}}{m}$$

(Equation 2.1.9)

This yields an RSD of 2.0×10^{-3} mg/kg-day.

The RSD is used in Equation 2.1.10 with the same input parameters (body weight, drinking water intake, fish intake, and BAF) as those used for the MoE approach:

$$AWQC = RSD \times \left(\frac{BW}{DI + (FI \times BAF)} \right)$$

(Equation 2.1.10)

This yields an AWQC of 0.019 mg/L (rounded from 0.0189 mg/L) for a target risk of 10^{-6}. (As noted above, this approach is appropriate for water bodies used as drinking water sources. See Section 2.1.3.4 for non-drinking water sources).

2.1.4.4 Use of the LMS Approach for Compound Y

This section is provided strictly for purposes of comparing the use of the MoE approach with the traditional linearized multistage (LMS) method for deriving AWQC for carcinogens. As discussed above, the LMS approach would not be used in practice to quantify risk and derive the AWQC for Compound Y given the hazard characteristics described for this substance.

First, the LMS approach was used to fit the male rat tumor data shown in Table 2.1.1 with the computer program GLOBAL86. This program calculates the 95th percentile upper confidence limit on the linear slope (i.e., the q_1*) in the low dose range. A human equivalent dose was calculated using the $BW^{2/3}$ interspecies dose scaling factor for purposes of illustrating the results obtained applying the 1980 AWQC derivation methodology. The human equivalent doses obtained using this scaling factor are shown in Table 2.1.1 above. (The same data set, using differently scaled doses, was employed for both the new linear and LMS approaches.) The q_1* value obtained using the LMS approach is 6×10^{-4} $(mg/kg\text{-}day)^{-1}$.

Equation 2.1.9 was used with a reference incremental cancer risk of 10^{-6} to calculate an RSD of 1.7×10^{-3}. Equation 2.1.10 was then used to calculate the AWQC with the same input parameters (body weight, drinking water intake, fish intake, and BAF) as those used for the MoE approach. (As noted above, this approach is appropriate for water bodies used as drinking water sources. See Section 2.1.3.4 for non-drinking water sources.) The AWQC was calculated to be 0.016 mg/L and was rounded from 0.0157 mg/L.

2.1.4.5 Comparison of Approaches and Results for Compound Y

The results of the three approaches used for Compound Y are summarized in Table 2.1.2. The AWQC calculated using the MoE approach is substantially higher than that obtained using the default linear and LMS approaches. If larger or smaller SFs were used in the MoE calculations, the AWQC obtained using the MoE approach would decrease or increase accordingly. The quantitative relationship between AWQC derived using different methods will vary depending on the nature of the data set and the SFs and Pdp selected for use in the MoE approach.

Table 2.1.2: Comparison of AWQC Obtained for Compound Y Using the MoE, Default Linear, and LMS Approaches

Method	AWQC (mg/L)
MoE Using hyperplasia as a precursor for determining the Point of Departure (Pdp) and a SF of 30.	6.7
Default Linear Using linear extrapolation from the LED_{10} with a 10^{-6} risk level and an interspecies scaling factor based on $BW^{3/4}$.	0.019
LMS Using the linearized multistage approach with a 10^{-6} risk level and an interspecies scaling factor based on $BW^{2/3}$.	0.016

2.1.5 References

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2.2 Noncancer Effects

2.2.1 Introduction

The evaluation of risks from noncarcinogenic chemicals traditionally has been based on the assumption that noncarcinogens have a dose or level below which no adverse effects are expected to occur. The risk parameter developed by EPA for noncarcinogens is called the Reference Dose (RfD). The Integrated Risk Information System (IRIS) Background Document entitled *Reference Dose (RfD): Description and Use in Health Risk Assessments* (USEPA, 1988) defines an RfD as "an estimate (with uncertainty spanning approximately an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects over a lifetime." The RfD is acknowledgedly an estimate and, thus, may not be completely protective of every individual within a highly variable population, conversely, neither are exposures above the RfD necessarily unsafe. Some individuals may have better adaptive or protective capacities than others and responses may vary with age and state of health; thus, individuals respond differently to toxicant exposure (Barnes and Dourson, 1988).

The key step in deriving water quality criteria for the protection of human health from noncancer effects is the determination of the RfD. As described in Section 1.4, the RfD is used in concert with additional information regarding exposure and the bioaccumulation potential of the substance to derive an AWQC for noncancer effects. The procedures presented in USEPA (1988)

for deriving the RfD using an experimentally derived No Observed Adverse Effect Level (NOAEL)/Lowest Observed Adverse Effect Level (LOAEL) approach are incorporated into this chapter. The Agency is also investigating alternative methods for estimating the RfD; thus, this guidance document contains information on two alternative methods, the Benchmark Dose (BMD) and Categorical Regression approaches. The Agency continues to conduct research on the utility of both of these methods in the noncancer risk assessment process and recommends their application in circumstances where the data are sufficient. The Agency used the BMD approach to derive a RfD for methyl mercury (USEPA, 1994a).

This section begins with a discussion of hazard identification and dose-response characterization. This is followed by a description of factors to be considered in the selection of critical data sets for use in the risk assessment evaluation. The procedures for deriving an RfD for a substance using the traditional NOAEL/LOAEL approach are presented as the accepted current risk assessment practice used by USEPA. Next, the BMD method for deriving an RfD is discussed and an example of its application is provided for illustrative purposes. A brief discussion of Categorical Regression is also included, with references to the relevant literature. The chapter concludes with specific sections on several issues relevant to noncancer risk assessment, including practical nonthreshold effects and risks from short-term exposures and mixtures.

While the intent of this guidance is to provide sufficient information to apply methods for deriving RfDs, this document does not detail all relevant issues and underlying theory associated with these methods. For further information, the reader is referred to the sources cited in the reference list (in particular, USEPA, 1988; Crump et al., 1995; and Hertzberg and Miller, 1985).

2.2.2 Hazard Identification

The first step in the risk assessment involves preparing a hazard identification, based on a review of data available to characterize the health effects associated with chemical exposure. The RfD Background Document (USEPA, 1988) outlines considerations for choosing data upon which to base a hazard identification for noncancer health effects.[10] Assessors should prepare a hazard identification document that describes the nature of exposure, the type and severity of effects observed, and the quality and relevance of data to humans. Well-conducted human studies are considered the best for establishing a link between exposure to an agent and manifestation of an adverse effect. In the absence of adequate human data, the Agency relies primarily on animal studies. In such cases, the principle studies are drawn from experiments conducted on laboratory mammals, most often rat, mouse, rabbit, guinea pig, dog, monkey, or hamster. Well-designed animal studies offer the benefit of controlled chemical exposures and definitive toxicological analysis. Supporting evidence provides additional information for dose-response assessment and may come from a wide variety of sources, such as metabolic and pharmacokinetic studies. *In vitro* studies seldom provide

[10]The Agency has also developed guidelines that explain the process of hazard identification for developmental (USEPA, 1991a) and reproductive (USEPA, 1994b) effects. Please refer to these EPA documents for guidance in these areas.

definitive hazard identification data, but they can often provide insight into the compound's potential for human toxicity.

Important to the hazard identification is consideration of the biological and statistical significance of observed effects. The determination of whether an effect is adverse requires professional judgment. For guidance, adverse health effects are those deleterious effects which are or may become debilitating, harmful, or toxic to the normal functions of an organism, including reproductive and developmental effects. Adverse effects do not include such effects as tissue discoloration without histological or biochemical effects, or the induction of the enzymes involved in the metabolism of the substance. Guidelines for defining the severity of adverse effects have been suggested by Hartung and Durkin (1986). EPA has also developed guidelines for the ranking of observed effects (USEPA, 1995) and a ranking scheme for slight to severe effects. Distinguishing slight effects such as reversible enzyme induction and reversible subcellular change from more serious effects is critical in distinguishing between a NOAEL and LOAEL.

It is also important to evaluate the reversibility of an effect. Reversibility refers to whether or not a change will return to normal or within normal limits either during the course of or following exposure. However, even a reversible effect may be adverse to an organism. In performing a hazard identification, irreversible effects should be distinguished from less serious, but still adverse, reversible changes.

The exposure conditions for toxicity tests, including the route (e.g., inhaled versus ingested), source (e.g., water versus food), and duration, should be discussed in the hazard identification. The hazard identification should also include an evaluation of the quality of studies. Elements that affect the quality of studies include the soundness of the study protocol, the adequacy of data analysis, the characterization of the study compound, the types of species used, the number of individuals per study group, the number of study groups, dose spacing, the types of observations recorded, sex and age of animals, and the route and duration of exposure (USEPA, 1988).

The hazard identification should conclude with a weight-of-evidence discussion. In general, the discussion should review the results of different studies and develop an overall picture of the chemical's toxicity. Evidence for possible toxicity in humans is supported by similar results across species and across investigators. A plausible mechanism of action for the effect, as well as similar toxic activity in chemicals of similar structure, also add to the weight-of-evidence.

2.2.3 Dose-Response Assessment

The dose-response assessment involves the evaluation of toxicity data to identify doses at which statistically and/or biologically significant effects occur and identify NOAEL and/or LOAEL values. The effects data are also evaluated to see if there is a quantitative relationship between dose and the magnitude of the effect. Dose-response relationships can be linear, curvilinear or U-shaped. The RfD is traditionally estimated by identifying the most appropriate NOAEL for the critical effect. The LOAEL may be used to estimate the RfD if no appropriate NOAELs have been identified.

2.2.4 Selection of Critical Data

2.2.4.1 Critical Study

Ideally, the scientific data for noncancer effects should include sufficient information to characterize quantitatively the incidence and severity of response as dose increases. However, complete data are frequently lacking. Instead, the Agency bases the derivation of the RfD on the NOAEL or LOAEL from a critical study or collection of critical studies. The choice of the critical study or studies to use in the derivation of the chronic RfD requires professional judgment concerning the quality of the studies, the definition of adverse effects and their level of occurrence. As part of the hazard identification, all relevant toxicity data on a chemical should be evaluated to support the establishment of the RfD. Those studies representing the best quality and most appropriate data should be considered for defining adverse effects and their level of occurrence.

In choosing a study on which to base the RfD, the Agency recommends a hierarchy of acceptable data. Most preferable is a well-conducted epidemiologic study that demonstrates a positive association between a quantifiable exposure to a chemical and human disease. Use of acceptable human studies avoids the problems of interspecies extrapolation, and thus, confidence in the estimate is often greater. At present, however, human data adequate to serve as a basis for quantitative risk assessment are available for only a few chemicals. Most often, inference of adverse health effects for humans must be drawn from toxicity information gained through animal experiments with human data serving qualitatively as supporting evidence. Under this condition, health effects data must be available from well-conducted animal studies and relevant to humans based on a defensible biological rationale, e.g., similar metabolic pathways. In the absence of data from a more "relevant" species, data from the most sensitive animal species tested, i.e., the species demonstrating an adverse health effect at the lowest administered dose via a relevant route of exposure, shall generally be used as the critical study.

The route of administration must be considered when choosing the critical study from among quality toxicity tests. The vehicle in which the chemical is administered is also relevant. For example, within the oral route of exposure, the bioavailability of a chemical ingested from one source (e.g., food) may differ from when it is ingested from another source (e.g., water). Usually, the toxicity data base does not provide data on all possible routes, sources, and/or durations of administration. In general, the preferred exposure route is that which is considered most relevant to environmental exposure. For example, when developing drinking water standards, the Agency has placed greater weight on oral studies in experimental animals, especially those studies in which the contaminant is administered via water. However, in the absence of data on the exposure route and/or source of concern, it is the Agency's view that the potential for the toxicity manifested by one route and/or source of exposure may be relevant to other exposure routes and/or sources. EPA guidelines for the development of interim inhalation reference concentrations (USEPA, 1989) discuss specific issues relevant to route-to-route extrapolation. These include issues of portal-of-entry effects, available pharmacokinetic data for the routes of interest, measurements of absorption efficiency by each route of interest, comparative excretion data when the associated metabolic pathways are equivalent by

each route of interest, and comparative systemic toxicity data when such data indicate equivalent effects by each route of interest.

Preference should be given to studies involving exposure over a significant portion of the animal's lifespan since this is anticipated to reflect the most relevant environmental exposure. Studies with shorter time frames can miss important effects. In selected cases, studies of less than 90 days can be used for quantification but the study must be of exceptionally high quality. In general short-term tests should not be used for anything other than interim RfDs or for developmental RfDs. However, developmental effects can sometimes be the critical effect and serve as the basis of an RfD. The duration of a developmental study is generally less than 15 days.

2.2.4.2 Critical Data and Endpoint

The experimental exposure level representing the highest dosage level tested at which no adverse effects were demonstrated in any of the species evaluated should be used for criteria development. By basing criteria on the critical toxic effect, it is assumed that all toxic effects are prevented (USEPA, 1988). In the absence of such data, the lowest LOAEL dosage may be used for criteria development and an additional uncertainty factor for LOAEL to NOAEL extrapolation is applied. When two or more studies of equal quality and relevance exist, the geometric means of the NOAELs or LOAELs may be used.

Often a chemical may elicit multiple effects, each with a different NOAEL and LOAEL. From among these effects, the Agency selects a critical endpoint. The critical endpoint is the effect that exhibits the lowest LOAEL (USEPA, 1988).

2.2.5 Deriving RfD Using the NOAEL/LOAEL Approach

The IRIS background document (USEPA, 1988) describes methods used to derive an RfD for a given chemical and criteria for selection of the critical NOAEL or LOAEL. Appropriate uncertainty factors (UF) and modifying factors (MF) are then applied to the selected endpoint to derive the RfD.

The general equation for deriving the RfD is (USEPA, 1988):

$$\text{RfD (mg/kg-day)} = \frac{\text{NOAEL}}{\text{UF} * \text{MF}} \text{ or } \frac{\text{LOAEL}}{\text{UF} * \text{MF}}$$

(Equation 2.2.1)

where:

NOAEL = An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of observed adverse effects between the exposed population and its appropriate control; *some effects may be produced at this level, but they are not considered as adverse, nor precursors to specific adverse effects.*

LOAEL = The lowest experimental exposure level at which there are statistically or biologically significant increases in frequency or severity of observed adverse effects between the exposed population and its appropriate control group. The LOAEL may be used if the NOAEL cannot be determined.

UF = An uncertainty factor which reduces the dose to account for several areas of scientific uncertainty inherent in most toxicity data bases. Standard UFs are used to account for variation in sensitivity among humans, extrapolation from animal studies to humans, and extrapolation from less than chronic NOAELs to chronic NOAELs. An additional UF may be employed if a LOAEL is used to define the RfD.

MF = A modifying factor, to be determined using professional judgment. The MF provides for additional uncertainty not explicitly included in UF, such as completeness of the overall data base and the number of species tested. (The value for MF must be greater than zero and less than or equal to 10; the default value for the MF is 1).

The RfD is generally expressed in units of milligrams per kilogram of body weight per day (mg/kg-day).

2.2.5.1 Selection of Uncertainty Factors and Modifying Factors

The choice of appropriate UFs and MFs must be a case-by-case judgment by experts and should account for each of the applicable areas for uncertainty and nuances in the available data that impact uncertainty. Several reports describe the underlying basis of UFs (Zielhuis and van der Kreek, 1979; Dourson and Stara, 1983) and research into this area (Calabrese, 1985; Hattis et al., 1987; Hartley and Ohanian, 1988; Lewis et al., 1990; Dourson et al., 1992).

The uncertainty factors (UFs) summarized in Table 2.2.1 account for five areas of scientific uncertainty inherent in most toxicity data bases: inter-human variability (H) (to account for variation in sensitivity among the members of the human population); experimental animal-to-human extrapolation (A); subchronic to chronic extrapolation (S) (to account for uncertainty in extrapolating

from less-than-chronic NOAELs (or LOAELs) to chronic NOAELs); LOAEL to NOAEL extrapolation (L); and data base completeness (D) (to account for the inability of any single study to adequately address all possible adverse outcomes). Each of these five areas is generally addressed by the Agency with a factor of 1, 3, or 10. The default value is 10.

In addition, a modifying factor (MF) may be used to account for areas of uncertainty that are not explicitly considered using the standard UF. This value of the MF is greater than zero and less than or equal to 10, but it should generally be used on a log 10 basis (i.e., 0.3, 1, 3, 10) as are the standard UFs. The default value for this factor is 1.

Table 2.2.1: Uncertainty Factors and the Modifying Factor

Uncertainty Factor	Definition
UF_H	Use a 1-, 3-, or 10-fold factor when extrapolating from valid data in studies using long-term exposure to average healthy humans. This factor is intended to account for the variation in sensitivity (intraspecies variation) among the members of the human population.
UF_A	Use an additional 1-, 3-, or 10-fold factor when extrapolating from valid results of long-term studies on experimental animals when results of studies of human exposure are not available or are inadequate. This factor is intended to account for the uncertainty involved in extrapolating from animal data to humans (interspecies variation).
UF_S	Use an additional 1-, 3-, or 10-fold factor when extrapolating from less-than-chronic results on experimental animals when there are no useful long-term human data. This factor is intended to account for the uncertainty involved in extrapolating from less-than-chronic NOAELs to chronic NOAELs.
UF_L	Use an additional 1-, 3-, or 10-fold factor when deriving an RfD from a LOAEL, instead of a NOAEL. This factor is intended to account for the uncertainty involved in extrapolating from LOAELs to NOAELs.
UF_D	Use an additional 1-, 3-, or 10-fold factor when deriving an RfD from an "incomplete" data base. Missing studies, e.g., reproductive, are often encountered with chemicals. This factor is meant to account for the inability of any study to consider all toxic endpoints. The intermediate factor of 3 (½ log unit) is often used when there is a single data gap exclusive of chronic data. It is often designated as UF_D.

Modifying Factor

Use professional judgment to determine the MF, which is an additional uncertainty factor that is greater than zero and less than or equal to 10. The magnitude of the MF depends upon the professional assessment of scientific uncertainties of the study and data base not explicitly treated above (e.g., the number of species tested). The default value for the MF is 1.

Note: With each UF or MF assignment, it is recognized that professional scientific judgment must be used.

The Agency's reasoning in its use of the MF is that the areas of scientific uncertainty labeled H, A, S, L, or D do not represent all of the uncertainties in the estimation of an RfD. For example, the fewer the number of animals used in a dosing group, the more likely it is that no adverse effect will be observed at a dose point which may have had an effect in a larger population. Such a case might argue for modifying the usual 10-fold factors—a 100-fold UF might be raised to 250 if too few animals were used in a chronic study. While this increase is scientifically reasonable, it introduces two difficulties: the adjustments applied could differ between risk assessors, and the applied precision of the result might not be justified by the data. For example, a UF of 250 has an implied precision of 2 digits and is not appropriate in relation to the variability of the biological response. The Agency intends to avoid these difficulties through limiting the options for the modifying factor (1, 3, 10).

In practice, the magnitude of the overall UF is dependent on professional judgment as to the total uncertainty in all areas. When uncertainties exist in one, two or three areas, the Agency generally uses 10-, 100-, and 1,000-fold UF respectively. When uncertainties exist in four areas, the Agency generally uses an UF no greater than 3,000. It is the Agency's opinion that toxicity data bases that are weaker and would result in UFs in excess of 3,000 are too uncertain as a basis for quantification. In such cases, the Agency does not estimate an RfD, and additional toxicity data are sought or awaited. For a few chemicals, an UF of 10,000 was applied. However, in such cases, the risk assessment was completed before current policies for the maximum UF were in place.

The Agency occasionally uses a factor of less than 10 or even a factor of 1, if the existing data reduce or obviate the need to account for a particular area of uncertainty. For example, the use of a 1-year rat study as the basis of an RfD may suggest the use of a 3-fold, rather than 10-fold, factor to account for subchronic to chronic extrapolation, since it can be empirically demonstrated that 1-year rat NOAELs are generally closer in magnitude to chronic values than are 3-month NOAELs (Swartout, 1990). Lewis et al. (1990) more fully investigate this concept of variable uncertainty factors through an analysis of expected values.

The modification of UFs from their standard values should follow the general guidelines for composite UFs and the overall precision of one digit for UFs. The composite uncertainty factor to use with a given data base is again strictly a case-by-case judgment by experts. It should be flexible enough to account for each of the applicable five areas of uncertainty and any nuances in the available data that might change the magnitude of any factor. The Agency describes its choice for the composite UF and sub-components for individual RfDs on its Integrated Risk Information System (IRIS). Because of the high degree of judgment involved in the selection of uncertainty and MFs, the risk assessment justification should include a detailed discussion of the selection of uncertainty factors, along with the data to which they are applied.

2.2.5.2 Confidence in NOAEL/LOAEL-Based RfD

As stated previously, when available, adequate data from acceptable human studies should be used as the basis for the RfD. Use of good epidemiology studies generally give the highest

confidence in RfDs. In the absence of such data, RfDs are estimated from studies in experimental animals.

The Agency generally considers a "complete" data base for calculating a chronic RfD for noncancer health effects to include the following:

- Two adequate mammalian chronic toxicity studies, by the appropriate route in different species, one of which must be a rodent.

- One adequate mammalian multi-generation reproductive toxicity study by an appropriate route.

- Two adequate mammalian developmental toxicity studies by an appropriate route in different species.

For a "complete" data base, the likelihood that additional toxicity data may change the RfD is low. Thus, the Agency usually has confidence in such an RfD because additional toxicity data are not likely to change the value.

The Agency considers a NOAEL from a well-conducted, mammalian subchronic (90-day) study by the appropriate route as a minimum data base for estimating an RfD. However, for such a data base, additional toxicity data may change the RfD. Thus the Agency generally has less confidence in such an RfD.

For some chemicals, an acute health hazard is the critical effect of concern. These could include neurotoxic or immunotoxic effects of acute exposures at environmental levels of contaminant. In such cases, longer term studies (subchronic or chronic) that would typically be included in a review of the toxicity literature may not capture the critical endpoint. Under such circumstances, greater emphasis should be placed on characterizing the acute threshold as opposed to the potential chronic effects.

Developmental toxicity data, if they constitute the sole source of information, are not considered an adequate basis for chronic RfD estimation. This is because such data are often generated from short-term chemical exposures, and, thus, are of limited relevance in predicting possible adverse effects from chronic exposures. However, if a developmental toxicity endpoint is the critical effect established from a "complete" data base, a chronic RfD can be derived from such data, applying the uncertainty and MFs normally required. Developmental data are the basis for developmental reference doses (RfD_{DT}).[11] The term RfD_{DT} is used to distinguish the developmental value from the chronic RfD which refers to chronic exposure situations. Uncertainty factors for developmental toxicity include a 10-fold factor for interspecies variation and a 10-fold factor for

[11]A RfD for developmental toxicity (RfD_{DT}) is discussed in USEPA (1991a).

intraspecies variation; in general, an uncertainty factor is not applied to account for duration of exposure. In some cases, additional factors may be applied due to a variety of uncertainties that exist in the data base. For example, the standard study design for developmental toxicity study calls for a low dose that demonstrates a NOAEL, but there may be circumstances where a risk assessment must be based on the results of a study in which a NOAEL for developmental toxicity was not identified. For details regarding risk assessment for developmental toxicants, refer to EPA risk assessment guidelines (USEPA, 1991b).

2.2.5.3 Presenting the RfD as a Single Point or as a Range

Although the RfD has traditionally been presented and used as a single point estimate, its definition contains the phrase ". . . an estimate (with uncertainty spanning perhaps an order of magnitude) . . ." (USEPA, 1988). Underlying this concept is the reasoning that during the derivation of the RfD, the selection of the critical effect and of the total uncertainty factor is based on the "best" scientific judgment of the Agency Work Group and that other groups of competent scientists examining the same database would reach a similar conclusion, within an order of magnitude. For example, although EPA recently verified a single number as the RfD for arsenic (0.3 µg/kg-day), there was not a clear consensus on the oral RfD. Applying the Agency's RfD methodology, "strong scientific arguments can be made for various values within a factor of 2 or 3 of the currently recommended RfD value, i.e., 0.1 to 0.8 µg/kg/day" (USEPA, 1993).

Presenting the RfD as a range may be more appropriate than expressing it as a point estimate because rarely are sufficient data available to precisely determine a lifetime threshold for a human. Even when there are good, reliable data, the variability of response in the human population argues for expressing the RfD as a range. However, although EPA supports the use of a range that spans one order of magnitude for most RfDs, there are a number of potential interpretations of the term "order of magnitude" as described below:

- **Range = x to 10x.** (where point estimate of RfD=x). This view is supported by those who believe that the risk assessment process is so inherently conservative that the RfD should be considered to be the lowest estimate, with the range of imprecision all resting <u>above</u> this point estimate.

- **Range = 0.3x to 3x.** This view is held by many EPA scientists who have developed RfDs. The RfD point estimate, x, is the midpoint of a range that spans an order of magnitude.

- **Range = 0.1x to x.** This is the view held by many risk managers. Regulatory decisions (e.g., setting of standards or cleanup levels) are made based on the assumption that standards or cleanup levels are protective as long as they do not exceed the RfD.

- **Range = 0.1x to 10x.** This range represents the assumption that the order of magnitude range could be on either side of the point estimate x.

The Agency is considering a risk management approach where the upper and lower bounds of the range are correlated to the uncertainty. Because the uncertainty around the dose response relationship increases as extrapolation below the observed data increases, the use of a range for the RfD may be more appropriate in characterizing risk than the use of a point estimate. Therefore, as a matter of risk management policy, it is proposed that if the product of the UFs and MF used to derive the RfD is 100 or less, there would be no consideration of a range. When greater than 100 but less than 1,000, the maximum range that could be considered would be one half of a $\log_{10}$ (3-fold) or a number ranging from the point estimate divided by 1.5 to the point estimate multiplied by 1.5. At 1,000 and above the maximum range would be a $\log_{10}$ (10-fold) or a number ranging from the point estimate divided by 3 to the point estimate multiplied by 3.

EPA advocates the use of the point estimate of the RfD as the default to derive the AWQC. The use of another number within the range defined by the uncertainty would then have to be justified. As used in this document, justification means that there are scientific data which indicate that some value in the range other than the point estimate may be more appropriate than the point estimate, based on human health or environmental fate considerations. Table 2.2.2 gives examples of some factors to consider when determining whether to use the point estimate of the RfD or values higher or lower than the point estimate. The factors presented in Table 2.2.2 should be considered in making the decision as to whether or not to use a value other than the point estimate within a range; the uncertainty will influence the magnitude of the range.

Table 2.2.2: Some Scientific Factors to Consider When Using the RfD Range

Use point estimate RfD	- Default position - Total UF/MF product is 100 or less - Essential nutrient
Use lower range of RfD	- Increased bioavailability from medium - The seriousness of the effect and whether or not it is reversible - A shallow dose-response curve in the range of observation - Exposed group contains a sensitive population (e.g., children or fetuses)
Use upper range of RfD	- Decreased bioavailability with humans - RfD based on minimal LOAEL and a UF/MF of 1,000 or greater - A steep dose-response curve in the range of observation - No sensitive populations identified

The use of an order of magnitude may not be appropriate for all chemicals. There are many factors that can affect the degree of "precision" of the RfD, and thereby affect the magnitude of the RfD range. The completeness of the data base plays a major role. Observing the same effects in several animal species, including humans, can increase confidence in the RfD point estimate and thereby narrow the range of uncertainty. Other factors that can affect the precision are the slope of the dose-response curve, seriousness of the observed effect, spacing of doses, and the route of exposure. For example, a steep dose-response curve indicates that relatively large differences in effect occur with a given change in dose; thus, there will be a greater chance that the data will allow scientists to distinguish clearly (i.e., statistically) between doses that produce an effect and those that do not. For a situation where the RfD is derived from a LOAEL for a serious effect, an additional uncertainty factor is often used in the RfD derivation to protect against less serious effects that could have occurred at lower doses had lower doses been evaluated. Dose spacing and the size of the study groups used in the experiment can also affect the confidence in the RfD. The "true" NOAEL can fall anywhere between the experimentally determined NOAEL (the highest dose administered without an adverse effect) and the LOAEL (the lowest dose administered causing an observable adverse effect). The wider the dose spacing, the greater the margin of uncertainty about where the "true" NOAEL may fall. Finally, for some RfDs, the route of exposure in the experiment may not match the route of exposure in the environment, and interroute extrapolation may be considered using assumptions about differences in absorption rates between routes.

There are cases when a range should not be used. For example, the RfD for zinc (USEPA, 1992) is based on consideration of nutritional data, a minimal LOAEL, and a UF of 3. If the factor of 3 were used to bound the RfD for zinc, then the upper-bound level would approach the minimal LOAEL. This situation must be avoided, since it is unacceptable to set a standard at levels that may cause an adverse effect. The risk manager must be informed of those specific cases when it is not scientifically correct to use the RfD range. Table 2.2.2 provides managers with guidelines on the scientific basis for using the range.

2.2.6 Deriving an RfD Using a Benchmark Dose Approach

A number of issues have been raised regarding the development of the RfD based on the traditional NOAEL/LOAEL approach. These concerns include the following:

- The traditional approach does not incorporate information on the shape of the dose-response curve, but focuses only on a single point (the NOAEL or LOAEL).

- The value of the NOAEL depends on the number and spacing of the doses in the experiment. The possible NOAEL values are limited to the discrete values of the experimental doses. Theoretically, the experimental no adverse effect level could be any value between the experimental NOAEL and the LOAEL, and typically the true NOAEL is below the observed NOAEL.

- Data variability is not directly taken into account. For example, studies based on a larger number of animals may detect effects at lower doses than studies with fewer animals; as a result, the NOAEL from a small study may be higher than the NOAEL from a similar but larger study in the same species. The traditional approach does not have a mechanism to account for such data variability.

- The determination of the NOAEL is dependent on the background incidence of the effect in control animals; therefore, statistically significant differences between the dose groups and the control group are more difficult to detect if background incidence is relatively high, even if biologically significant effects occur.

- In conjunction with exposure data, the NOAEL-based RfD can be used to estimate the size of the population at risk, but not the magnitude of the risk.

In response to these concerns, alternative approaches have been developed that attempt to address some of these shortcomings. One such alternative, the BMD approach, has been the subject of extensive research over the past decade (Crump 1984, 1995; Gaylor, 1983, 1989; Dourson et al., 1985; Brown and Erdreich, 1989; Kimmel, 1990; Faustman et al., 1994; Allen et al., 1994a, 1994b). The following discussion presents the general methods for calculation of a RfD using the BMD approach; for more extensive discussion, the reader is referred to Crump et al. (1995). To date, the Agency has used the BMD approach for deriving the RfD for methyl mercury (USEPA, 1994a) and the RfC for several compounds.

2.2.6.1 Overview of the Benchmark Dose Approach

A benchmark dose (BMD) or concentration (BMC) is defined as a statistical lower confidence limit on the dose producing a predetermined level of change in response (the benchmark response-BMR) relative to controls The BMD/BMC is intended to be used as an alternative to the NOAEL in deriving a point of departure for low dose extrapolations. The BMD/BMC is a dose corresponding to some change in the level of response relative to background and is not dependent on the doses used in the study. The BMR is based on a biologically significant level of response or on the response level at the lower detection limit of the observable dose range for a particular endpoint in a standard study design. The BMD/BMC approach does not reduce uncertainty inherent in extrapolating from animal data to humans (except for that in the LOAEL to NOAEL extrapolation), and does not require that a study identify a NOAEL, only that at least one dose be near the range of the response level for the BMD/BMC.

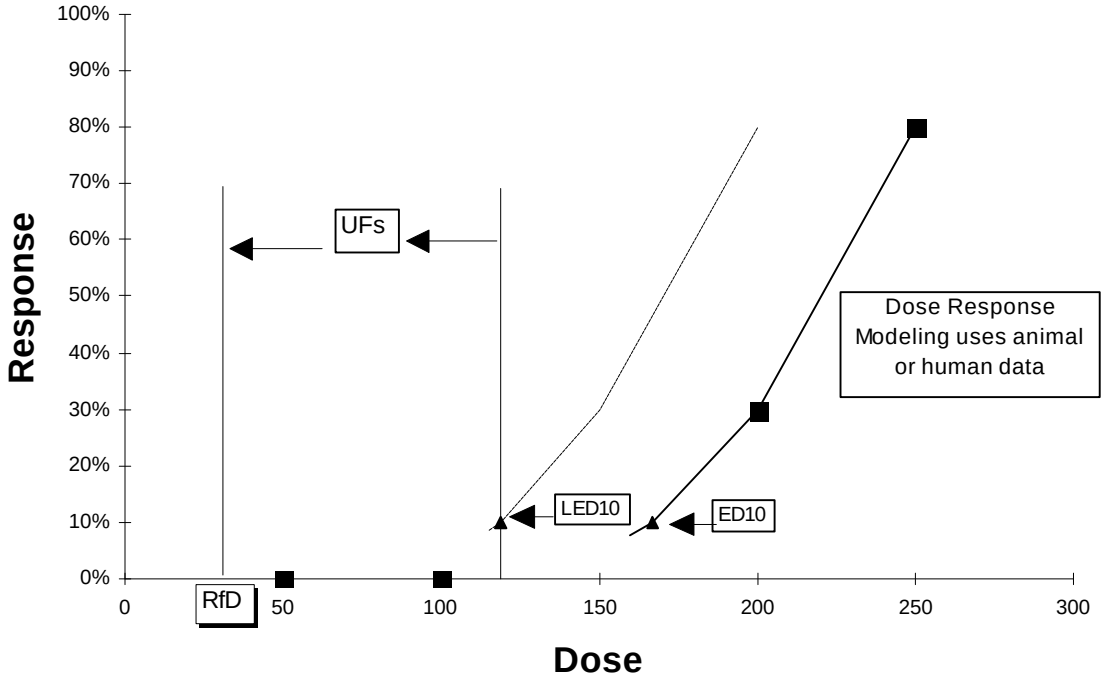
The central step in deriving a BMD is to calculate lower bounds directly on the dose estimate. This modeling process is limited to the experimental range and no attempt is made to extrapolate to doses far below the experimental range. Generally, the models used in the BMD approach are statistical rather than biologically-based models; thus, they cannot be reliably used to extrapolate to low doses without incorporating detailed information on the mechanisms through which the toxic agent causes the particular effect being modeled.

Once a mathematical dose-response curve and its corresponding curve of confidence limits are established, the assessor selects a point on the lower confidence dose curve corresponding to the chosen BMR (e.g., 1 percent, 5 percent, or 10 percent increase in the incidence of an effect). This point on the lower confidence curve is the lower confidence bound of the effective dose for that BMR (denoted as the BMD) (see Exhibit 2.2.1). A BMD may be calculated for each agent for which there is an adequate data base.

The BMD approach offers a number of advantages over the traditional approach for the derivation of the RfD from the NOAEL/LOAEL divided by uncertainty factors. The advantages of the BMD approach are that it considers the dose-response curve, including its shape; better accounts for statistical variability in the data; is not overly sensitive to dose spacing and, thus, is not limited to experimental doses for determining the effect level. In addition, studies with small group sizes and evaluation of a limited number of endpoints, which may identify artificially high NOAELs, will tend to yield lower BMD values because the confidence bands will be wider. The BMD analyses for developmental effects shows that the NOAELs from studies are actually at about a 5 percent response level (Faustman et al., 1994). Therefore, the BMD approach provides an incentive to conduct more robust studies, since better studies give narrower confidence bands.

Exhibit 2.2.1

Derivation of RfD Using BMD Approach



2.2.6.2 Calculation of the RfD Using the Benchmark Dose Method

The determination of an RfD using the BMD approach involves four basic steps. The first step involves the selection of the experiments and responses that will be used for modeling the BMD. Second, BMDs are calculated for the selected responses; BMD values should be calculated for all endpoints that have the potential for yielding the critical BMD. Third, a single BMD is selected from among those calculated. Finally, the RfD is calculated by dividing the chosen BMD by appropriate uncertainty factors. The decision points associated with these steps are outlined in Table 2.2.3. The discussion below summarizes the critical issues unique to the BMD approach. The following discussion of the issues largely incorporates the information from Crump et al. (1995).

Table 2.2.3: Steps and Decisions Required in the BMD Approach

Step	Decisions
1. Selection Study/Response	**1. Experiments to include** **2. Responses to model**
2. Model dose-response	**1. Format of data** **2. Mathematical model(s)** **3. Handling model fit** **4. Measure of altered response**
3. Select BMD(s)	**1. Critical BMR** **2. Confidence limit calculation**
4. Calculate RfD	**1. Uncertainty factors**

Source: Crump et al., 1995

Selection of Response Data to Model

The selection of experiments and responses suitable for BMD modeling involves considerations similar to those for identifying the appropriate studies upon which to base a NOAEL. There may be several appropriate studies and relevant health effects that could be modeled for a chemical. Ideally, BMD calculations would be performed for the complete set of relevant effects. However, utilizing all relevant responses for the calculation of BMDs may be resource-intensive. Further, it is difficult to interpret results from a large number of dose-response analyses. When selecting the data to model it is often considered appropriate to limit attention to those responses for

which there is evidence of a dose-response relationship. Statistically, such a relationship may be indicated by significant trends (either increasing or decreasing) in the response as dose level increases. Considerations of biological significance may also be warranted. Another alternative is to focus efforts on modeling the most critical effects as seen at the LOAEL. However, limiting the number of responses modeled may potentially misrepresent the minimum BMD.[12]

Use of Categorical Versus Continuous Data

A central issue in the selection of data to model concerns the form of the data used. Categorical data, particularly quantal data, are relatively straightforward to use in the BMD approach, since the data are expressed as the number (or percent) of subjects exhibiting a defined response at a given dose. Data may also be of the continuous form, where results are expressed as the measure of a continuous biological endpoint, such as a change in organ weight or serum enzyme level. With continuous data the results are generally presented in terms of means and standard deviation for dose groups but are most valuable when data for individual animals are available. To perform dose-response modeling of such data, the way the data are expressed must be decided. Continuous data can be modeled by looking at the mean response for each dose group as a fraction of the mean response of the control group or as the percentage of animals showing an adverse response at each dose level. (Gaylor and Slikker, 1990; Crump, 1995). Such approaches take advantage of the continuous nature of the response data, but express the results in terms that are directly comparable to those derived from analysis of categorical data, i.e., in terms of additional or extra risk, rather than in terms of changes in mean response. In particular, Crump (1995) has extended those considerations so that the model used for analysis of a continuous endpoint yields the same model type as used for analysis of any quantal endpoints. Such developments have enhanced the consistency of results across different endpoints for any particular chemical. In any case, application of the BMD approach to continuous data requires professional judgment in order to determine what level or category of response constitutes an abnormal (adverse) effect. The BMD approach is not recommended for routine use but may be used when data are available and justify the extensive analyses required.

Choice of Mathematical Model

Various mathematical approaches have been proposed for determining the BMD. Table 2.2.4 shows a number of dose-response models that may be used for estimating the BMD with quantal or continuous data.

Information generally required for application of dose-response models for categorical (including quantal) data includes the experimental doses, the total number of animals in each dose group, and the number of these whose responses are in each of the categories of response. For continuous data, the experimental doses, number of animals in each dose group, mean response in each group, and sample variance of response in each dose group are needed.

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[12]This is due to the fact that an effect seen only at doses above the LOAEL but having a shallow dose-response could produce a lower BMD than an effect seen at the LOAEL, which has a steeper dose-response.

The BMD approach should not be applied to data sets with only two experimental groups (a control and one positive dose). In such cases, much of the advantage of the BMD approach with respect to consideration of the dose-response shape will be lost; such data supply little information about the shape of the dose-response curve. The more doses available, especially at lower doses, the greater the expected benefit of the BMD approach as compared to the NOAEL-based approach.

Table 2.2.4: Dose-Response Models Proposed for Estimating BMDs

Model	Formula
Quantal Data	
Quantal linear regression (QLR)	$P(d) = c + (1-c)\{1-\exp[-q_1(d-d_0)]\}$
Quantal quadratic regression (QQR)	$P(d) = c + (1-c)\{1-\exp[-q_1(d-d_o)^2]\}$
Quantal polynomial regression (QPR)	$P(d) = c + (1-c)\{1-\exp[-q_1d_1-...q_kd^k]\}$
Quantal Weibull (QW)	$P(d) = c + (1-c)\{1-\exp[-q_1d^k]\}$
Log-normal (LN)	$P(d) = c + (1-c)N(a+b \log d)$
Continuous data	
Continuous linear regression (CLR)	$m(d) = c + q_1(d-d_0)$
Continuous quadratic regression (CQR)	$m(d) = c + q_1(d-d_0)^2$
Continuous linear-quadratic regression (CLQR)	$m(d) = c + q_1d+q_2d^2$
Continuous polynomial regression (CPR)	$m(d) = c + q_1d+...+q_kd^k$
Continuous power (CP)	$m(d) = c + q_1(d)^k$

Notes: P(d) is the probability of a response at the dose, d; m(d) is the mean response at the dose, d. In all models, c, $q_1,...q_k$, and d_o are parameters estimated from the data. For the quantal models, $0 \le c \le 1$ and $q_i \ge 0$. For the CPR model proposed by Crump (1984), all the q_i have the same sign. In the CLQR model discussed by Gaylor and Slikker (1990), q_1 and q_2 were not constrained to have the same sign. For all models, $d_0 \ge 0$, $k \ge 1$. N(x) denotes the normal cumulative distribution function.

SOURCE: Crump et al., 1995.

Fitting the models to experimental data gives estimates of the parameters that describe each model. This fitting, usually accomplished through maximum likelihood methods, estimates the probability of response (for quantal data) or the mean response (for continuous data) for each dose level. Goodness-of-fit tests can be used to determine if a model adequately describes the dose-response data.

In many cases, several models may fit the data well. In these cases, other considerations can be used to select an appropriate model. For example, the statistical assumptions underlying the model should be reasonable for the given data. Quantal results, for example, are assumed to follow a binomial distribution around a dose-dependent expected value. This assumption requires that each subject responds independently and all have an equal probability of responding. Continuous responses for each dose level are assumed to follow a normal distribution and are also assumed to be independent. When biological factors may be important (e.g., intralitter correlation for developmental toxicity data) they may also be used to select appropriate models. Another biological consideration may be whether or not a threshold is assumed to exist. If a threshold is expected for the given effect, then a model that allows for a threshold dose may be chosen for modeling. The biological plausibility of the dose-response curve shape should also be a consideration in model selection.

Even with these considerations, several different models may often adequately describe the data. In these cases, the choice of the model may not be critical, especially since the estimation will be confined to the observed dose range. Thus, any model that suitably fits the empirical data is likely to provide a reasonable estimate of a BMD.

In certain data sets, none of the standard models may provide a reasonable fit to the data. Fit is assessed statistically by comparing the model predictions to the observations. Goodness-of-fit statistics formalize that comparison and provide p-values, ranging between 0 and 1, as a measure of fit. When using a χ^2 statistic, larger p-values are indicative of good fit; smaller p-values of poorer fit. Sufficiently small p-values (e.g., less than 0.01 or 0.05) are typically viewed as an indication that the model was not adequate for describing the observed dose-response pattern.

Poor fit is often due to reduced responses at higher doses that are inconsistent with the dose-response trend for lower doses, perhaps due to competing toxic processes or saturation of metabolic systems related to the toxic response of interest. Several procedures can be used to adjust the modeling process in these circumstances. For example, responses at the highest doses could be eliminated, since those doses are usually least informative of responses in the lower dose region of interest. In the case of saturated metabolic pathways, pharmacokinetic data can be used to estimate delivered dose to the organ of interest. The BMD modeling can then be conducted on the delivered dose. (Andersen et al., 1987, 1993; Gehring et al., 1978).

A particularly valuable exercise with respect to all of these fit issues is a visual (graphical) examination of the model predictions in relation to the observations. This supplements the formal

statistical assessment of fit and may, in fact, be equally or more informative. The statistical test assesses overall fit. For the purposes of BMD estimation, fit is most crucial in and around the response level used to define the BMD (i.e., the BMR). Thus, for example, models that have similar fits to the entire data set may differ with respect to their predictions near the BMR, and it may be possible to select one over another on the basis of that more local behavior.

Measure of Altered Response

Crump (1984) proposed two measures of increased response for quantal data. These are additional risk and extra risk. Additional risk is simply the probability of response at dose d, P(d), minus the probability of response at zero dose (control response), P(0). It describes the additional proportion of animals that respond in the presence of a dose. Extra risk is additional risk divided by [1-P(0)]. It describes the additional proportion of animals that respond in the presence of a dose, divided by the proportion of animals that would not respond under control conditions. These measures are distinguished in the way they account for control responses. For example, if a dose increases a response from 0 to 1 percent, both the additional risk and the extra risk is 1 percent. However, if a dose increases risk from 90 to 91 percent, the additional risk is still 1 percent, but the extra risk is 10 percent. The choice of extra risk versus additional risk is based to some extent on assumptions about whether an agent is adding to the background risk. Extra risk is viewed as the default because it is more conservative.

Analogous measures of risk have been proposed for continuous data (Crump, 1984). First, altered response can be expressed as the difference between the mean response to dose d minus the mean control response. The second measure is simply the difference between dose and control means divided by (i.e., normalized by) the control mean response. The second measure expresses change as a fraction of the control response rather than as an absolute change.

More recent consideration of BMDs for continuous endpoints have suggested other alternatives. Allen et al. (1994a, 1994b) and Kavlock et al. (1995) determined that normalizing changes in mean responses by a multiple of the background standard deviation produced BMDs that were comparable, on average to NOAELs. For the developmental endpoints that those investigators studied, the preferred multiple for the standard deviation was 0.5.

It is not clear when measures of risk expressed relative to the background (e.g., extra risk) are preferable to measures expressed as absolute changes. Additional research is required to provide guidance regarding the measure of altered response that is most appropriate in particular circumstances.

Selection of the BMR

A critical decision for deriving the BMD is the selection of the Benchmark level of risk (BMR). Since the BMD is used like a NOAEL in the derivation of the RfD, the BMR should be selected near the low end of the range of increased risks that can be detected in a bioassay of typical size. The ED_{10} is frequently chosen as the BMR. The ED_{10} is the dose predicted to cause a 10 percent increase in the incidence of the effect in the test population. For some data, it may be possible to adequately estimate the ED_{05} or ED_{01}, which are closer to a true no-effect dose. Levels between the ED_{01} and the ED_{10} are usually the lowest levels of risk that can be estimated adequately for binomial endpoints from standard toxicity studies (Crump, 1984). Another consideration is the goal of model independence. Different dose-response models may fit the data equally well yet give very different estimates of risk far below the observable range (Crump, 1984). This argues for use of a BMR close to the range of responses that can be reliably measured in typical studies.

During a BMD Workshop, sponsored by EPA, participants generally agreed that the appropriate BMR should either be 5 percent or 10 percent, but acknowledged that future research might demonstrate the advisability of selecting one value over another (ILSI, 1993). Research by Allen et al. (1994a, 1994b) and Faustman et al. (1994) indicates that BMDs defined in terms of 10 percent increases in probability of response tend to be, on average, similar to corresponding NOAELs for quantal developmental toxicity studies. For the purposes of water quality criteria derivation, EPA recommends the use of the ED_{05} or ED_{10} when deriving a BMD.

Calculating the Confidence Interval

The BMD is defined to be the lower confidence bound on the dose corresponding to the selected BMR. A statistical lower confidence limit is used rather than a maximum likelihood estimate (MLE) for several reasons. The use of confidence limits accounts for the sample size of the experiment; the fact that NOAELs do not account for sample size is a major criticism of NOAEL-based derivation of the RfD. Furthermore, a lower confidence limit is more stable to minor changes in data and, rarely, may be estimable where a MLE is not.

To calculate the upper confidence bound on response, and subsequently, the lower bound on effective dose, decisions must be made regarding the selection of the procedure for calculating confidence limits and the size of the confidence limits.

The recommended method used to calculate the confidence bounds on the curve relies on maximum likelihood theory. This approach is the same one used by EPA in the computer program for cancer dose-response modeling. The approach can be applied to BMD modeling using commercially available software. A detailed explanation of theory supporting this approach is found in Crump (1984).

By convention, the size of the statistical confidence limits can range from 90 to 99 percent. The methods of confidence limit calculation and choice of confidence limits are critical. The Agency

recommends the use of one-sided 95th percentile confidence limits for BMD modeling. This is consistent with the size of the confidence limits used in cancer dose-response modeling.

Selection of the BMD As the Basis for the RfD

An important decision is the choice of the appropriate BMD to use in the RfD calculation when multiple BMDs are calculated. Multiple BMDs can be calculated when different models fit the response data for a single study, when more than one response is modeled in a single study, and when there are different BMDs from different studies. When multiple BMDs exist because several models fit a single data set, the analyst may select the smallest BMD or combine BMDs by using the geometric average. When multiple BMDs are calculated due to different responses or different studies that examine the same endpoint, the choice among BMDs may also involve the selection of the "critical effect" and the most appropriate species, sex, or other relevant feature of experimental design.

Use of Uncertainty Factors with BMD Approach

Once a single or averaged BMD is selected, the RfD can be calculated by dividing the BMD by one or more uncertainty factors. It is still necessary to use uncertainty factors with a BMD, because the BMD can miss sensitive subpopulations and is still subject to interspecies extrapolation uncertainties. As a default, all applicable uncertainty factors used in the traditional NOAEL-based RfD approach, except for the LOAEL-NOAEL extrapolation factor, should be retained. Other factors, such as the size of the BMR and confidence bounds, biological considerations (such as the possibility of a threshold), severity of the modeled effect, and the slope of the dose-response curve, may affect the choice and magnitude of uncertainty factors (see Crump et al., 1995, for more detailed discussion).

2.2.6.3 Limitations of the BMD Approach

The BMD approach has been proposed as an alternative procedure that can be used until biologically motivated approaches are available for some or all effects. It provides specific improvements over NOAEL-based approaches, but by no means does it resolve all issues or difficulties associated with noncancer risk assessment. The BMD approach allows for objective extrapolation of animal response data to human exposures across the different study designs encountered in noncancer risk assessment.

2.2.6.4 Example of the Application of the BMD Approach

The following provides a simple example of the application of the BMD approach to quantal toxicity data. The example given is taken from Crump et al. (1995) for acrylamide. The purpose of presenting this example is to illustrate the method only; no actual risk value nor AWQC for acrylamide is derived.

Selection of Data to Model

This example takes the approach of identifying a critical study rather than modeling all endpoints seen in valid studies. For this example, a 6-month dietary study of neurological effects in rats is used as the critical study for acrylamide (Johnson et al., 1986, as cited in Crump et al., 1995). The endpoint examined in this study was tibial nerve degeneration. The researchers recorded the occurrence of nerve degeneration in two categories: none or mild, and moderate or severe. Since mild nerve degeneration occurs spontaneously in older rats, and because mild degeneration showed no dose-response relationship, only moderate and severe degeneration were recorded as responses. The data are presented in quantal form, with no or mild degeneration considered "no response," and moderate to severe degeneration recorded as a response. The dose levels and number of animals responding in each dose group are shown in Table 2.2.5.

Table 2.2.5: Rats Experiencing Moderate or Severe Nerve Degeneration in Response to Acrylamide Dose

Dose (mg/kg-day)	Number affected	Number tested
0	9	60
0.01	6	60
0.1	12	60
0.5	13	60
2.0	16	60

Choice of Mathematical Model

From Table 2.2.4, we can select from among the various models available for quantal data. Fitting is accomplished through the use of maximum likelihood estimation to estimate the probability of a response at each dose level. The actual fitting exercise is done through the use of computer software.

Results of Information Above

All of the models can be tried to see which achieves the best fit. The following Exhibits illustrate the best-fit modeling of the study data for the Weibull model (Exhibit 2.2.2) and the quadratic model (Exhibit 2.2.3). Table 2.2.6 provides the best-fit model parameters for the two equations.

Exhibit 2.2.2 Quantal Weibull Regression - Extra Risk

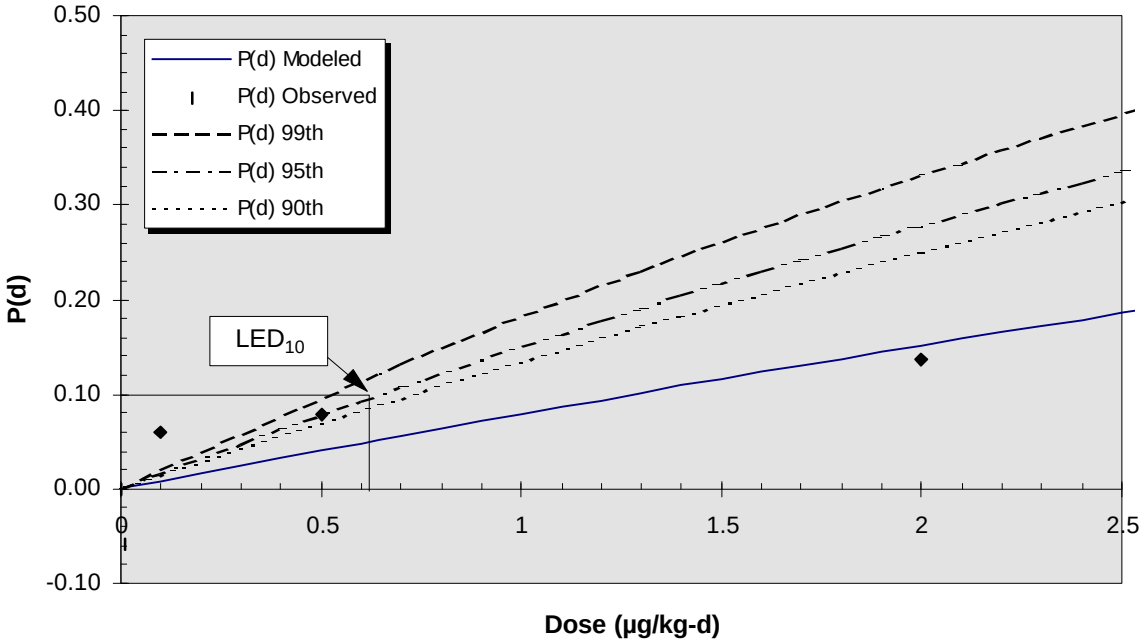

Exhibit 2.2.3 Quantal Quadratic Regression - Extra Risk

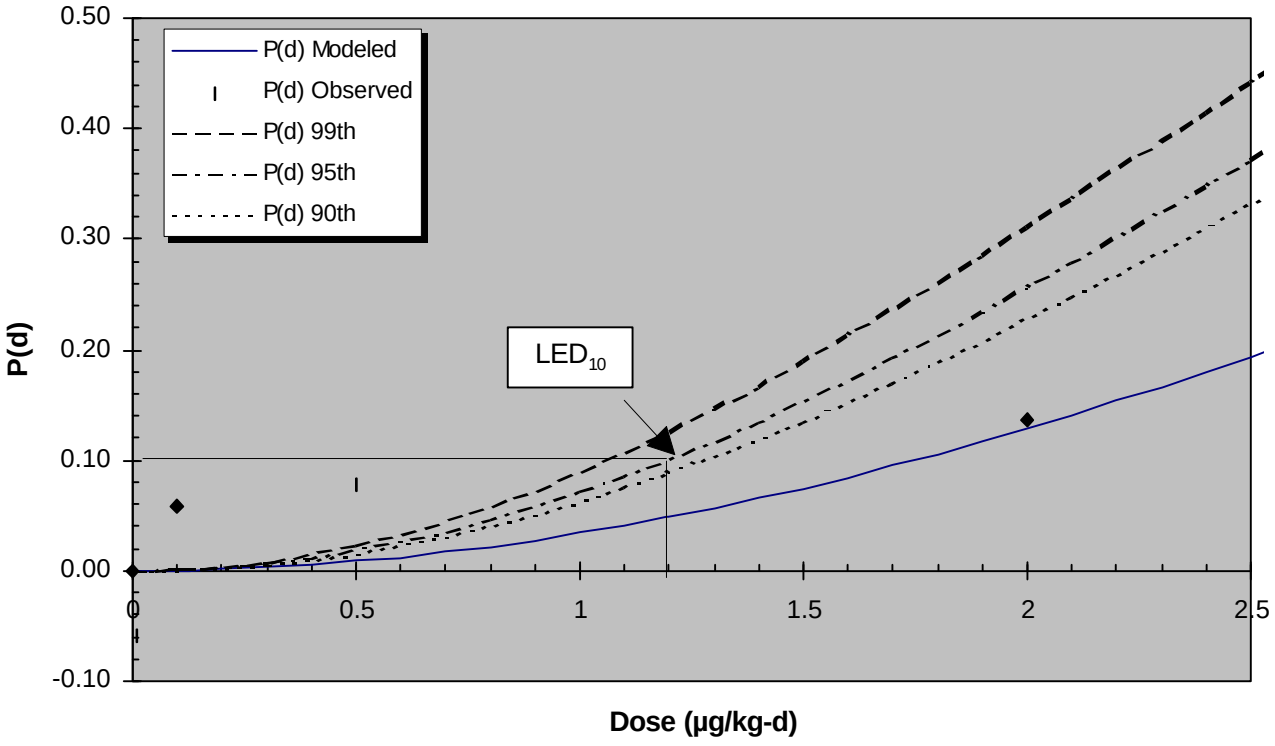

Table 2.2.6: Best-Fit Model Parameters from Modeling of the Acrylamide Data

Model	Background rate	q1	k	chi-square p value
Quantal Weibull	0.15	0.08	1	0.48
Quantal quadratic	0.16	0.034	--	0.34

Note that in example given here, the measure of altered response is extra risk, which is defined as:

$$ER(d) = [P(d) - (P(0)]/[1 - P(0)]$$

(Equation 2.2.2)

Extra risk is the fraction of animals that respond when exposed to a dose, d, among animals who otherwise would not respond.

Both models fit the data adequately as shown in Table 2.2.6. In both cases the chi-squared goodness of fit yields P-values greater than 0.05. Therefore, either model can be used for derivation of BMD. Neither model, as fitted to this data set, suggests a threshold for this response. However, both models do indicate a background rate in the absence of exposure to acrylamide.

Selection of the BMR

For the data set discussed above, the BMDs were calculated using the quantal Weibull and the quantal quadratic models for 1, 5, and 10 percent extra risk (Table 2.2.7 estimates are in units of mg/kg-day):

Table 2.2.7: BMD Values Calculated Using Quantal Weibull and Quadratic Models

Model	BMR	BMD (mg/kg-day) for Confidence Limit:		
		90th percentile	95th percentile	99th percentile
Weibull	10	0.73	0.64	0.52
	5	0.35	0.31	0.25
	1	0.07	0.06	0.05
Quadratic	10	1.28	1.19	1.06
	5	0.89	0.83	0.74
	1	0.39	0.37	0.33

The calculated BMDs are about a factor of two apart for the BMD_{10} values, but are about a factor of six apart for the BMD_1. This demonstrates the model dependence of the BMD values when low BMR levels are selected.

Calculating the Confidence Interval

As shown in Table 2.2.7, the BMDs were calculated for 90th, 95th, and 99th percentile confidence limits. The effect of the confidence limit on the estimated BMD was slightly less for the quantal quadratic than for the quantal Weibull. Model results were most comparable for the 90th and 95th percentile confidence limits and least comparable for the 99th percentile confidence limits. These results demonstrate that the BMD tends to be more model-dependent for wider (higher percentile) confidence intervals. For the remainder of the example, the 95th percentile confidence limit estimate is used.

Selection of the BMD as the Basis for the RfD

The example above yields different 95th percentile BMD_{10} values based on the two models. Since there is no basis upon which to eliminate one of the BMDs (i.e., goodness of fit, statistical assumptions and biological considerations), both must be considered. Either the smaller estimate may be used, or a geometric average may be used. In this case, the selection of which BMD to use is a risk management decision. In the example, the lower of the two BMDs (0.64) was chosen for the RfD calculation.

Use of Uncertainty Factors with BMD Approach

Once the BMD is chosen, the RfD is derived by dividing the BMD by uncertainty factors. The same uncertainty factors applied to a NOAEL are used. In this case a factor of 10 was selected for interspecies extrapolation and a factor of 10 for human interspecies variability. Using an total UF of 100 and applying it to the 95th percentile confidence limit BMD for 10 percent response derived with the quantal Weibull model yields an RfD of 0.006 mg/kg-day.

2.2.7 Categorical Regression

2.2.7.1 Summary of the Method

Categorical regression is another method under investigation to estimate risks associated with systemic toxicity (Dourson et al., 1997; Guth et al., 1997). In this approach, health effects are grouped into ordered severity categories (ranging from no effect to severe effect). This simplification allows for the incorporation into the analysis of both quantal and continuous data, as well as data that are reported qualitatively rather than quantitatively. Furthermore, information on many health effects can be considered together. Logistic regression analysis techniques are then applied to the data: the cumulative odds of falling into severity categories is the dependent variable, and exposure concentration, exposure duration, and other parameters are the independent variables. Using the regression results, the RfD is then specified as the dose at which the probability of adverse effects is sufficiently small at some level of confidence, modified, as in the NOAEL and BMD approaches, by appropriate uncertainty factors. For example, the dose of interest, D, might be defined as that dose for which one could conclude with 95 percent certainty that the probability of an adverse effect was less than 0.01. The value D would then be adjusted by uncertainty factors to derive the RfD.[13]

2.2.7.2 Steps in Applying Categorical Regression

The categorical regression approach begins with a review of the toxicological data base for the chemical. For each valid study, the toxic responses observed are assigned to one of several ordered severity categories, based on biological and statistical considerations. For example, responses may be grouped into four categories: (1) no effect; (2) no adverse effect; (3) mild-to-moderate adverse effect; and (4) severe or lethal effect. These correspond to the dose categories used in setting the RfD, namely the No Observed Effect Level (NOEL), NOAEL, LOAEL, and Frank Effect Level (FEL), respectively.

Since all response data are used in categorical regression analysis, there is no need to specify the lowest dose showing "mild-to-moderate" adverse effects. Accordingly, a more general term, adverse-effect level (AEL), is generally used in categorical regression in place of the term LOAEL to describe mild-to-moderate effects.

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[13]Note that the logistic regression could be used to estimate the response to exposures greater than the RfD. BMD models could be used similarly, but caution is warranted when doing so in either case.

The probability of observing a response in a category at a given dose level is estimated by dividing the number of responses observed in that severity category divided by the total number of observations recorded for that dose level. Sufficient numbers of dose groups in each of several categories are required for the categorical regression. Judgment is required to define the types of effects that correspond to the severity categories.

The log odds for each dose and severity level is calculated, and then regressed against dose. The resulting regression equation can be used to calculate the probability of an effect of given severity for any dose.

Several model structures (logistic, Weibull, or others) may be used to perform the categorical regression. Logistic regression on the ordered categories (Harrell, 1986; Hertzberg, 1989) allows the dependent variable (e.g., severity parameter) to be categorical and the independent variables to be either categorical or continuous.

The goodness of the fit of the model to the data can be judged using several statistical measures, including the overall χ^2, model parameter standard errors and their χ^2 significance levels, concordance statistics and correlation coefficients for the overall model, and the model covariates (Hertzberg and Wymer, 1991). A variety of criteria are currently being investigated.

Some advantages of using the categorical regression to derive the RfD include the following: data concerning different health effects can be incorporated; it allows for refinement through improved data and statistical methodology; and several indicators of uncertainty in the estimates are provided. In addition, the categorical regression approach can be used to evaluate likely responses to exposures above the RfD.

2.2.8 Chronic, Practical Nonthreshold Effects

Noncarcinogens are generally assumed to exhibit a threshold below which adverse effects are unlikely to occur. There are, however, exceptions to this general rule. Of particular concern are teratogenic and reproductive toxicants that may act through a genetic mechanism. EPA has recognized the potential for genotoxic teratogens and germline mutagens and discussed this issue in the 1991 *Amendments to Agency Guidelines for Health Assessments of Suspect Developmental Toxicants* (USEPA, 1991a) and in the 1986 *Guidelines for Mutagenicity Risk Assessment* (USEPA, 1986a). Various statements within these guidelines raise concern for the potential for future generations inheriting chemically induced germline mutations or suffering from mutational events occurring in utero. An awareness of the potential for such teratogenic/mutagenic effects should be established in order to deal with such data. At this time, genotoxic teratogens and germline mutagens should be considered an exception and the traditional uncertainty factor approach the rule for calculating criteria or values for chemicals demonstrating developmental/reproductive effects. In the absence of adequate data to support a genetic or mutational basis for developmental or reproductive effects, the default becomes an uncertainty factor approach. For such chemicals, this guidance recommends the procedures described above for noncarcinogens assumed to have a threshold.

Where evidence for a genetic or mutational basis does exist, a nonthreshold mechanism shall be assumed for genotoxic teratogens and germline mutagens. Since there is no well established mechanism for calculating criteria protective of human health from the effects of these agents, criteria will be established on a case-by-case basis.

2.2.9 Acute, Short-Term Effects

States may choose to derive criteria that correspond to acute or short-term exposures. These criteria should correspond to a level of exposure that is "without appreciable risk of deleterious effects during some relatively short period of time" (USEPA, 1991c). The derivation of such values follows the same general approaches described above for criteria based on chronic effects. The primary difference lies in the type of toxicity data used as the basis for the evaluation. Generally, studies that mimic the exposure pattern and duration of interest will be considered more relevant to the development of acute or short-term criteria. This is especially important where acute or short-term effects are of a substantially different nature than low-level chronic effects. Where toxicity data do not match the exposure of interest, professional judgment is required to evaluate the relevance of the available data. Factors such as the pharmacokinetics, potential recovery periods, and potential for bioaccumulation should be considered in judging the relevance of the data.

The Office of Water has established procedures for deriving Health Advisories (HAs) for one day, ten days, and longer-term. In general HAs are developed by using NOAELs or LOAELs from studies with similar duration to the exposure period of concern, though there is some flexibility in this regard. Studies used for HAs should provide information on the critical endpoint. Studies that identify only frank toxic responses should not be used since these levels are far above the protective level targeted by HAs. More information on the derivation of HAs is given in Ware (1988).

2.2.10 Mixtures

Exposures to multiple noncarcinogens may occur simultaneously. Possible interactions among chemicals in a mixture are usually placed in one of three categories:

- Antagonistic, where the chemical mixture exhibits less toxicity than is suggested by the sum of the toxic effects of the components.

- Synergistic, where the chemical mixture exhibits greater toxicity than is suggested by the sum of the toxic effects of the components.

- Additive, where the toxicity of the chemical mixture is equal to the sum of the toxicities of the components.

In only a few instances have the interactive effects of chemical mixtures been specifically studied. Where data on the effects of chemical mixtures exist, they should be used to characterize risk. Using the available data is especially important in cases where the resulting toxic effect from the

mixture has been demonstrated to be greater than the sum of the individual effects. Where specific data are not available on the interactive effects of particular chemical mixtures, the methods described below can be used by states to characterize risks from chemical mixtures. When risks from multiple chemicals are added, the quality of experimental evidence that supports the assumption of dose addition should be stated clearly (USEPA, 1986b).

In cases where the chemicals in the mixture induce the same effect by similar modes of action, contaminants may be assumed to contribute additively to risk (USEPA, 1986b), unless specific data indicate otherwise. To characterize risks from multiple chemical exposure to noncarcinogens, the dose for each chemical with a similar effect first is expressed as a fraction of its RfD. These ratios are added for all chemicals to obtain the chemical mixture hazard index:

$$HI_{mix} = \sum_{m=1}^{n} \frac{E_m}{RfD_m}$$

(Equation 2.2.3)

where HI_{mix} is the hazard index of the mixture (unitless), E_m is the exposure to chemical *m*, RfD_m is the reference dose for chemical *m*, and *n* is the number of chemicals in the mixture. A hazard index greater than one implies that the individual is at some risk of the non-carcinogenic effect, and the concern is the same as if exposure from an individual chemical exceeded the acceptable level by the same amount (USEPA, 1986b). However, the numerical value of the hazard index does not indicate the magnitude and severity of the risk.

Some chemical mixtures may contain chemicals that cause dissimilar health effects. Methods currently do not exist for combining dissimilar health effects to characterize overall health concerns from chemical mixtures. Instead, States should characterize and present the risks from these contaminants separately.

2.2.11 References

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2.3 Exposure Analyses

2.3.1 Role of Exposure Data in Setting AWQC

The AWQC are primarily established to protect individuals from adverse health effects caused by pollutants in United States' inland and estuarine waters. To achieve this goal, exposure factors representative of the population to be protected should be used in the equations to derive the criteria (see Section 2.3.4.2 for the equations to derive criteria). In addition, exposures from other non-water sources such as air and food should be taken into account so that the criteria are protective of individuals who may be exposed to a particular pollutant from multiple exposure routes.

The following sections describe data available to determine exposure factors and discuss methods for incorporating non-water sources of exposure, including EPA's recommended default values and methods. In addition, Table 2.3.1 presents sources of exposure-related information. While not intended to be a comprehensive list, Table 2.3.1 does indicate some of the readily available sources for contaminant concentration data and exposure intake parameters.

2.3.2 Exposure Factors in AWQC Algorithms

Several exposure factors are included in the equations to derive AWQC. These factors include (1) body weight of the individuals exposed; (2) drinking water ingestion rates; (3) fish consumption rates; (4) incidental ingestion of water; and (5) the relative source contribution factor to account for other exposures. Body weights and fish intake assumptions are used in each criterion.

The uses of and values for these factors differ based on several considerations. One consideration in the choice of values for a specific exposure parameter depends on whether the water body has been designated as a drinking water supply source or as a recreational, non-potable source. The drinking water ingestion rate is recommended for use for those waters designated as public drinking water supply sources. This rate represents the amount of water an individual drinks per day (see Section 2.3.2.2 for further discussion of the general policy to include a drinking water ingestion rate when setting AWQC). For waters that are used for recreational purposes, an individual may incidentally swallow water when swimming or waterskiing. Thus, an incidental ingestion rate would be applied in these circumstances. Although it is possible that individuals would incidentally ingest water from drinking water sources, incidental ingestion is not included for these sources of intake because the incidental ingestion rate is negligible when the assumed daily drinking water ingestion rate is utilized.

Another consideration in determining the exposure factors used is whether health effects result from chronic exposure or whether developmental health effects are being evaluated. For example, if a chemical causes both developmental and chronic health effects, a State or Tribe may wish to evaluate the chemical using relevant chronic or developmental exposure factors associated with those health effects, respectively, to determine whether to set criteria based on chronic or developmental effects. For chronic health effects, intake rates and body weights of adults or rates relevant to lifetime exposures are the most applicable because the health effects are associated with a long period of exposure. However, for pollutants that may cause health effects after shorter-term exposure to a chemical, exposure factors for children may be most useful when setting criteria for RfDs based on health effects in children, because children often have a higher intake per body weight than adults. In addition, children may be more susceptible to certain contaminants than adults, and may have less capability to detoxify contaminants (USEPA, 1994a). Thus, for such potential situations, EPA default values include intake rates for children.

Table 2.3.1: Sources of Contaminant Concentration and Exposure Intake Information

Name of Source	Type of Information	Agency/Author
Aerometric Information Retrieval System (AIRS)	An updated air data base of many different sites (from rural to urban/industrial) that includes Federally required information, as well as data submitted voluntarily by States.	Office of Air Quality Planning and Standards, EPA
Continuing Survey of Food Intake by Individuals (CSFII)	A national food consumption survey conducted approximately annually.	U.S. Department of Agriculture (USDA)
Exposure Factors Handbook	Summarization of studies and data bases to provide statistical data on factors used in assessing exposure.	National Center for Environmental Assessment, EPA

Table 2.3.1: Sources of Contaminant Concentration and Exposure Intake Information		
Name of Source	**Type of Information**	**Agency/Author**
Inventory of Exposure-Related Data Systems Sponsored by Federal Agencies	Compilation of information on Federally managed data systems that contain exposure information.	Agency for Toxic Substances and Disease Registry; Centers for Disease Control; EPA
National Food Consumption Survey (NFCS)	A national food consumption survey conducted each decade by USDA. The last survey was conducted in 1987-88.	USDA
National Health and Nutrition Examination Survey (NHANES)	A national health and nutrition survey conducted each decade. Based on a probability sample of noninstitutionalized people residing in the U.S.	National Center for Health Statistics
National Inorganics and Radionuclides Survey (NIRS)/National Pesticides Survey (NPS)	Most recent Federal surveys (mid to late 1980s) conducted to characterize occurrence of a series of inorganic and radionuclide chemicals (NIRS) and pesticides (NPS) in public drinking water supplies from ground water sources (and rural domestic wells with the NPS).	EPA
National Sediment Inventory (NSI)	Compilation of available data bases on sediment contamination/sediment chemistry data. These include data on fish tissue residues of chemical contaminants.	EPA
Safe Drinking Water Information System (SDWIS)	Compiled data that includes monitoring required and provided under the program for unregulated contaminants (Section 1445 of the Safe Drinking Water Act).	EPA
Total Diet Study (TDS) - also known as Market Basket Survey	Contaminant concentrations in foods purchased from supermarkets or grocery stores throughout the U.S. four to five times a year. Food items in the TDS are of similar type included in the NFCS and the second NHANES (both described above).	Food and Drug Administration
Total Water and Tap Water Intake in the United States: Population-Based Estimates of Quantities and Sources	Presents estimates of total water (includes water intrinsic to foods) and tap water intake in the population of the continental U.S. Data used are based on the NFCS (described above).	Ershow and Cantor (NCI/NIH)

Shorter-term exposures may also pose risks to other people with special susceptibilities due to illness (e.g., persons with kidney, liver, or other diseases may be especially vulnerable to toxins which attack those systems). When States and Tribes assess intake from pollutants that cause toxicity resulting from such exposures, they may wish to investigate intakes for these other population groups that may also have a high intake per body weight, and/or may be highly subject to adverse effects

from these toxicants. It may be appropriate to calculate criteria using developmental and chronic toxicity and exposure assumptions to see which criterion is more stringent.

Developmental effects resulting from prenatal exposure to contaminants have become an area of significant concern (USEPA, 1994a). Thus, in addition to considering use of exposure factors specific to adults or children, States and Tribes may wish to use exposure factors specific to women of childbearing age in cases where developmental health effects may be of concern. These exposure factors are described below.

Fish consumption intake rates may also differ based on the target population to be protected. Some states may have a large population of recreational fishers who may fish a few times a year or during a fishing vacation. Other States may have populations that subsist on fish for a large portion of a year. Thus, the fish intake exposure factor may differ depending on the population that is to be protected. Different types of fishers are discussed in greater detail, below, in the section that describes fish intake rates.

When setting AWQC, it is preferable to use exposure information reflective of individuals who actually use the water body for which AWQC are to be determined. When dealing with such diverse populations as those throughout the United States, extreme ranges of behaviors and activities are likely. Therefore, EPA explicitly recommends that, for certain exposure factors that may be highly variable (e.g., fish intake rates), States use available local data. These data should be used especially in cases that result in AWQC that are more stringent than criteria derived using default exposure assumptions suggested by EPA. In many situations, local exposure data may not be available. Therefore, EPA also recommends default values for each of the exposure values discussed below.

The following sections discuss available data and describe some of the above issues in greater detail. In addition, the sections discuss EPA's recommendations for use of the exposure factors and present EPA's suggested default values. The incorporation of these exposure factors into equations to derive criteria are described in detail in Section 2.3.4.2.

2.3.2.1 Body Weight

The 1980 AWQC National Guidelines used a body weight of 70 kg in the derivation of AWQC, which represents EPA’s Agency-wide adult body weight assumption used in its risk assessments and approximates the average adult body weight of 71.8 kg from an analysis of the National Health and Nutrition Examination Survey (NHANES II), as reported in the Exposure Factors Handbook (USEPA, 1997a). In the current, updated guidance, EPA recommends several default body weight values, depending on whether chronic effects or acute effects are being evaluated. The use of these data in equations to derive AWQC are described in Section 2.3.4.2.

Chronic Exposure Scenarios

For chemicals that cause chronic effects, EPA recommends using a default body weight of 70 kilograms. This value approximates the mean for adults from two sets of data. The first set of data comes from NHANES II, which was conducted from 1976 through 1980 and for which information on a variety of health and nutritional characteristics of individuals were collected (adapted from NCHS, 1987). The National Center for Health Statistics compiled body weight data from NHANES II for over 20,000 individuals aged 6 months to 74 years. Weighted mean body weights were determined from this data. The mean body weight value for men and women ages 18 to 74 years old, using data from NHANES II, is 71.8 kg. The median body weights for men and women from this study are 76.9 and 62.4 kilograms, respectively. Table 2.3.2 includes a distribution of mean and median adult body weights, by age group, based on NHANES II data. Body weights are presented for men, women, and both sexes combined.

The second set of body weight data come from Ershow and Cantor (1989). These authors used data collected during the 1977-1978 Nationwide Food Consumption Survey (NFCS), which surveyed 30,770 individuals who constituted a stratified random sample designed to represent the noninstitutionalized U.S. population living in households (USDA, 1988). Body weights were self-reported by participants. The mean value for body weight for adults ages 20 - 64 years old is 70.5 kg. Means and percentile values of body weight from Ershow and Cantor (1989) listed by sex and age are presented in Table 2.3.3. The revised EPA Exposure Factors Handbook (USEPA, 1997a) recommends a value of 71.8 kg for adults, based on the NHANES II data. However, the Handbook also acknowledges the 70 kg value commonly used in EPA risk assessments and cautions assessors on the use of values other than 70 kg. Specifically, the point is made that the 70 kg value is used in the derivation of cancer slope factors and unit risks that appear on IRIS. Consistency is advocated between the dose-response relationship and exposure factors assumed.

Table 2.3.2: Body Weight (in kilograms) of Adults from NHANES II

Age	Men		Women		Men and Women
	Mean	Median	Mean	Median	Mean
18 - 24 years	73.7	72.0	60.6	58.0	67.2
25 - 34 years	78.7	77.5	64.2	60.9	71.5
35 - 44 years	80.9	79.9	67.1	63.4	74.0
45 - 54 years	80.9	79.0	68.0	65.5	74.5
55 - 64 years	78.8	77.7	67.9	65.2	73.4
65 74 years	74.8	74.2	66.6	64.8	70.7
Overall: 18 - 74 years	78.1	76.9	65.4	62.4	71.8

Source: Adapted from NCHS (1987)

Developmental Effects Exposure Scenarios

In certain cases, pregnant women may represent a more appropriate target population for consideration when setting water quality criteria than all adults in cases where developmental effects may be of concern (USEPA, 1994b). In these types of cases, body weights representative of women of childbearing age may be appropriate to adequately protect offspring from such health effects. For example, in the Great Lakes Water Quality Initiative, EPA chose women of childbearing age as the target population for development of the mercury criterion (USEPA, 1995). To determine a mean body weight value appropriate to this population, separate body weight values for women in individual age groups within the range of 15 to 44 years old, taken from NHANES II (adapted from NCHS, 1987), were combined and weighted by current population percentages (U.S. Bureau of the Census, 1996) to obtain a value applicable to the current population. The resulting mean body weight value for this age group is 63.8 kg.

Ershow and Cantor (1989) also present data on mean and median body weights for pregnant women, of 65.8 and 64.4 kilograms, respectively. Based on these data, States may wish to use a value of 65 kilograms in combination with relevant developmental toxicity data when assessing risks for pregnant women and for setting AWQC.

Likewise, for some contaminants, RfDs based on health effects in children may be of primary concern. As stated in the *Federal Register* notice, because children generally eat more fish and drink more water per body weight than adults, higher intake rates per body weight may be more appropriate in the derivation of AWQC to provide adequate protection for these individuals. In

addition, because children may be more susceptible to the effects of some pollutants than adults (USEPA, 1994b), they should be especially considered when assessing adverse effects that occur following such exposures. Information on children's body weights (from NHANES II) are included in Tables 2.3.3 and 2.3.4.

To protect children against health effects from water and fish intake when RfDs are based on health effects in children, EPA recommends a default body weight of 28 kilograms, which represents a mean body weight for children 0 to 14 years old. This is only recommended for chemicals for which adverse effects for children are the most critical endpoint in the chemical's toxicological profile. This body weight can be used with fish intake rates for children in the same age group when deriving criteria for protection against such health effects from eating fish. The default recommendation is made, in part, due to the limitations of the default fish consumption data. Specifically, the limited sampling base prohibits the use of finer age group divisions due to unacceptable confidence intervals with such finer fish intake divisions. However, finer age divisions are provided in Tables 2.3.3 and 2.3.4 for States and Tribes to consider using along with more robust fish consumption data. As with other recommended body weight values, the default estimate is based on information from analyses of NHANES II data (adapted from NCHS, 1987). Current population estimates (U.S. Bureau of the Census, 1996) were used to weight information on body weights for individuals in several age groups up to age 14 years, using body weight information from NCHS (1987) to represent values applicable to the current population. This calculation resulted in weighted mean body weight values of 28 kg for this age group. A similar analysis using body weights for separate age groups within the 0-14 year range from Ershow and Cantor (1989), and weighting by current population estimates also resulted in a mean body weight of 28 kilograms.

If States wish to specifically evaluate infants and toddlers, EPA recommends a lower default body weight of 10 kilograms, as has been used in previous water program guidance and regulations. The body weight is representative of children up to three years old. EPA recommends using data from this particular age group because these children may be particularly susceptible to acute effects from water-based formula intake (e.g., nitrate). Data used to determine this body weight value come from Ershow and Cantor (1989) and the analysis of NHANES II data (adapted from NCHS, 1987). The analysis of NHANES II data indicate 10th, 25th, and 50th percentile values for children less than three years old as 8.5, 9.6, and 11.3 kilograms for females, and 9.1, 10.3, and 11.8 kilograms for males, respectively. Mean body weights from NHANES II are 9.1 for children ages 6-11 months, 11.3 for 1-year-olds, and 13.3 for 2-year-olds (adapted from NCHS, 1987). From the Ershow and Cantor study, the 10th, 25th, and 50th percentile values for children 1-3 years old are 10.4, 11.8, and 13.6 kg, respectively, with a mean value of 14.1 kg (Ershow and Cantor 1989).

States and Tribes may instead wish to consider certain general developmental ages (e.g., pre-school, pre-adolescent, adolescent, etc.) or certain specific developmental landmarks (e.g., neurological development in the first four years, etc.) depending on the chemical of concern. EPA encourages States and Tribes to use Tables 2.3.3 and 2.3.4 to choose a body weight intake, if they believe a particular age subgroup is more appropriate due to these developmental ages or landmarks.

Table 2.3.3: Self-Reported Body Weight (kilograms) for Both Sexes from Ershow and Cantor (1989)[ab]

Sex	Age (yr)	Mean	Standard Deviation	Percentile Distribution				
				1	5	10	25	50
Both	<0.5	5.8	1.8	c	3.2	3.6	4.5	5.4
	0.5-0.9	9.2	2.0	c	6.8	7.3	8.2	9.1
	1-3	14.1	3.2	8.6	10.0	10.4	11.8	13.6
	4-6	20.3	4.6	12.7	13.6	15.4	17.2	20.0
	7-10	30.6	7.8	18.1	20.4	22.7	24.9	29.5
	11-19	55.2	13.4	28.6	34.0	38.6	45.4	54.4
	20-64	70.5	15.2	44.5	49.9	52.2	59.0	68.0
	65+	68.6	13.1	40.8	48.5	52.2	59.0	68.0
	All	59.3	22.6	9.1	15.9	22.7	48.5	61.2
Males	<0.5	6.2	1.8	c	3.6	3.6	5.0	6.4
	0.5-0.9	9.6	2.1	c	6.8	7.3	8.2	9.1
	1-3	14.4	3.3	9.1	10.0	10.9	12.2	13.6
	4-6	20.5	4.5	13.6	14.5	15.9	18.1	20.4
	7-10	31.0	7.9	18.1	20.9	22.7	24.9	29.5
	11-19	58.3	14.9	29.0	34.0	38.6	47.2	59.0
	20-64	79.4	13.0	54.4	61.2	64.0	70.3	78.0
	65+	74.4	11.5	49.9	56.7	61.2	67.1	73.9
	All	63.8	25.3	9.1	15.4	20.9	49.9	70.3
Females	<0.5	5.5	1.8	c	2.7	3.6	4.1	5.4
	0.5-0.9	8.8	1.7	c	6.8	6.8	7.7	8.6
	1-3	13.7	3.0	8.6	9.5	10.0	11.3	13.6
	4-6	20.0	4.6	12.7	13.6	15.0	17.2	19.1
	7-10	30.2	7.6	18.1	20.4	21.8	24.9	29.5
	11-19	52.1	11.0	28.1	34.0	38.6	45.4	52.2
	20-64	64.1	13.4	43.1	47.6	49.9	54.4	61.2
	65+	64.5	12.6	39.9	45.4	49.9	55.8	63.5
	All	55.7	19.5	9.1	15.9	24.9	48.1	56.7

[a] Does not include pregnant women, lactating women, or breast-fed children.
[b] Individual values may not add to totals due to rounding.
[c] Value not reported due to insufficient number of observations.

Table 2.3.4: Mean Body Weights (kilograms) of Children from NHANES II

Age	Boys	Girls	Boys and Girls
6-11 months	9.4	8.8	9.1
1 year	11.8	10.8	11.3
2 years	13.6	13.0	13.3
3 years	15.7	14.9	15.3
4 years	17.8	17.0	17.4
5 years	19.8	19.6	19.7
6 years	23.0	22.1	22.6
7 years	25.1	24.7	24.9
8 years	28.2	27.9	28.1
9 years	31.1	31.9	31.5
10 years	36.4	36.1	36.3
11 years	40.3	41.8	41.1
12 years	44.2	46.4	45.3
13 years	49.9	50.9	50.4
14 years	57.1	54.8	56.0

Source: Adapted from NCHS (1987)

2.3.2.2 Drinking Water Intake

The 1980 AWQC National Guidelines used a value of 2 liters/day to represent the drinking water intake of an individual. In these updated guidelines, EPA recommends the same value when setting chronic criteria. In addition, EPA recommends a drinking water intake specific to children for protecting against certain health effects (with those chemicals for which the critical effect of concern is based on children) because young children may intake a large amount of water per body weight.

Chronic Exposure Scenarios

To protect against health effects due to chronic exposure, EPA recommends an adult-specific drinking water intake of 2 liters per day. This value has been used as a nationwide estimate of adult daily water consumption in the drinking water program for setting Maximum Contaminant Level Goals (MCLGs) and Maximum Contaminant Levels, to be protective of a majority of the population over the course of a lifetime. The value is also suggested by the Exposure Factors Handbook to be supported by studies analyzed in the Handbook for use as an upper-percentile intake rate (USEPA, 1997a). In addition, the value was recommended in the Technical Support Document for setting water quality criteria for human health in the Great Lakes Region (USEPA, 1995). Based on the study data from Ershow and Cantor (1989, summarized below), EPA also recommends a 2 liters per day intake for women of childbearing age.

The value of 2 liters/day has been estimated as being somewhere between the 75th and the 100th percentiles, as reported by different studies of drinking water intake. Thus, using this higher than average value in combination with recommended default body weights and fish intake rates would protect most individuals in the population. However, certain individuals who work or exercise in hot climates may consume water at rates significantly higher than 2 liters/day. Some of the most highly exposed individuals, such as migrant workers, may not be captured in national surveys of drinking water intake. Several studies that have estimated drinking water intake are described below.

One study by the National Cancer Institute (NCI) estimated intake from tap water (which includes water directly from the tap and tap water added to foods and beverages during preparation) using data from the NFCS (Ershow and Canter, 1989). For 11,700 adults ages 20 - 64 years old, this study reports 50th, 75th, and 90th percentile tap water intakes of 1.3, 1.7, and 2.3 liters/day, respectively. Table 2.3.5 includes the distribution of intake values by age from this study.

NCI determined drinking water intake values from a study in which 9,000 individuals were questioned in a population-based, case-control study investigating a possible relationship between bladder cancer and drinking water (Cantor et al., 1987). This study estimated an overall average tap water consumption rate of 1.39 liters of water per day. The 100th percentile consumption rate was estimated to be about 1.96 liters per day as shown in Table 2.3.6.

A survey of drinking water literature by the National Academy of Sciences (NAS) has calculated the average per capita water consumption to be 1.64 liters per day. NAS estimates that daily water consumption may vary with physical exercise and fluctuations in temperature and humidity. It is reasonable to assume those living in arid, hot climates will consume higher levels of water. However, NAS adopted the 2 liters/day volume to represent the intake of the majority of water consumers (NAS, 1977). In another survey, the Food and Drug Administration's (FDA) Total Diet Study estimated rates for water and water used to make drinks and soups for two groups of adults to be 1.04 and 1.26 liters per day with an average of 1.15 liters per day. Finally, EPA estimates based on the U.S. Department of Agriculture’s (USDA) 1977-78 Nationwide Food

Table 2.3.5: Tap Water Intake (g/day) for Both Sexes from Ershow and Cantor (1989)[ab]

Sex	Age (yr)	Mean	Standard Deviation	Percentile Distribution				
				50	75	90	95	99
Both Sexes	<0.5	272	247	240	332	640	800	c
	0.5-0.9	328	265	268	480	688	764	c
	1-3	646	390	567	820	1162	1419	1899
	4-6	742	406	660	972	1302	1520	1932
	7-10	787	417	731	1016	1338	1556	1998
	11-19	965	562	867	1246	1701	2026	2748
	20-64	1366	728	1252	1737	2268	2707	3780
	65+	1459	643	1367	1806	2287	2636	3338
	All	1193	702	1081	1561	2092	2477	3415
Males	<0.5	250	232	240	320	569	757	c
	0.5-0.9	322	249	264	408	634	871	c
	1-3	683	406	606	867	1228	1464	2061
	4-6	773	414	693	1033	1336	1530	1900
	7-10	802	437	738	1046	1391	1609	2055
	11-19	1050	605	942	1364	1856	2179	2967
	20-64	1460	798	1339	1841	2485	2949	4083
	65+	1570	704	1448	1952	2460	2790	3712
	All	1250	759	1123	1634	2205	2673	3760
Females	<0.5	293	259	240	358	672	800	c
	0.5-0.9	333	281	278	500	712	759	c
	1-3	606	368	532	783	1114	1339	1806
	4-6	709	395	622	930	1231	1491	1932
	7-10	772	395	726	992	1299	1475	1888
	11-19	882	503	799	1147	1540	1825	2424
	20-64	1297	664	1207	1655	2147	2491	3359
	65+	1382	584	1309	1687	2167	2472	3071
	All	1147	648	1049	1505	1988	2316	3097

[a] Does not include pregnant women, lactating women, or breast-fed children.
[b] Individual values may not add to totals due to rounding.
[c] Value not reported due to insufficient number of observations.

Consumption Survey identified daily beverage intakes ranging from 1.48 to 1.73 liters per day. Both the FDA and USDA studies were cited in USEPA (1997a). Based on these studies, EPA estimated an average adult drinking water consumption rate to be 1.41 liters per day and the 90th percentile value to be 2.35 liters per day (USEPA, 1997a).

Table 2.3.6: Frequency Distribution of Tap Water Consumption Rates*

Consumption Rate (L/day)	Cumulative Frequency (%)
0.80	19.2
0.81 - 1.12	39.6
1.13 - 1.33	59.7
1.45 - 1.95	79.9
1.96	100.0

*Represents consumption in a "typical" week.
Source: Cantor et al. (1987)

Developmental Effects Exposure Scenarios

As noted above, for some contaminants, RfDs based on health effects in children are of primary concern. Because infants and small children have a higher water consumption per body weight compared to adults, a higher water consumption rate per body weight may be needed for comparison with doses from relevant toxicity studies. Use of these higher water consumption rates when setting criteria based on health effects associated with children should result in adequate protection for infants and children. Estimating a mean drinking water intake for children ages 0-14 years old, which combines drinking water intake for five age groups within the larger age group of 0-14 years from Ershow and Cantor (1989) and weighting by current population estimates (from U.S. Bureau of the Census, 1996) results in a drinking water intake of approximately 750 ml. As a slightly more protective measure than using 750 ml, EPA proposes a drinking water intake of 1 liter. This value is equivalent to about the 75th percentile value, of 960 ml for children ages 1-10 years old (Ershow and Cantor, 1989). The distribution of drinking water intakes for age groups within the 0-14 year-old group from Ershow and Cantor (1989) is included in Table 2.3.5. This value is also appropriate to use for evaluating smaller children ages 1-3 years old and has been used as a default by EPA's water program office for small children in past regulatory efforts.

Inhalation and Dermal Exposure

A number of water contaminants are volatile and thus diffuse from water into the air where they may be inhaled. In addition, drinking water is used for bathing and ambient waters for swimming

and thus, there is at least the possibility that some contaminants in water may be dermally absorbed.

Dermal absorption and the inhalation of volatilized drinking water contaminants may be responsible for significant increases in exposure over and above that due to ingestion. However, this issue is quite complicated. A significant fraction of the water that is ingested is either boiled or allowed to stand prior to ingestion. In both cases, it is reasonable to assume that volatilization will decrease the concentration of volatile contaminants in the water that is actually ingested. In addition, because volatilization can decrease the concentration of volatile contaminants in the water that comes in contact with the skin, it follows that volatilization can decrease the extent of dermal absorption.

Thus, volatilization may increase exposure via inhalation and decrease exposure via ingestion. The net effect of volatilization and dermal absorption upon total exposure to volatile contaminants in water is unclear. Although several approaches can be found in the literature, including various models that have been used by EPA, the Agency currently does not have a proposed methodology for explicitly incorporating inhalation (i.e., from volatilization) and dermal absorption exposures from household water uses in the derivation of health-based criteria (i.e., MCLGs or AWQC). The Agency is currently exploring the effect of volatilization and dermal absorption upon exposure to drinking water contaminants. For example, the Agency has a joint agreement with the International Life Sciences Institute (ILSI) to develop guidance on estimating exposures of inhalation and dermal absorption from contaminants in water. It is anticipated that this guidance would be incorporated into this methodology when it is available.

2.3.2.3 Fish Intake Rates

Fish intake rates (expressed in grams/day) are used in the equations to derive AWQC. Throughout this section, the terms “fish intake” or “fish consumption” are used. They generally refer to the consumption of finfish and shellfish, and the national survey described in this section (the CSFII) includes both. States and Tribes should ensure that when selecting local or regionally-specific studies, both types are included when the population exposed are consumers of both types. If the population of concern are also believed to consume aquatic plants from the water body, this source should be accounted for with the estimate of other exposures (i.e., the relative source contribution analysis). Ideally, fish intake rates should be representative of individuals who eat fish from a given water body for which AWQC are to be set. In addition, priority should be given to identifying and protecting the most highly exposed fish eaters in the area. Although highly exposed populations cannot be precisely defined and may differ depending on the water body to be protected, such fish eaters may generally be separated into two groups: (1) sportfishers, defined generally as the group of anglers who eat the fish they catch recreationally; and (2) subsistence fishers, individuals who rely on fish for a large part of their protein intake. A more detailed description, as well as examples, of these highly exposed groups follows.

Sportfishers may vary widely in their catch and consumption rates. Some may eat fish for short periods throughout the year or during certain fishing seasons. Others may fish for much longer periods during a year. Although sportfishers may primarily fish recreationally and only supplement their regular diets with the fish they catch, some sportfishers may eat large amounts of fish throughout the year.

Populations which have been identified as eating a larger portion of sport-caught fish than the general population (e.g., Native Americans) yet are not recreational fishers are distinguished from the above group of sportfishers. Such fishers (called subsistence fishers here) may rely on catching and eating fish to meet nutritional needs or because of cultural traditions. Subsistence fishers may catch fish year round (CRITFC, 1994) or preserve fish to eat throughout the year. Some of these fishers, such as Asian-Americans, often consume portions of the fish that recreational fishers do not often consume (including liver, kidneys, brains, and eyes). In addition, fish may be prepared whole, providing greater exposure to contaminants (e.g., organs and remains are often used as soup stock) (Pestana, 1994; Shubat, 1994; Allbright, 1994; Cung, 1994; Nehls-Lowe, 1994; University of Wisconsin SeaGrant, 1994; Den, 1994; Young, 1994; Lorenzana, 1994). Subsistence fishers are often (although not always) low income individuals, and may reside in either urban or rural areas.

Several ethnic groups have been identified as having members who subsist on fish. Several specific groups of Native American fishers have been identified in the Northwest and the Great Lakes Region (Kmiecik, 1994; CRITFC, 1994; Den, 1994; Young, 1994; Eng, 1994). Asian-American fishers are a group that includes numerous populations such as Laotian, Hmong, Cambodian, and Vietnamese, each with differing consumption patterns and cultural traditions. Asian-American fishers in particular may eat a larger portion of the fish than generally recommended, including consumption of additional organs or the whole fish (Pestana, 1994; Shubat, 1994; Allbright, 1994; Cung, 1994; Nehls-Lowe, 1994; University of Wisconsin SeaGrant, 1994; Den, 1994; Young, 1994; Lorenzana, 1994).

When estimating fish intake for the population of concern, EPA recommends that central tendency values (i.e., median or mean values) or higher percentile values from studies of fish consumption relevant to the identified group be used in the derivation of criteria. Values lower than the median or mean should not be used because the identified populations would not be adequately protected. Furthermore, when considering median values from fish consumption studies, States need to ensure that the distribution is based on survey respondents who reported consuming fish because surveys based on both consumers and non-consumers typically result in median values of zero.

Because fish consumption habits may vary among different types of populations and among States, EPA prefers that States use information on fish consumption rates directly relevant to the population being addressed. However, such information may not always be available. Thus, EPA proposes the hierarchy of preferences for consideration of fish consumption data described below. Although Preferences #1 and #2 are likely to result in higher intake rates than the default recommendations of Preference #4, if the converse is true (i.e., if site-specific or similar geographic/population studies indicate lower intake rates than the recommended defaults), States

may choose the lower intake rates determined from the first two preferences. However, if a State chooses values (whether central tendency or high end) that particularly target highly exposed consumers, they should be compared to high-end fish intake rates for the general population to make sure that the highly exposed consumers within the general population would also be protected by the chosen intake rates. As discussed in the *Federal Register* presentation of the Methodology, it is recommended that cooked weight values of intakes be used.

Preference #1: Use of Local Information

Once a State has identified the particular population, which, if a protected subgroup, will also afford acceptable protection to the entire population, EPA recommends that States use results from fish intake surveys conducted in the geographic area where the State is located to estimate fish intake rates (measured in grams/day) that are likely to most closely represent the defined populations being addressed. Generally, the more specific the data are to the individuals who use the water body of interest, the better the data are considered to be for estimating accurate fish intake rates.

Information on local fish consumption habits may not be already available to States. Thus, if time and money permit, States are encouraged to conduct their own surveys in order to obtain estimates of fish consumption (in grams/day) and to characterize fisher populations within the State, and specifically, the locality of interest. The EPA guidance manual entitled *Guidance for Conducting Fish and Wildlife Consumption Surveys* (USEPA, 1997b) may be useful in planning and conducting surveys. This guidance document reviews five methods of obtaining fish consumption data:

- Recalled information collected by telephone.
- Recalled information collected by in-person interviews.
- Recalled information from self-administered mailed questionnaires.
- Diaries maintained by anglers.
- On-site creel censuses (obtaining harvest data collected on-site from single anglers).

The advantages and disadvantages of each method are addressed, and suggestions about procedures to solve problems associated with each survey method are given.

In addition, *Consumption Surveys for Fish and Shellfish* lists several suggestions regarding the type of information to collect when conducting these surveys. Examples of this information include: (1) *sociodemographic characteristics* such as age of the angler, number of household members, and pregnancy or lactation status of women in the household; (2) *fishing activities* including seasonal and temporal distribution of fishing activities, whether the angler fishes for sport or consumption, and the type of fish captured (whether bottom feeders or pelagic); and (3) *preparation and consumption patterns* including portions of the fish consumed, methods of preparation prior to cooking, and procedures for cooking. Such information can be used to investigate patterns of consumption among high-risk groups, and can aid in most accurately characterizing consumption rate information using as few assumptions as possible.

The document presents a variety of guidelines for conducting surveys, and is intended to provide methods for efficiently and cost-effectively collecting information necessary for valid statistical analyses of risks to subsistence and recreational anglers. States should refer to USEPA (1997b) for more detailed information on methods of conducting fish consumption surveys.

A couple of issues not addressed in detail in USEPA (1997b) should be emphasized when planning a fish consumption survey. The first issue involves identification of subsistence fisher populations. Because it may be difficult to identify subsistence fisher populations solely through traditional approaches such as mail or phone surveys, it may be necessary for surveyors to use other methods to target these populations. A couple of methods may be of use. One method involves contact with community organizations that represent these populations (e.g., Indian tribal organizations) that have already established a relationship with community members. In addition, creel clerks (those who interview fishers at specific fishing locations) may be good sources of information on fisher demographics because they have direct contact with individuals at fishing sites (Shubat, 1993). It is important to anticipate cultural and language requirements of each ethnic group and to try and follow the community-based approach indicated above. Asians and Pacific Islanders are currently the fastest growing minority population in the U.S. For many first and second generation immigrants and refugees, survey methods which utilize creel, mail-in, telephone or door-to-door techniques are ineffective in obtaining reliable data characterizing fish and seafood consumption patterns (Nakano, 1996; USEPA, 1996). Informal studies indicate a preference for bottom dwelling fish; therefore, Asian and Pacific Islander surveys should include an appropriate species list (Soukhaphonh et al., 1996).

A second issue important to emphasize is that, if States intend to consider health effects resulting from acute exposures when setting AWQC, surveyors may wish to obtain information regarding maximum amounts of fish that may be eaten at a meal. Because many surveys are designed to obtain information simply on the number of fish meals eaten by an individual over a specific time period, rather than the size of the fish meals, maximum meal sizes may not generally be obtained by a fish consumption survey. As noted above, such large acute exposures may be especially

problematic to children, people with special susceptibilities, and pregnant women. In addition, such high doses may be more likely to occur at specific times during the year, such as periods when certain types of fish are available or during specific events (e.g., summer vacation, Native American religious festivals, or fishing tournaments). Thus, surveyors may wish to consider obtaining information on such maximum intake rates and determine whether these rates are likely to occur during specific times during the year.

Preference #2: Use of Surveys from Similar Geographic Areas and Population Groups

For those States and Tribes that do not have resources available to conduct a survey of consumption rates of local populations and when such information is otherwise not available, EPA's second preference in determining fish intake rates is for States and Tribes to use results from existing fish intake surveys that reflect similar geography and/or population groups. For instance, States or Tribes with subsistence fisher populations may wish to use consumption rates from studies that focus specifically on these groups, or, at minimum, use rates that represent high-end values from studies that measured consumption rates for a range of types of fishers (e.g., recreational/sport fishers, subsistence, minority populations). A State or Tribe in a particular region of the country may consider using rates from studies that surveyed the same region; for example, a State or Tribe that has a climate that allows year-round fishing may underestimate consumption if rates are used from studies taken in regions where individuals fish for only one or two seasons per year. A State or Tribe that has a high percentage of a particular age group (such as elderly individuals, who have been shown to have higher rates in certain surveys) may wish to use age-specific consumption rates, which are available from some surveys.

Fish intake rates estimated from available surveys that have investigated the fish consumption habits of individuals are described below and presented in Tables 2.3.7 and 2.3.9. These surveys are divided into the two previously identified groups of highly exposed fisher populations (sportfishers and subsistence fishers) described above. Although the surveys are divided into these two categories for ease of presentation, it should be noted that these two categories cannot always be strictly delineated. In particular, there may be individuals included in the sportfisher surveys that exhibit habits indicative of subsistence fishers (i.e., eating fish as a large part of their diet). Also, some members of identified subsistence populations may not subsist on fish as a major portion of their diets.

These surveys use a variety of methods. The methods used in the surveys to estimate the fish intake rates are included in Tables 2.3.8 and 2.3.10. A few points should be made about the methods used in these studies to estimate the consumption rates. One major issue regarding these rates is that although they are presented as grams per day in Tables 2.3.7 and 2.3.9, they should be considered to be approximations of actual gram/day amounts only. For example, the estimates are generally obtained by memory recall, not strict daily log-keeping of grams eaten per day. In addition, surveys generally ask respondents to estimate the *number* of meals they have eaten over a given period of

time. Although some surveys include questions about approximate size of the meals, others do not ask any questions about the actual size of the meals eaten during that time and, instead, assume all meals are a given size (most often 227 grams, or a half pound).

A second major issue to be addressed is that the estimates of fish intake may vary across surveys for reasons which depend on the type of fish included in the survey. For instance, surveys may report consumption of only certain types of fish. Some surveys have focused primarily on either freshwater or saltwater fish, whereas others have collected information on both types. In addition, some surveys have queried individuals about whether they have eaten recreational fish only, whereas others have questioned respondents about intake of commercial fish, or both.

Methods of averaging fish consumption information also differ among studies. Some studies average the consumption rates over all individuals, regardless of whether they ate fish, while other surveys average the information only for those individuals who reported eating fish. For example, Cox, Vaillancourt, and Hayton (1993) report consumption rates averaged for the fish-eating population, whereas the Alabama Department of Environmental Management (1993) report a rate averaged for both individuals who eat fish and those who do not eat fish.

As discussed in the *Federal Register* notice, fish consumption surveys also vary in terms of whether reported rate values are for cooked fish, uncooked fish, or whether the study is unclear as to which is reported. States and Tribes should check to see if the survey study clearly identifies whether weights represent cooked or uncooked fish.

Many of the differences in survey methods are highlighted in the text and accompanying Tables 2.3.8 and 2.3.10. However, States should consult the individual surveys to obtain the most complete descriptions of the study and resulting consumption rates. USEPA's *Guidance for Conducting Fish and Wildlife Consumption Surveys* (USEPA, 1997b) includes detailed descriptions of the various methods for conducting surveys, including their strengths and limitations.

Sportfishers

As noted above, sportfishers differ with respect to their catch and consumption habits. Surveys of the general sportfishing population may include those who primarily fish for recreational purposes or eat fish for a small portion of the year but may also include some individuals who eat fish as a main staple in their diets. Results of sportfisher surveys are described in the following paragraphs, and are included in Tables 2.3.7 and 2.3.8.

Alabama Fishers. The Alabama Department of Environmental Management (1993) conducted a survey from August 1992 to July 1993 on-site at various fishing locations. In this survey, 1,586 individuals were interviewed and asked about the number of fish that were caught and kept for consumption. Demographic information on age, gender, income, and region was also collected. Two survey methods, which differed in determining meal size of the fish catch that was to be eaten, were used to estimate consumption rates. Mean and 95th percentile consumption rates

for the harvest method were 45.8 and 50.7 grams/day, respectively, and the rates for the serving method were 43.1 and 50.9 grams/day, respectively. Both were averaged over a year. Although consumption rates were not found to vary across major ethnic groups, some specific subpopulations had higher than mean consumption as a function of age and income. Black anglers with incomes less than $15,000 ate a mean of 63 grams/day, and anglers over 50 years old consumed a mean of 76 grams/day of sport-caught fish (Alabama DEM, 1993).

California Fishers. The Santa Monica Bay Restoration Project contracted with the Southern California Coastal Water Research Project and MBC Applied Environmental Sciences to conduct a seafood consumption study from September 1991 to August 1992 (SCCWRP and MBC, 1994). The purpose of the study was to characterize recreational anglers fishing in the Santa Monica Bay, including identifying ethnic subgroups of the population with the highest consumption. Information on household income was also evaluated. The survey form included a census and a questionnaire. Twenty-nine sites were surveyed on 99 days of sampling, with 2,376 anglers included in the census and over 1,200 interviews (71%). Of these, 555 anglers (45%) provided enough information to be used to derive consumption rates. The overall median and mean consumption rates were 21.4 and 49.6 grams/day, respectively, with the highest median and mean consumption rates (85.7 and 137.3 grams/day) in the Other category (i.e., primarily Pacific Island origin). Among ethnic groups, the 90th percentile rates ranged from 64.3 to 173.6 grams/day, with the Hispanic category having the lowest and the Other category having the highest rates. With respect to income, the study showed that the lowest income group (<$5,000/year) had the highest median consumption rate (32.1 grams/day) but the highest income group (>$50,000/year) had the highest mean consumption rate (58.9 grams/day) and the highest 90th percentile (128.6 grams/day). However, it should be noted that two-thirds of the survey population was comprised of higher income anglers.

Louisiana Fishers. The Louisiana Department of Environmental Quality conducted a seafood consumption survey in 1993 (Dellenbarger, et al., 1993). A telephone survey was conducted of 1,100 households in Houma, LA, a coastal community. Households sampled were stratified by ethnic characteristics; however, the households were otherwise randomly selected. Other high-end consumers were individuals over 50 years old, who consumed a mean value of 40 grams/day. Rates for all types of fish consumed were 65 grams/day, comprised of 17 grams/day of fresh water fish, 15 grams/day of saltwater fish, and 33 grams/day of shellfish. These rates include both sport-caught and commercial fish and are averaged for only those people who ate fish and seafood.

New York Fishers. Based on a survey of 4,530 anglers, the New York State Department of Environmental Conservation (Connelly, et al., 1990) estimated that consumption of fish (all types) by New York State anglers averaged about 45.2 meals per year, or 28.1 grams per day (assuming 227 grams per meal). Averages are also listed by age of the angler, income group, and the area within New York State where the angler lives. The highest average was recorded for the two Long Island counties of Nassau and Suffolk, whose populations consumed a combined mean value of 37 grams/day of fish. Other high-end consumers were individuals over 50 years old, who consumed a mean value of 40 grams/day.

Table 2.3.7: Sportfishers[a] Fish Intake Data

Fisher Group[b]	Fish Intake Rates (g/day)					Fish Type[c]	
	mean	median	80%ile	90%ile	95%ile		
Alabama fishers[1]	45.8				50.7	F+S	R+C
Louisiana (coastal) fishers[2]		65				F+S	R+C
New York fishers[3]	28.1					F	R
New York (Hudson River) fishers[4]	23 (typical)						
Michigan fishers[5]	14.5		30	62	80	F+S	R
Michigan fishers[6]	18.3			50 (approx.)	70 (approx.)	F+S	R+C
Michigan fishers[7]	44.7					F	R
Wisconsin fishers (10 counties)[8]	12.3				37.3	F	R
Wisconsin fishers (10 counties)[8]	26.1				63.4	F	R+C
Ontario fishers[9]	22.5					F	R
Ontario fishers[10]	31 (average)						
Los Angeles Harbor fishers[11]		37	120.8	225	338.8		
Washington State (Commencement Bay) fishers[12]		23		54		S	R
Washington State (Columbia River) fishers[13]	7.7					F+S	R+C
Maine fishers (inland waters)[14]	6.4	2.0		13	26		
Washington State (Columbia River) fishers[15]	1.8						

NOTES:
[a]Sportfishers may include individuals who eat fish as a large portion of their diets
[b]Fisher groups refer to the same headings as those that appear in the text
[c]Fish Type: F= Freshwater, S = Saltwater (may indicate either estuarine or marine waters), R = Recreationally caught

SOURCES:
[1]AL Dept. Env. Mgt., 1993
[2]Dellenbarger, et al., 1993
[3]Connelley, et al., 1990
[4]Barclay, 1993
[5]West, et al., 1993
[6]West, et al., 1989
[7]Humphrey, 1976
[8]Fiore, et al., 1989
[9]Cox, Vaillancourt, and Hayton, 1993
[10]Sonstegard, 1985
[11]Puffer, et al., 1982
[12]Pierce, et al., 1981
[13]Honstead, et al., 1971
[14]Ebert et al., 1993
[15]Soldat, 1970

Table 2.3.8: Sportfishers[a] Survey Methods

Fisher Group[b]	Methods (See Key)[c]							
	Number Surveyed	Contact Method	Instrument	Reporting Method	Catch vs. Consump-tion	Individual vs. Household	Data Available	Duration
Alabama fishers[1]	1,586	on-site	int	log	catch	individual	age, eth, inc, reg, sex	12 mos
Louisiana (coastal) fishers[2]	1,100	random[d]	tele	recall	consump-tion	household	age, edu, eth, inc, oth	1 mos
New York fishers[3]	4,530	license	mail/follow up by tele	recall	catch	individual	age, inc, reg	12 mos
New York (Hudson River) fishers[4]	336	on-site	int	recall	consump-tion			
Michigan fishers[5]	2,684	license	mail	recall	consump-tion	household	age, edu, eth, inc, reg, sex	12 mos
Michigan fishers[6]	1,104	license	mail	recall	consump-tion	household	age, edu, eth, inc, reg, sex	6 mos
Michigan fishers[7]	182	license		log	catch	individual		24 mos
Wisconsin fishers (10 counties)[8]	801	license	mail	recall	consump-tion	individual	age, edu, eth, reg, sex	
Wisconsin fishers (10 counties)[8]	801	license	mail	recall	consump-tion	individual	age, edu, eth, reg, sex	
Ontario fishers[9]	494	license	mail	recall	consump-tion	individual	age, reg, sex	summer, fall
Ontario fishers[10]								
Los Angeles Harbor fishers[11]	1,059	on-site	int	recall	catch	individual	age, eth	12 mos
Washington State (Commencement Bay) fishers[12]	508	license	int/follow up by tele	recall	catch	individual		summer, fall

Table 2.3.8: Sportfishers[a] Survey Methods

Fisher Group[b]	Methods (See Key)[c]							
	Number Surveyed	Contact Method	Instrument	Reporting Method	Catch vs. Consump-tion	Individual vs. Household	Data Available	Duration
Washington State (Columbia River) fishers[13]	10,900	license	int	recall	consump-tion	household		12 mos
Maine fishers (inland waters)[14,e]								
Washington State (Columbia River) fishers[15,e]								

KEY:

Contact Method:	Census/Random/Fish Licenses/On-Site/Tribal Members
Instrument:	Personal Interview/Mail Survey/ Telephone Survey
Log/Recall:	Respondents recorded consumption information in a log or recalled consumption information during interview
Catch/Consumption:	Catch: Original data from catch rates extrapolated to consumption rates Consumption: Data obtained on consumption patterns
Individual/Household:	Consumption information obtained either for individuals or for households
Data Available:	Study may have data on: Age/Education/Ethnicity/Income/Region/Sex/Other

NOTES:

[a]Sportfishers may include some individuals who eat fish as a large portion of their diets.
[b]Fisher groups refer to the same headings as those that appear in the text.
[c] Blank cells indicate information is not available.
[d]A "stratified random" approach was used to obtain information with adequate representation of the population of interest.
[e]Data available only from draft documents. Consequently, detailed information was not available at the time of publications. Additional information will be provided in future revisions of this document.

SOURCES:

[1]AL Dept Env Mgt, 1993
[2]Dellenbarger, et al., 1993
[3]Connelley, et al., 1990
[4]Barclay, 1993
[5]West, et al., 1993
[6]West, et al., 1989
[7]Humphrey, 1976
[8]Fiore, et al., 1989
[9]Cox, Vaillancourt, and Hayton, 1993
[10]Sonstegard, 1985
[11]Puffer, et al., 1982
[12]Pierce, et al., 1981
[13]Honstead, et al, 1971
[14]Ebert et al., 1993
[15]Soldat, 1970

Barclay (1993) conducted direct interviews with 336 shore-based anglers on the Hudson River at sites including the upper Hudson, mid-Hudson, and lower Hudson sites, at both urban and rural sites. These surveys were conducted between June and November of 1991 and April and July of 1992. Because the survey did not reach anglers in boats or all river areas, the authors of the survey note that the results cannot be directly extrapolated to the entire population of Hudson River anglers. Over 58 percent of the individuals eat their catch. The survey reports that the average frequency of fish consumption reported was 3 meals over the previous month, but did not ask respondents about the size of their fish meals. Assuming 227 grams (8 ounces) of fish would be eaten per meal and assuming 4.3 weeks per month, the results translate to an average fish consumption rate of 23 grams/day.

Michigan Fishers. West et al. (1993) completed a survey of Michigan fishers over a one year period. For this survey, 2,684 individuals who purchased fishing licenses responded to mailed surveys. Consumption of commercial and sport-caught fish was estimated through a 7-day recall, and data were separated demographically by age, education, ethnicity, income, region and gender. Mean consumption was estimated to be 14.5 grams/day. The 80th percentile was 30 grams/day, 90th percentile consumption rate was 62 grams/day and the 95th percentile rate was 80 grams/day. Several specific subpopulations surveyed in this study had higher than average consumption rates. Minority fishers (primarily black and non-reservation Native Americans) with annual incomes less than $25,000 averaged the highest consumption rate of all Michigan angler groups surveyed, consuming a mean of 43.1 grams/day of sport-caught fish.

An older survey by West et al. (1989) evaluated Michigan fishers as part of a revision of exposure pathways for the Michigan Toxic Substance Control Commission. This earlier study was only conducted over a six month period, but its results were corroborated by the more recent survey data. The population studied was sport anglers, and consumption of both self-caught and commercial fish was considered. The survey relied on seven-day recall in order to estimate mean fish consumption; the percentage of respondents consuming no fish was high (56.6 percent). The study concluded that mean fish consumption for Michigan sport anglers and their families is 16.1 grams/day, after adjustment for non-response bias. The 90th percentile consumption is approximately 50 grams/day, the 95th percentile is about 70 grams/day, and the maximum reported fish consumption is over 200 grams/day.

The Michigan Department of Natural Resources conducted a survey of 381,000 sport-fishers in 1974 (Humphrey, 1976, as cited in Rupp et al., 1979). This survey obtained mean catch of 36 lbs. of fish per year (44.7 grams per day) for consumption.

Wisconsin Fishers. In a survey of anglers in Wisconsin, the annual mean number of sport-caught meals was 18. Using the assumed fish meal size of 8 ounces (227 grams) from this survey, the estimated mean daily consumption of sport-caught fish in Wisconsin is about 11 grams/day. When respondents who consumed no sport-caught fish were excluded, the mean daily sport-caught fish intake was 12 grams/day (Fiore et al., 1989). The 95th percentile value, counting only those individuals who consumed any sport-caught fish, was determined to be 37 grams/day.

Ontario Fishers. Another study was completed by Ontario sports fishers in 1992 (Cox, Vaillancourt, and Hayton, 1993). Questionnaires were inserted randomly into 10,000 copies of *1992 Guide to Eating Ontario Sports Fish*, and 494 replies were received. Questions regarding fish preferences and catch rate, consumption rate and portion sizes, and use of consumption advisories were asked. A mean daily consumption of 22.5 grams/day was calculated based on estimated average meal size and frequency of eating sport-caught sportfish. Anecdotal evidence provided by one researcher studying the Ontario sportfishers during an earlier survey from 1985 (Sonstegard, 1985 as cited in Kleiman, 1985) found that an average sportfisher consumed a mean of 31 grams/day, while a high-end consumer ate 62 grams/day (the percentile value was not specified). The maximum amount consumed was over 310 grams/day.

Idaho Fishers. One study was conducted in the Lake Coeur d'Alene region in Idaho (West, 1993; Richter and Rondinelli, 1989). 933 individuals were surveyed, including Native Americans living both on and off reservations, individuals selected randomly from individuals with fishing licenses in Idaho, and volunteers who were recruited for the study. Tribal members were surveyed in person, while others were surveyed primarily by telephone. All respondents were asked to recall fish consumption patterns. This study was conducted over a period of three months, so data must be extrapolated to the rest of the year. Consumption rates for the licensed fisher population ranged from 16 to 27 grams/day.

Los Angeles Harbor Fishers. From January to December of 1980, 1059 interviews with sportfishers were conducted in several fishing areas of the Los Angeles Harbor area (Puffer et al., 1982). No fisher was sampled more than once. Data was collected on the following: amount of fish caught on the day of the interview, the primary use of the fish (whether eaten by the fisher's family, given away, thrown back, etc.), frequency of fishing, and other variables. Based on this data and assuming that only an edible portion (1/4 to 1/2) of the caught fish would be eaten, median and 90th percentile consumption rates of 37 grams per day and 225 grams per day were determined. The 95th percentile was 338.8 grams/day. Consumption rates were also estimated by age, race, and species caught. This study indicates that median consumption rates for Orientals/Samoans are 71 grams/day and 113 grams/day for individuals over 65 years old.

Washington State Fishers. Interviews were conducted with fishers in Commencement Bay, Washington from July to late November; 304 interviews were conducted in summer and 204 were conducted in the fall (Pierce, 1981). Data were collected on size and amount of specific species caught, size of the fishers' families, frequency of fishing, and planned use of the fish. The fishers were later called about whether the fish had been eaten. USEPA (1989a) used these data to estimate a median consumption rate value of 23 grams per day and a 90th percentile of 54 grams per day (also reported in USEPA, 1997a). The authors note that although a survey of night/dawn fishing was conducted only once, fish caught at this time could represent a significant part of the total fish caught from the bay. Therefore, these values may underestimate fish consumption.

Honstead et al. (1971, as cited in Rupp et al., 1979) conducted a study of the consumption patterns of sportfishers on the Columbia River in the Tri-City area of Hanford, Washington. This

survey monitored 10,900 persons, each of which were members of households where a Columbia River angler resides. The surveyors required respondents to recall the number of fish meals consumed over a 12-month period and, using an estimate of 200 grams per meal, calculated the mean annual consumption to be 2.8 kg per year (7.7 grams/day).

Lake Ontario Fishers. Connelly et al. (1996) surveyed 1,202 Lake Ontario anglers through mail questionnaires, diaries, and telephone interviews. The mail questionnaires were based on a 12 month recall of 1991 fishing trips; the diaries involved self-recording of 1992 fishing trips. Of the 1,202 participants, 853 returned a diary or provided diary information by telephone. Participants were instructed to record in the diary the species of fish eaten, meal size, method by which fish was acquired (sport-caught or other), fish preparation and cooking techniques used, and the number of household members eating the meal. Due to changes in health advisories for Lake Ontario which resulted in less Lake Ontario fishing, only 43 percent, or 366 persons indicated that they fished Lake Ontario in 1992. The mean fish intake from all sources was 17.9 grams/day and from sport-caught sources was 4.9 grams/day. The median rates were 14.1 grams/day for all sources and 2.2 grams/day for sport-caught; the 95th percentiles were 42.3 grams/day and 17.9 grams/day for all sources and sport-caught, respectively. Residents of large cities and younger people had lower intake rates on average. The authors note that although diaries tend to provide more accurate information than studies based on 12 month recall, a considerable portion of the respondents participated in the study for only a portion of the year and some errors may have been generated in extrapolating the results to an entire year.

Alaska Communities. Wolfe and Walker (1987) analyzed a data set from 98 Alaska communities (four large urban population centers and 94 small communities) for harvests of fish, land mammals, marine mammals, and other wild resources. The data set was developed by various researchers in the Alaska Department of Fish and Game, Division of Subsistence, between 1980 and 1985. Respondents were asked to estimate the quantities of particular species that were harvested and used by members of their households during the previous 12 month period. Urban sport fish harvests were derived from a survey that was mailed to a randomly selected statewide sample of anglers. For the four urban centers, fish harvests ranged from 6.2 grams/day to 26.2 grams/day. The range for the 94 small communities was 31 grams/day to 1,541 grams/day. For the 94 communities, the median per capita fish harvest was 162 grams/day. Dressed weight, the portion brought into the kitchen for use, varied by species and community, but in general was 70 to 75 percent of total fish weight. The authors used a factor of .5 to convert harvest to intake rates, yielding a median per capita consumption rate in the 94 small communities of 81 grams/day, and a range of 15.5 to 770 grams/day.

Savannah River Fishers. Turcotte (1983) estimated fish consumption from the Savannah River in Georgia based on total harvest, population studies, and a Georgia fishery survey. The angler survey data, which included the number of fishing trips per year as well as the number and weights of fish harvested per trip, were used to estimate the average consumption rate in the angler population. The study found an average consumption rate of 31 grams/day and a maximum rate of 58 grams/day.

Alabama Fishers. Meredith and Malestuto (1996) studied anglers in 29 locations in Alabama to estimate freshwater fish consumption. The purpose of their study was to compare two methods of estimating fish consumption: the harvest or krill survey, and the serving-size method. The two techniques yielded comparable estimates of mean fish intake: 43 and 46 grams/day, respectively.

Florida Fishers Who Receive Food Stamps. As part of a larger effort, the Florida Department of Environmental Regulation attempted to identify fish consumption rates of anglers who were thought to consume higher rates of fish. Interviews with twenty-five households' primary seafood preparers were conducted at each of five food stamp centers per quarter for an entire year. The respondents were asked to recall fish consumption at home within the previous seven days. Sekerke et al. (1994) found that adult males in the study consumed 60 grams/day of finfish and 50 grams/day of shellfish; adult females consumed 40 grams/day and 30 grams/day, respectively, of finfish and shellfish.

Subsistence Fishers

Subsistence fishers consume fish as a major staple of their diet. As noted above, subsistence fishers often have higher consumption rates than other fisher groups; however, consumption rates vary considerably among subsistence fishers. Consequently, generalizations should not be made about this fisher group. If studies contained in this section are used to estimate exposure patterns for a subsistence population of concern, care should be taken to match the dietary and population characteristics of the two populations as closely as possible. Several surveys evaluating the consumption patterns of subsistence fishers have been initiated in the last several years. Some of these have been completed and many more are currently being carried out, with results expected in the near future. Although many of these surveys provide only a range of consumption rates, a great deal of qualitative information has been gained through these surveys, both about the individual populations that were studied and about effective survey methods for different groups of subsistence fishers. The consumption rates reported by these surveys are presented below. Results of these surveys and the methods used to collect the data are summarized in Tables 2.3.9 and 2.3.10.

Great Lakes Tribes. The Great Lakes Indian Fish and Wildlife Commission conducted a survey of spear fishing for walleye among Native Americans living on reservations in the Great Lakes Region (Kmiecik, 1994). This study was designed to evaluate the concern about mercury among spear fishers in the tribes of the Great Lakes Region. The results of this study showed that people were modifying their behavior about where to fish and types and sizes of fish to keep based on concerns about mercury. Although consumption rates had no baseline for comparison prior to mercury concerns, many respondents indicated that they modified their consumption of fish due to concerns about mercury contamination. Despite these possible decreases in fish consumption, the rates of consumption of walleye were still extremely high; the mean value was 351 grams/day, while the maximum amount consumed was 1,426 grams/day. These daily consumption rates were calculated by multiplying the average portion size, as reported by the respondents, by the respondents' average consumption of 2.75 meals per week (that is the average of each season's meals/wk), and

then dividing by 7 days/wk. Assuming individuals may have been eating other fish in addition to walleye, the rates may be higher than these values.

Idaho Fishers. As described above, a study conducted in the Lake Coeur d'Alene region in Idaho surveyed Native Americans, individuals with fishing licenses, and volunteers (West, 1993; Richter and Rondinelli, 1989). This study was conducted over a period of three months, so data must be extrapolated to the rest of the year. Consumption rates of tribal members ranged from 28 to 49 grams/day.

Columbia River Tribes. One of the most comprehensive surveys of fishing patterns among Native Americans has been conducted by the Columbia River Inter-Tribal Fisheries Commission. The study surveyed four of the tribes living in the Columbia River Basin (CRITFC, 1994). From four tribes both on and off the reservation, 717 individuals were surveyed in person regarding their consumption patterns of self-caught fish, wild game, and wild rice. The responses were based on memory recall, and the survey was conducted over a full year. Mean consumption from this study was calculated as 58.7 grams/day and the 95th percentile is 170 grams/day.

American Samoan Fishers. A number of surveys have been conducted in American Samoa that have attempted to assess the potential risk of industrial development in the major harbor on the main island of American Samoa where most of the population also lives and fishes (Den, 1994; Young, 1994; Eng, 1994). The local EPA conducted a pilot scoping survey to assess the extent of the contamination in the fisheries resources and heavy metal poisoning in blood and urine of sample populations; a brief survey of consumption rates was included in this survey. The results of this study (the toxicity of the harbor and the fisheries resources) encouraged the local EPA to apply for a study to be conducted by the Centers for Disease Control (CDC). Results indicated fish consumption at a rate of approximately 12 grams/day (Ponwith, 1991; ATSDR, 1995).

Wisconsin Chippewa Indians. Peterson et al. (1994) investigated the extent of exposure of Chippewa Indians who consume fish caught in northen Wisconsin lakes to methylmercury. The study, conducted in May 1990, included 175 randomly selected and 152 nonrandomly selected participants. The authors reported that both groups had similar fish consumption rates. Participants were asked to complete a questionnaire describing their routine fish consumption and, more extensively, their fish consumption during the previous two months. Results from the survey showed a mean fish consumption of 1.2 meals per week. This includes fish from all sources. The consumption figure translates to a fish intake of 20 grams/day, using 117 grams/meal as the average weight of fish consumed per fish meal in the general population. Consumption varied seasonally, with the highest consumption during April and May, the spearfishing season for walleye. During peak consumption months, males and respondents under 35 consumed more fish than females and respondents 35 and over.

Miccousukee Indian Tribes. The Centers for Disease Control (1993) administered dietary questionnaires to 2 children and 183 adults from the Miccousukee Indian Tribes of South Florida. The survey found that 31 percent ate fish from the Everglades during the previous six months; 57

percent consumed marine fish during the previous six months. The median consumption of local fish was 3.5 grams/day; the maximum consumption was 168 grams/day. Blue gill was the most common species of local fish consumed; largemouth bass were consumed in greatest quantity.

Wisconsin Tribes. A 1992 EPA report entitled *Tribes at Risk* (The Wisconsin Tribes Comparative Risk Project) reported an average total fish intake for Native Americans living in Wisconsin of 35 grams/day. The average daily intake of locally harvested fish was 31.5 grams.

Tribes of Puget Sound. In November 1994 Toy et al. (1995) completed a study of fish consumption among 190 adult members of the Tulalip and Squaxin Island Tribes of Puget Sound. The study was conducted between February and May 1994. Fish consumption practices were assessed using dietary recall methods, food models, and a food frequency questionnaire. Fish consumed were categorized into anadromous fish (e.g., king salmon and sockeye salmon), pelagic fish (e.g., cod and pollock), bottom fish (e.g., halibut and sole), and shell fish (e.g., manila clams, scallops, and mussels). Anadromous fish and shell fish were consumed in greatest quantities.

The 50th percentile consumption rate for all fish combined for the Tulalip Tribe was 0.55 grams/kg body weight/day and 0.52 grams/kg body weight/day for the Squaxin Tribe. If an average body weight is assumed to be 70 kg, the daily fish consumption rate for adults in the Tulalip Tribe was 38.5 grams/day and 36.4 grams/day for the Squaxin Tribe. The weighted combined median daily fish consumption for both tribes was 37.1 grams.

Native Americans near Clear Lake, California. Harnly et al. (1997) found that Native Americans living near Clear Lake, California consumed an average of 84 grams/day of fish (60 grams/day of sport fish plus 24 grams/day of commercial fish). The most popular species of sportfish were: catfish, perch, hitch, bass, and carp. Commercial species most commonly eaten were: snapper, tuna, salmon, crab, and shrimp.

Hawaiian Islands. The Mercury Study Report to Congress (1997) cites a number of studies on the commercial utilization of seafood [i.e., Higuchi and Pooley (1985) and Hudgins (1980)] and analyses of epidemiology [i.e., Wilkens and Hankin (1996)] which provide a basis to describe general patterns of fish consumption among Hawaiians. These studies indicate that, on average, Hawaiians consumed 30.5 grams/day of fish in 1972 and 24.0 grams/day in 1974. A 1987 State of Hawaii study of 400 residents cited by the authors found that shrimp and mahimahi were the most popular seafoods.

Alaska Natives. Nobmann et al. (1992) performed a nutrient analysis of the food consumed in eleven communities that represented different ethnic and socioeconomic regions of Alaska. The survey sample included 351 adults aged 21-60 years. Information was obtained using 24 hour dietary recalls during five seasons over an 18-month period. The mean daily intake of fish and shellfish of Alaska Natives was 109 grams/day.

Table 2.3.9: Subsistence Fishers[a] Consumption Data

Fisher Group[b]	Fish Intake Rates (g/day)			Fish Type[c]	
	mean	95%ile	max		
Great Lakes tribes[1]	351		1426	F	R
Columbia River tribes[2]	58.7	170		F	R
Florida residents receiving food stamps[3]	23			F+S	
Florida Asian residents[3]	59			F+S	R+C
High-end Caucasian consumers on Lake Michigan[4]	54		132		
Wisconsin tribes[5]	31.5				
Chippewa tribes in Wisconsin[6]	55				
Native Alaskan Adults[7,c]	109			F+S	

NOTES:
[a]Subsistence fishers include groups (such as the Florida residents receiving food stamps) that may eat sport-caught fish at high rates but do not subsist on the fish as a large part of their diet
[b]Fisher groups refer to the same headings as those that appear in the text
[c]Fish Type: F= Freshwater, S = Saltwater (may indicate either estuarine or marine waters), R = Recreationally caught.

SOURCES:
[1]Kmiecik, 1994
[2]CRITFC, 1994
[3]Degner et al., 1994
[4]Hovinga, 1992; 1993
[5]USEPA, 1992
[6]Peterson et al., 1995
[7]Nobmann et al., 1992

Table 2.3.10: Subsistence Fishers[a] Survey Methods

Fisher Type[b]	Methods (See Key)[c]							
	Number Surveyed	Contact Method	Instrument	Reporting Method	Catch vs. Consumption	Individual vs. Household	Data Available	Duration
Great Lakes tribes[1]	69	tribe	mail	recall	consumption	individual	NA	2 mos
Columbia River tribes[2]	717	tribe/ random	interview	recall	consumption	individual	age, eth, reg, sex	12 mos
Florida residents receiving food stamps[3]	500							
Florida Asian residents[3]	120	random[e]	telephone	recall	consumption	individual	age, eth, reg, sex, income	12 mos (of total study, not recall)
High-end Caucasian consumers on Lake Michigan[4,d]	115							
Wisconsin tribes[5,d]								
Chippewa tribes in Wisconsin[6,d]	323	tribe/ random	interview	recall	consumption	individual	sex, employmt., age, education	1 mo
Native Alaskan Adults[7,d]	351			recall	consumption			18 mos

KEY:

Contact Method:	Census/Random/Fish Licenses/On-Site/Tribal Members
Instrument:	Personal Interview/Mail Survey/Telephone Survey
Log/Recall:	Respondents recorded consumption information in a log or recalled consumption information during interview
Catch/Consumption:	Catch: Original data from catch rates extrapolated to consumption rates. Consumption: Data obtained on consumption patterns
Individual/Household:	Consumption information obtained either for individuals or for households
Data Available:	Study may have data on: Age/Education/Ethnicity/Income/Region/Sex/Other

NOTES:

[a]Subsistence fishers include groups (such as the Florida residents) that may eat sport-caught fish at high rates but not subsist on fish as a large part of their diets.

[b]Fisher groups refer to the same headings as those that appear in the text.

[c]Blank cells indicate information is not available.

[d]Data available only from draft documents.

[e]Number sampled per county was proportionate to population in county compared to the entire State.

SOURCES:

[1]Kmiecik, 1994

[2]CRITFC, 1994

[3]Degner et al., 1994

[4]Hovinga, 1992; 1993

[5]USEPA, 1992

[6]Peterson et al., 1995

[7]Nobmann et al., 1992

Surveys in Progress

The Wisconsin Department of Health is currently conducting a study of the Hmong populations of Sheboygan and Manitowac (Nehls-Lowe, 1994; University of Wisconsin Sea Grant, 1994). These surveys have resulted from a larger project that was designed to inform the Asian-American populations of the potential dangers of eating too much contaminated fish.

The EAGLE project (EAGLE, 1991; Cole, 1994) is a Canadian collaboration of the Assembly of First Nations and Health and Welfare Canada. This project is a several year study of the health of First Nation communities throughout the northern Great Lakes region. Consumption patterns by these communities of local food sources have been obtained, and preliminary results of this project have been compiled. The results will not be ready, however, until sometime in 1997 (Wheatley, 1996).

Another study is underway among the Ojibway peoples (Chippewa) of the upper Great Lakes region (Dellinger, 1993 and 1996) and is currently being finalized. This study is designed primarily to study the correlation between fish consumption habits, body burdens, and neurobehavioral effects.

EPA Regions 9 and 10 have begun studies of the Asian-American/Pacific Islander communities in Washington and California (Den, 1994; Young, 1994; Eng, 1994; Lorenzana, 1994). In order to most effectively reach the communities that they wish to survey, Region 10 awarded the project to a local Asian-American community. Specifically called the Asian Pacific American Seafood Consumption Study and conducted via the Refugee Federation Service Center and the University of Washington, the community group designed the study with input from technical advisors (statisticians, toxicologists, epidemiologists), agency representatives and various community groups (USEPA, 1996). Personal interview surveys conducted in the King County area of Seattle, Washington were completed during the of summer 1997, and a report is expected by September 1998 (Lorenzana, 1998). A study of the Laotian community in the San Francisco Bay Area (specifically, west Contra Costa County) was funded by EPA Region 9 and conducted via the Asian Pacific Environmental Network, a non-profit organization that coordinates environmental health projects. This represents a community-based survey where the survey questions were designed with input from the Pacific Asian community, interested agencies and academia, and where the actual survey was conducted by an elder and junior person from each of the various ethnic groups composing the Laotian community. Data collection was completed during the Summer of 1997, and a draft report developed. This underwent subsequent peer review and the report was finalized in March 1998 (Den, 1998).

Preference #3: Use of Distributional Data from National Food Consumption Surveys

If information from existing regional studies is not relevant to a given State, EPA's third preference is that States use distributional information for intake of fresh/estuarine species for different population groups from national food consumption surveys. EPA has analyzed one such

national survey, the combined 1989, 1990, and 1991 Continuing Survey of Food Intake by Individuals (CSFII). EPA recommends use of the CSFII (see Tables 2.3.11 through 2.3.22), but believes similar nationally-based surveys are appropriate for consideration (see Table 2.3.1 on sources of exposure information). The 1989 through 1991 CSFII data are the most recent analyzed by EPA for developing estimates. As more current data become available, these estimates may be revised by EPA.

In addition to providing nationally-based information, which offers a greater quantity of data points, the CSFII information is also presented here for regional break-outs from the same data set. States may wish to consider these regional values if they have at least some information as indicated with Preferences #1 and #2, and if they believe that the consumption rates of the particular population of concern differ from the national rates. However, if a State has not identified a separate well-defined population of highly-exposed consumers and believes that the national data from the CSFII are representative, EPA recommends these national data. Although the regional break-outs are provided for the States to consider, EPA believes that there is less confidence in the regional estimates due, in part, to the relatively small sample size that results when these break-outs are made (see Tables 2.3.12 through 2.3.20). For example, the Mountain Region is indicative of a very small sample size with few respondents who reported consumption during the study period and is skewed by a few high consumers (e.g., a mean of 3.23 grams/day and a 90th percentile of 0.48 grams/day). It is, therefore, not recommended that these breakouts be used by themselves to represent regional/State intakes. In addition, the geographic divisions, as created, may not accurately reflect the consumption patterns of each State within a given division. For example, whereas the Pacific geographic division (i.e., California, Oregon, Washington) may be reasonable to use for West Coast populations, it is doubtful that the values for the West South Central division apply equally to each State (Table 2.3.18). That is, fish consumption in Louisiana may be vastly different than fish consumption in Oklahoma.

A detailed set of fish consumption tables from the CSFII is presented in Appendix A of this document. The tables indicate consumption rates for adults, children under 14, women of child-bearing age (considered to be ages 15-44), as well as per capita values. Both average and acute values are presented for the adults and per capita groups, whereas only acute values are given for children under 14 and women of childbearing age. The procedures for determining average and acute consumption are described on pages 107 and 117, respectively. Appendix A includes the regional breakouts that are also listed in Tables 2.3.12 to 2.3.20. All of the aforementioned tables are presented in both grams/day and in mg/kg/day. Finally, the Appendix includes species breakouts by mean consumption for each of the four major groups in grams/day.

The U.S. Department of Agriculture conducts the CSFIIs, through which dietary intake data is collected for selected years from April of one year to March of the next (USEPA, 1998). About 25 percent of the interviews are conducted in a calendar quarter. These data are collected from the 48 conterminous States over 3 consecutive days. On the first day of the survey, participants give information to an in-home interviewer, and on the second and third days, data are taken from self-administered dietary records. Meals consumed both at home and away from home are recorded. However, it was not possible to distinguish between the intake of fish locally caught and that which

was not. Although the assumption that all freshwater/estuarine fish consumed comes from a particular water body is somewhat conservative, EPA believes that this is a reasonable assumption to ensure adequate protection from such fish subject to contamination.

The CSFII 1989-1991 did not draw samples from Alaska or Hawaii. As these two States could potentially contain a larger percentage of subsistence fishers than the population from the 48 conterminous States, the absence of data from these two States could result in a slight underestimate of per capita fish consumption for the entire population. This underestimate is probably insignificant given that the populations of Alaska and Hawaii are quite small compared with that of the total conterminous States (USEPA, 1998). However, as indicated above, Alaska and Hawaii are encouraged to make decisions on fish intake via Preferences #1 and #2, if possible, to ensure the most accurate estimates.

The CSFII survey is a national multi-stage, stratified-cluster area probability sample. The 48 conterminous States were divided into 60 strata. Within these strata, counties, cities, and areas within cities were grouped into relatively homogeneous units called primary sampling units (PSUs). Two of these units were sampled, with replacement, from each of the strata. Each PSU was sampled with probability proportional to its 1985 projected population. These units were further divided into area segments, from which predetermined numbers of households were selected for participation. Each household within an area segment had equal probability of selection (USEPA, 1998). To allow the data for the three survey years to be combined, the area segments for each of the years were drawn from the same PSUs (USEPA, 1998).

Each of the surveys consists of "basic" and "low-income" samples. Individuals in all households, regardless of income, were eligible for inclusion in the basic sample. In the low-income sample, only households with gross income at or below 130 percent of the Federal poverty threshold were eligible for inclusion. Both samples are included in the distributional estimates using data from the three survey years.

Response rates for the three survey years and for the low-income and basic surveys varied from 40 to 53 percent. USDA corrected the survey weights for non-response.

Of the 6,000 food categorizations in the CSFII surveys, 465 relate to fish. Survey respondents with 3 days of dietary intake data reported consumption across 284 of these fish-related food codes. The amount of a fish-related food code reported was adjusted according to information in the USDA recipe file to reflect the proportion of fish in the recipe. For example, if fish was 80 percent of the recipe, then consumption of 100 grams of the food code was adjusted to 80 grams to represent the amount of fish consumed.

Food codes were assigned to either a freshwater/estuarine or marine habitat. Food codes containing flatfish (i.e., flounder, smelt, halibut, plaice, and sole), clams, scallops, crabs (with the exception of king crab) and salmon were apportioned between the freshwater/estuarine and marine

habitats based on the proportions of freshwater/estuarine and marine species landed during 1989, 1990, and 1991 reported by the National Marine Fisheries Service (NMFS, 1995-96).

In some cases habitat assignments are based on NMFS data *and* life-cycle considerations. If a particular species is listed by NMFS as commercially harvested in marine waters, but is known to spend at least part of it's life-cycle in estuarine or freshwater habitats, further evaluation was undertaken to determine the significance of a species' life-cycle with respect to exposure to chemical contaminants in freshwater and estuarine waters. Species with life-cycles utilizing both freshwater/estuarine and marine habitats identified as contributing significantly to the CSFII fish consumption rate determination include shrimp and salmon.

Shrimp, which are harvested in both marine waters and freshwater/estuarine waters, spend their juvenile years up to sexual maturity in freshwater/estuarine habitats. At sexual maturity, shrimp are nearly adult size and generally begin migration to marine waters where they spend the remainder of their adult life. Once shrimp reach sexual maturity, they are nearly full grown and available for commercial harvesting from both estuarine and marine waters. Though shrimp are harvested from both estuarine and marine waters, they have been assigned to the freshwater/estuarine habitat designation. This is because shrimp are harvestable from estuarine waters or immediately after migrating to marine waters (Zein-Eldin and Renaud, 1986; Kutkuhn, n.d.).

The six species of anadromous salmon found in North American waters spend their first 3 months to 3 years in freshwater/estuarine habitats before migrating to marine waters. At the time of out migration to marine waters, juveniles measure up to 5 inches in length. All six species will then spend 1-5 years maturing as adults in open sea before migrating back to freshwater lakes, rivers and streams for spawning. Depending on the species, spawning may occur from one to eight weeks after entering freshwater habitats (some unique populations of sockeye salmon may spend up to 6 months in lakes prior to spawning). Additionally (with the exception of these sockeye populations) most salmon fast, thus spending their energy making the trip to their spawning destination. Because these six species of salmon spend essentially their entire adult life in open seas prior to commercial harvesting from marine waters, all salmon have been designated marine habitat with the exception of 1 percent of the total U.S. harvest which accounts for salmon which are farmed raised or harvested from landlocked populations (Groot and Margolis, 1991).

Consumption for the given USDA food code with an unknown habitat designation was allocated across the freshwater/estuarine and marine habitat types in the same percentages as those observed across food codes from known habitat types.

Average daily individual consumptions for a given fish-by-habitat category were calculated by summing the amount of fish eaten by the individual across three reporting days for all fish-related food codes in a given fish-by-habitat category. The total individual consumption was then divided by three to obtain an average daily consumption. The three-day individual food consumption data collection period is one during which a majority of sampled individuals did not consume any finfish or shellfish. The non-consumption of finfish or shellfish by a majority of individuals, combined with

consumption data from high-end consumers, resulted in a wide range of observed fish consumption. This range of fish consumption data would tend to produce distributions of fish consumption with larger variances than would be associated with a longer survey period, such as 30 days. The larger variances would reflect greater dispersion, which results in larger upper-percentile estimates, as well as wider confidence intervals associated with parameter estimates. It follows that the estimates of the upper percentiles of per capita fish consumption based on three days of data will be conservative with regards to risk (USEPA, 1998).

For each type of criteria (chronic, acute, or consideration of developmental effects), percentile values from distributional data on intakes are presented below for consumption of freshwater and estuarine fish, as well as for consumption of all fish (including marine species).

Chronic Criteria

Table 2.3.11 and Exhibit 2.3.1 include distributional data on intake rates of fresh/estuarine fish for adults 18 years and older. These intake values represent "as consumed" weights; that is, they are primarily cooked weight intakes but also include any raw fish consumption (e.g., raw shellfish) reported. These estimates were determined by averaging information from both consumers and non-consumers of fish over the three days of the survey. This survey did not specifically ask questions on whether a respondent eats fish or how often and, therefore, it is not possible to identify consumers from non-consumers. Since the CSFII reporting period is only three days, long-term consumption distributions cannot be well characterized using the CSFII data. EPA is recommending adult intakes (i.e., specifically based on individuals age 18 years and over) for the general, sport fisher, and subsistence fisher populations to be consistent with the fact that the assumptions used for drinking water intake and body weight are also based on adults. These values represent reasonable intake rates for long-term exposure that result in chronic effects. As shown in Table 2.3.11, the arithmetic mean for adults is 5.59 g/day; the median is 0 g/day. The 90th percentile value is 17.80 g/day, the 95th percentile is 39.04 g/day, and the 99th percentile is 86.30 g/day. Ninety percent confidence intervals for the mean and 90 percent bootstrap intervals for the median and percentile values are also recorded in Table 2.3.11. EPA determined confidence interval estimates for the percentile estimates by using Efron's percentile bootstrap technique (USEPA, 1998). Exhibit 2.3.1 shows the cumulative distribution (via histogram), which States may wish to use to estimate intake rates at different percentile values from those values presented in Table 2.3.11.

Table 2.3.11: Daily Estimates of Fish Consumption (Finfish and Shellfish): Individuals of Age 18 and Over in the U.S. Population (g/day)

Statistic	Estimate	90% Interval*	
		Lower Bound	Upper Bound
Fresh/Estuarine			
Mean	5.59	4.91	6.28
50th Percentile	0	0.00	0.00
90th Percentile	17.80	14.89	20.63
95th Percentile	39.04	36.13	42.16
99th Percentile	86.30	81.99	96.67
All Fish (including marine)			
Mean	18.01	16.85	19.17
50th Percentile	0.00	0.00	0.00
90th Percentile	60.64	57.06	64.63
95th Percentile	86.25	80.29	91.00
99th Percentile	142.96	134.23	154.15

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications
Source: CSFII (1989-1991)

Geographic data are included for areas of the United States, as determined by the U.S. Department of Commerce for the 1980 Census of Population. Because of small sample size, these data are provided for all individuals rather than for those only $\geq$ 18 years old. The regions are broken out as follows:

New England:	Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont
Middle Atlantic:	New Jersey, New York, Pennsylvania
South Atlantic:	Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia
East North Central:	Illinois, Indiana, Michigan, Ohio, Wisconsin

East South Central: Alabama, Kentucky, Mississippi, Tennessee

West North Central: Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, South Dakota

West South Central: Arkansas, Louisiana, Oklahoma, Texas

Mountain: Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, Wyoming

Pacific: California, Oregon, Washington

As stated on page 104, States and Tribes should consider these data in combination with other regional studies and not by themselves because of the lack of confidence due to the small sample size.

Tables 2.3.12 through 2.3.20 include these breakouts for finfish and shellfish, again representing as consumed intakes:

Table 2.3.12: Distribution of Finfish and Shellfish Consumption: New England

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	4.94
50th Percentile	0.00
90th Percentile	17.58
95th Percentile	30.11
99th Percentile	72.04
All Fish (including marine)	
Mean	21.90
50th Percentile	0.00
90th Percentile	73.56
95th Percentile	91.33
99th Percentile	145.86

Source: CSFII (1989-1991)

Table 2.3.13: Distribution of Finfish and Shellfish Consumption: Middle Atlantic

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	3.79
50th Percentile	0.00
90th Percentile	12.13
95th Percentile	25.29
99th Percentile	61.72
All Fish (including marine)	
Mean	18.68
50th Percentile	0.00
90th Percentile	61.26
95th Percentile	80.54
99th Percentile	153.23

Source: CSFII (1989-1991)

Table 2.3.14: Distribution of Finfish and Shellfish Consumption: South Atlantic

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	4.92
50th Percentile	0.00
90th Percentile	16.72
95th Percentile	30.45
99th Percentile	77.54
All Fish (including marine)	
Mean	16.33
50th Percentile	0.00
90th Percentile	57.62
95th Percentile	83.39
99th Percentile	130.78

Source: CSFII (1989-1991)

Table 2.3.15: Distribution of Finfish and Shellfish Consumption: East North Central

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	2.88
50th Percentile	0.00
90th Percentile	5.10
95th Percentile	18.24
99th Percentile	58.24
All Fish (including marine)	
Mean	13.21
50th Percentile	0.00
90th Percentile	47.50
95th Percentile	72.05
99th Percentile	114.31

Source: CSFII (1989-1991)

Table 2.3.16: Distribution of Finfish and Shellfish Consumption: East South Central

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	10.66
50th Percentile	0.00
90th Percentile	37.64
95th Percentile	58.41
99th Percentile	165.12
All Fish (including marine)	
Mean	16.63
50th Percentile	0.00
90th Percentile	52.26
95th Percentile	69.94
99th Percentile	165.12

Source: CSFII (1989-1991)

Table 2.3.17: Distribution of Finfish and Shellfish Consumption: West North Central

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	4.48
50th Percentile	0.00
90th Percentile	4.41
95th Percentile	25.84
99th Percentile	104.32
All Fish (including marine)	
Mean	12.85
50th Percentile	0.00
90th Percentile	42.99
95th Percentile	63.05
99th Percentile	141.07

Source: CSFII (1989-1991)

Table 2.3.18: Distribution of Finfish and Shellfish Consumption: West South Central

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	7.04
50th Percentile	0.00
90th Percentile	23.85
95th Percentile	55.46
99th Percentile	112.68
All Fish (including marine)	
Mean	13.06
50th Percentile	0.00
90th Percentile	49.69
95th Percentile	74.77
99th Percentile	114.22

Source: CSFII (1989-1991)

Table 2.3.19: Distribution of Finfish and Shellfish Consumption: Mountain

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	3.23
50th Percentile	0.00
90th Percentile	0.48
95th Percentile	20.90
99th Percentile	78.60
All Fish (including marine)	
Mean	11.20
50th Percentile	0.00
90th Percentile	39.32
95th Percentile	58.55
99th Percentile	95.84

Source: CSFII (1989-1991)

Table 2.3.20: Distribution of Finfish and Shellfish Consumption: Pacific

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	3.93
50th Percentile	0.00
90th Percentile	10.16
95th Percentile	26.46
99th Percentile	68.74
All Fish (including marine)	
Mean	16.81
50th Percentile	0.00
90th Percentile	55.87
95th Percentile	83.44
99th Percentile	122.64

Source: CSFII (1989-1991)

Developmental Criteria

Table 2.3.21 presents as consumed weight distributional data for children ages 0 to 14 who are "acute" consumers of fish. Exhibit 2.3.2 graphically shows a more complete distribution of values for these consumers. The term “acute consumer” does not refer to adverse health effects or toxicity studies. It refers to the subset of survey responses where fish was actually consumed. That is, the distributional data from the CSFII for these “acute consumers” was determined by using only data from the individuals who ate fish during the survey period. “Acute consumers” were defined as individuals who reported consumption of a fish-related food code at least once in the three-day reporting period. In addition, if an individual consumed fish for two of the three days, the average daily consumption for that individual was calculated by summing the two daily consumption values and dividing by two. As noted above, these data may be most appropriate to use for evaluating exposures for children because they generally have higher intake rates per body weight than adults. EPA did not generate intervals around the estimates because variance estimation algorithms require data from at least two primary sampling units (PSUs) per stratum, and this criterion was not always met for these acute consumers (USEPA, 1998).

Table 2.3.21: Daily Estimates of Fish Consumption: Finfish and Shellfish - Acute Consumers,[14] Children 0 to 14 Years Old in the U.S. Population

Statistic	Estimate (g/day)
Fresh/Estuarine	
Mean	45.73
50th Percentile	28.35
90th Percentile	108.36
95th Percentile	136.24
99th Percentile	214.62
All Fish (including marine)	
Mean	74.80
50th Percentile	56.49
90th Percentile	153.70
95th Percentile	178.08
99th Percentile	337.46

Source: CSFII (1989-1991)

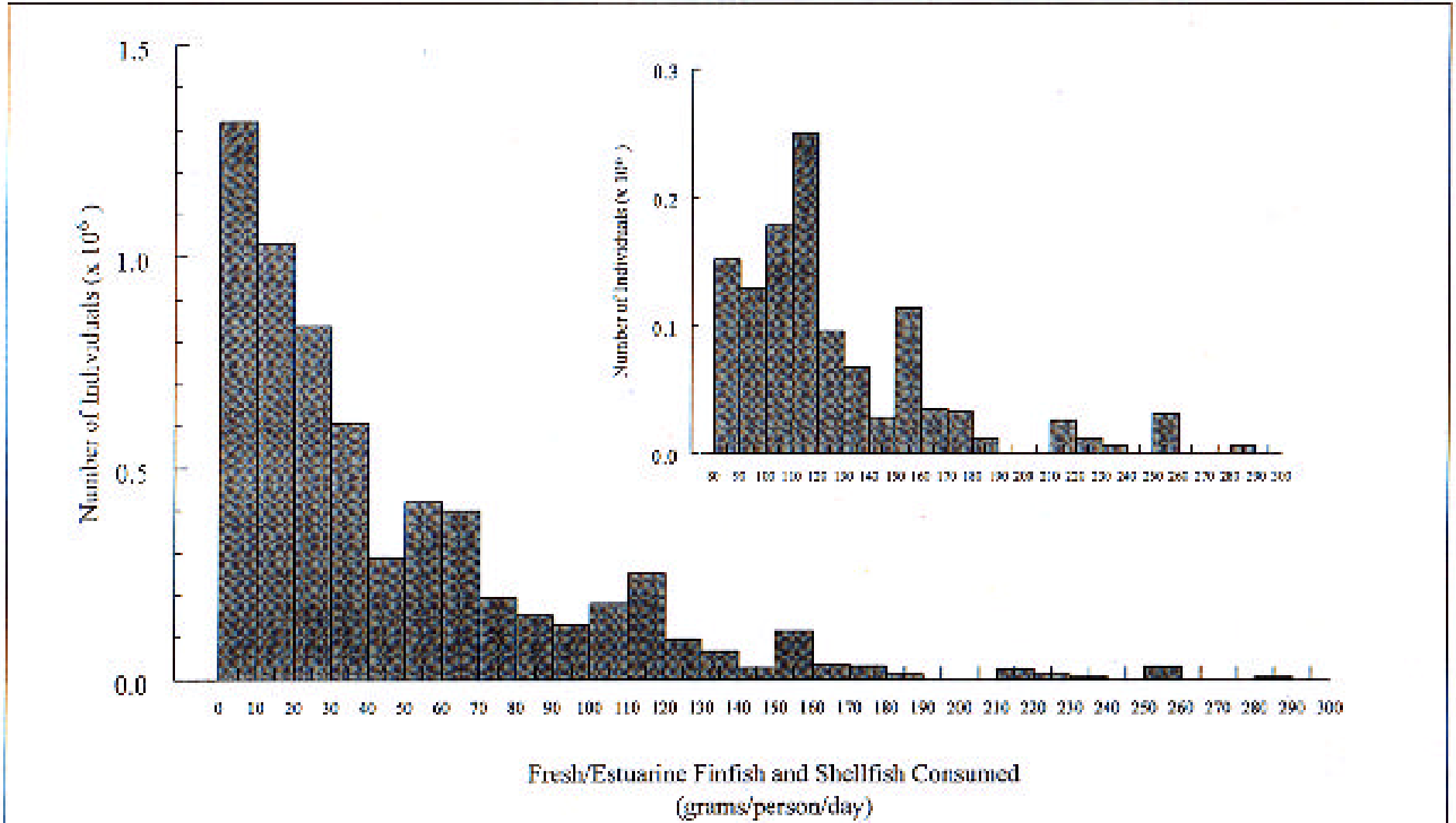
[14] Acute consumer refers to respondents who reported consuming fish during the 3-day survey period.

Exhibit 2.3.2. - HISTOGRAM OF DAILY AVERAGE
PER CAPITA FISH CONSUMPTION

As Consumed Fish

Individuals 14 Years of Age and Younger in the U.S. Population

Acute Consumers - Fresh/Estuarine Finfish and Shellfish



The CSFII data indicate that for median, mean, and upper percentile intakes, rates for children are higher per body weight than rates for adults, with differences of up to 8.6 g/kg-day at the 99th percentile (See Appendix A).

For in-utero developmental effects, intake rates for women of childbearing age may be most appropriate. Thus, Table 2.3.22 presents the distribution of as consumed fish intake values for women ages 15-44 years old who are acute consumers, as described above. Exhibit 2.3.3 graphically shows a more complete distribution of values for these acute consumers.

Table 2.3.22: Daily Estimates of Fish Consumption: Acute Consumers,[15] Women 15 to 44 Years Old in the U.S. Population (g/day)

Statistic	Estimate
Fresh/Estuarine	
Mean	61.40
50th Percentile	35.22
90th Percentile	148.83
95th Percentile	185.44
99th Percentile	363.56
All Fish (including marine)	
Mean	88.80
50th Percentile	69.95
90th Percentile	170.01
95th Percentile	212.56
99th Percentile	361.04

Source: CSFII (1989-1991)

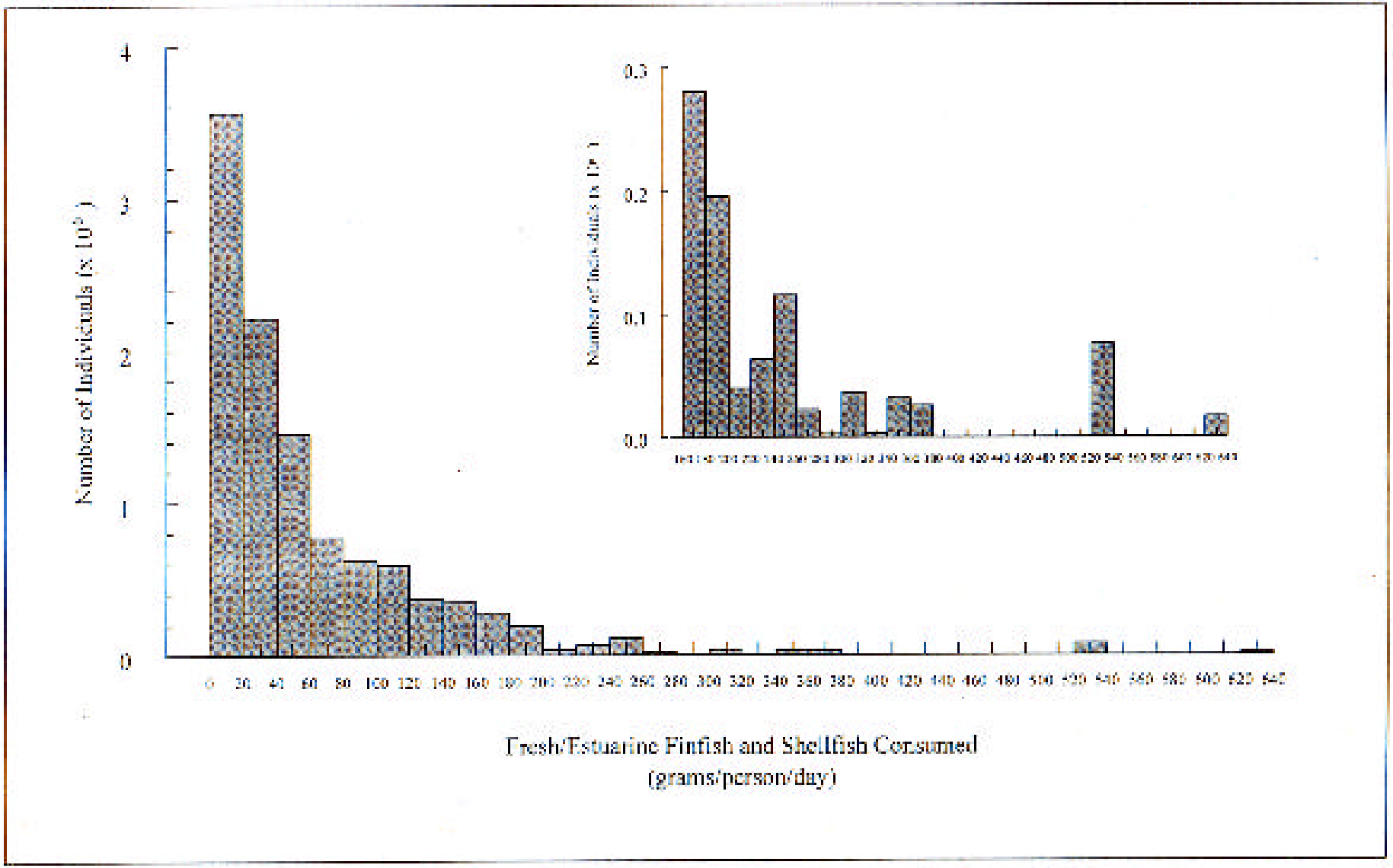
[15] Acute consumer refers to respondents who reported consuming fish during the 3-day survey period.

Exhibit 2.3.3. - HISTOGRAM OF DAILY AVERAGE PER CAPITA FISH CONSUMPTION

As Consumed Fish

Females of Age 15 to 44 in the U.S. Population

Acute Consumers - Fresh/Estuarine Finfish and Shellfish



Preference #4: Use of Default Intake Rates from the CSFII

The 1980 AWQC National Guidelines recommended a fish intake rate of 6.5 grams/day, based on the mean consumption rate of freshwater and estuarine finfish and shellfish from 30-day diary results reported in the 1973-74 National Purchase Diary Survey. These updated guidelines recommend several default intake rates depending on the population and type of effect (chronic or developmental) that is being considered.

Default Intake Rate for Chronic Effects

Although EPA prefers that States use one of the above methods to determine fish intake, this section presents two default intake rates that EPA believes represent appropriate fish intake values for different population groups, and are appropriate for determining intake related to contaminants that may cause chronic effects. EPA recommends using the following intake rates (of freshwater and estuarine finfish and shellfish) based on information for all adults from the CSFII: 17.80 g/day for the general adult population and sport fishers, and 86.30 g/day for subsistence fishers. These values represent the intake of freshwater/estuarine finfish and shellfish as consumed. By applying 17.80g/day as a default for the general adult population, EPA intends to select an intake rate that is protective of a majority of the population. EPA further considers that, although these rates are reflective of high-end consumers in the general population and do not directly reflect intakes specific to sportfishers and subsistence fishers, they are indicative of the average consumption among sport fishers and subsistence fishers, respectively. Specifically, comparison of the CSFII intake rates with results from state and regional surveys indicate that these rates may be appropriate for the defined sportfisher and subsistence fisher populations (refer to study summaries for sportfishers and subsistence fishers under Preference #2). As noted above, however, sportfisher and subsistence fisher populations are generalized terms and each group may encompass a variety of types of individuals. Thus, States should try to use intake rates more specific to the population addressed before considering the default intake rates suggested here (ensuring that the rates chosen meet the minimum discussed on page 86).

Default Intake Rate for Developmental Effects

For a few fish contaminants, health effects in children are of primary concern (e.g., cholinesterase inhibitors). Because children have a higher fish consumption rate per body weight compared to adults, using a higher fish consumption rate per body weight may be necessary for setting AWQC to assure adequate protection for children from toxicants that cause such effects. EPA advises that in absence of local data or other data approximating local information on values appropriate for children's intake, States use a value of 108.36 g/day. This value represents the 90th percentile from the combined 1989-1991 CSFII surveys for acute consumption (defined above under Preference #3, in the Developmental Criteria subsection) of freshwater/estuarine finfish and shellfish for children ages 0 to 14. The value represents only those children from the CSFII survey who ate fish during the 3-day survey period, and the intake was averaged over the number of days during which fish was actually consumed. It is recommended that this value be used with a body weight of

28 kilograms (discussed above) to protect individuals from adverse effects of eating fish when RfDs are based on health effects in children.

Developmental effects may be of concern for children or women of childbearing age. To provide additional protection from adverse effects when pregnant women are of particular concern, a default intake rate of 148.83 g/day, specific to women of childbearing age (15-44 years old), is suggested for setting AWQC to protect against such developmental effects. This value represents approximately the 90th percentile of acute consumption of freshwater/estuarine finfish and shellfish for women in this age group from the CSFII survey. As with the rate for children, this value represents only those women who consumed fish during the 3-day survey period.

2.3.2.4 Incidental Ingestion

The drinking water ingestion rate of 2 liters/day is used only for setting AWQC for those water bodies designated as public water supply sources. Individuals exposed to water from water bodies that are not listed as public water supply sources would not be likely to ingest 2 liters/day from these waters. However, even if a water body is not used for public drinking water supplies, it is possible that an individual may incidentally ingest some amount of water if he or she swims, fishes or boats in the water body. Literature on recreational exposure combined with assumptions about the average mouthful of water ingested for every hour of total body contact can be used to determine an incidental ingestion rate. EPA recommends an incidental ingestion rate of 10 ml/day based on data from studies below when developing chronic criteria. The criteria that would be calculated using incidental ingestion would include water bodies that are designated to be used for recreational purposes only.

Incidental ingestion can be determined by estimating the number of hours that an individual may be in contact with water during recreation and multiplying this value by an average mouthful of water assumed to be swallowed during each hour of recreational exposure which results in total body contact with water. The estimate of 10 ml/day is based on an assumption that an individual may be in total contact with water for 123 hours a year (which represents an hour of exposure per day throughout four summer months) and may ingest 30 ml of water per hour of total contact (State of Michigan, 1985).[16] The value is calculated by multiplying 30 ml/hour by 123 hours a year and dividing by 365. This value has been proposed for use in the proposed Water Quality Guidance for the Great Lakes (58 FR 20869).

Other studies of recreational exposure suggest much variation in this rate, with some similar estimates of exposure as a result of water skiing, swimming, boating, and fishing activities. These studies are discussed below.

EPA has reported exposure durations for swimming, water skiing, boating, and fishing. EPA recently estimated a national average frequency of swimming of 7 days/year with a 2.6 hour duration

[16] Superfund guidance suggests that an average mouthful of water may be 50 ml [SUPERFUND Risk Assessment Guidelines (USEPA, 1989b)].

(USEPA, 1989b). This value may be compared with an earlier EPA publication (USEPA, 1979), which estimated an average annual frequency of 9 days/year with a 2 hour duration of exposure per day. EPA estimated that approximately 20 million individuals participated in water skiing (which, like swimming, involves total body contact with water) for a total of 260 million hours per year. This averages to 14 hours of exposure per participant. USEPA (1979) also listed individuals that participated in other water activities. Sixty-eight million people were involved nationally in boating with an average duration of 24 hours per participant per year and 54 million people fished with 122 hours per participant per year. Total body contact with water during boating and fishing was identified as 40 percent and 20 percent, respectively (USEPA, 1979). These values were used to adjust the exposure duration for participants in these activities to yield exposures on a total contact basis. The resulting total contact exposures per year for swimming, water skiing, boating and fishing were calculated as 18, 14, 10, and 24 hours, respectively. Adding all exposures yields 66 hours of total body contact exposure from recreational activities.

Several recreational surveys have been conducted in Michigan which indicate up to 105 hours of total water exposure. Estimating total exposure suggests total hours of exposure per year that are higher than the national average. The calculation of these exposures involves assuming an individual participates in all activities for the number of days listed in the 1981 Michigan Travel and Recreation Survey and for the duration of hours per participation as identified in the 1976 Recreation survey. In addition to these assumptions, exposure was adjusted by the percentage of total body contact exposure involved in the activity. This adjustment was made assuming the same percentages for total body contact used in USEPA (1979). The calculation of total body exposure resulting from these activities is indicated in Table 2.3.23.

Although the default value of 10 ml/day for chronic ingestion is appropriate for situations in which exposure occurs daily for about four months, States and Tribes in warmer climates may wish to use higher incidental ingestion rates for chronic criteria to protect individuals who may swim in lakes or rivers for a greater portion of the year. For example, Louisiana uses 89 ml/day to account for exposure due to incidental ingestion when developing criteria for non-drinking water supplies. The assumptions used by the Louisiana Department of Environmental Quality in determining the 89 ml/day are described in Louisiana DEQ (1989, 1994).

In addition to chronic values for incidental ingestion, States and Tribes may wish to use an incidental ingestion rate for evaluating contaminants that cause adverse health effects from shorter-term exposures based on the amount of water that may be ingested in a given hour of recreational activity.

Table 2.3.23: Yearly Total Hours of Total Body Contact as Determined by Michigan Recreational Surveys

	Activity Days per Participant	Hours per Participation	Body Contact Adjustment	Hours of Exposure
Swimming	13.3	2.1 (ave.)	1.0	27.9
Fishing	14.3	3.7 (ave.)	0.2	10.6
Power Boating	24.5 (total)	3.2	0.4	31.4
Water Skiing	9.6	1.5	1.0	14.4
Sailing	10.4 (total)	3.2	0.4	13.3
Canoeing	4.8	3.9	0.4	7.5
			TOTAL	105.1

Source: Wells (1990)

2.3.3 Quantification of Exposure

In typical exposure assessments, the magnitude, frequency, and duration of exposure is quantified for a given population and specifically selected exposure pathways. After selecting exposure concentration values in each environmental medium to be addressed (e.g., water, food), pathway-specific intake rates are subsequently selected. Given an assumption that exposure occurs over a period of time, dividing the exposure assumption by the period of time will give an average exposure rate per unit time. Alternatively, exposure can be estimated by normalizing both the time and body weight factors, expressed in units of mg chemical/kg body weight-day. (This is discussed in the *Federal Register* notice and comment is requested on this alternative.)

The term "intake" used with this methodology describes the daily exposure estimate (normalized for a lifetime) and is expressed in units of mg chemical/liter. Specifically, for purposes of establishing AWQC which are, by and large, based on chronic health effects data and are intended to be protective of the general population over a lifetime of exposure, the criteria calculations are made in terms of a person's daily exposure. That is, the AWQC represent an acceptable daily exposure over a lifetime for which no adverse health effects associated with that chemical are expected to occur. Hence, the expression of the AWQC is in mg chemical/day. The AWQC calculation includes an assumption of body weight.

When selecting contaminant concentration values in environmental media and exposure intake values for the Relative Source Contribution (RSC) analysis, it is important to realize that each value selected (including those intakes recommended as default assumptions in the AWQC equation) is associated with a distribution of values for that parameter. Determining how various subgroups fall

within the distributions of overall exposure and how the combination of exposure variables defines what population is being protected is a complicated and, perhaps, unmanageable task, depending on the amount of information available on each exposure factor included. Many times, the default assumptions used in EPA risk assessments are derived from the evaluation of numerous studies and are generally considered to represent a particular population group or some national average. Therefore, describing with certainty the exact percentile of a particular population that is protected with a resulting criteria is often not possible.

General recommendations for selecting values to be used in exposure assessments for both individual and population exposures are discussed in EPA's *Guidelines for Exposure Assessment* (USEPA, 1992). The ultimate choice of the contaminant concentration values used in the RSC estimate and the exposure intake rates requires the use of professional judgment. In particular, when combining variable values for the AWQC estimate, the basis of the health effect (e.g., chronic) and the population (e.g., general population) must be kept in mind; for example, combining a 90th percentile intake with a 5th percentile body weight is not appropriate because it is not likely that the smallest person would have the highest intake and it would not be appropriate with such a chronic effect, general population scenario. Similar judgments must be made for less-than-lifetime health effects and different target population groups. The following are general recommendations. States and Tribes have the flexibility to consider other parameters based on site-specific information or other risk management considerations.

Contaminant concentration. The concentration values for all media used in the RSC analysis are arithmetic means when calculations are made for the general population. These are used to represent reasonable central tendency estimates for a typically exposed person. Higher concentration values may be considered when making evaluations for more highly exposed population groups (e.g., subsistence fishers) whose patterns of exposure with fish consumption are not the same as the general population. However, higher contaminant concentration values should not be used for all media (e.g., other dietary or air intake assumptions) unless it is clear that the specific population group is likely to experience higher concentrations from other media as well. For example, in the RSC analysis, choosing a higher concentration value for estimating fish exposure with a subsistence fisher, should not mean automatically using high concentration values for other foods (such as vegetables, fruit, etc.) or for air exposures.

Body weight. By and the large, the AWQC will be based on the arithmetic mean of the adult body weight for the general population. If the health effect of concern is one that specifically occurs in children, the arithmetic average child body weight is recommended. The same recommendation of an arithmetic mean is made for women of childbearing age.

Dietary intake (non-fresh/estuarine fish intake) and inhalation. Values recommended for these assumptions, which are a part of the RSC analysis, are based on the arithmetic means from the information sources utilized. Specifically, the dietary intake assumptions are taken from the Food and Drug Administration's Total Diet Study program (Pennington, 1983) and the inhalation rate is based on a study conducted by the International Commission on Radiological Protection (ICRP, 1981),

which has been historically used in EPA risk assessments. These studies are representative of the overall U.S. population.

Fresh/estuarine fish intake and drinking water. The intake rates recommended for these two parameters are higher than the arithmetic means for the U.S. population. The choice of default intake assumptions for these parameters represent a risk management decision under the goals of the Clean Water Act to establish AWQC that are protective of a majority of the population through the exposure routes of water and fish consumption. The default drinking water intake rate represents the 84th percentile value from the study on which it is based. The default intake rate for fish consumption of the general population represents the 90th percentile value from the study on which it is based. However, it should be kept in mind that the study does not enable accounting for fish consumers only and, therefore, the intake assumption likely represents less than the 90th percentile of the population potentially at risk from this exposure route.

EPA considers the national AWQC recommendations to be protective of a majority of the general population and believes that it has used appropriate professional judgment in recommending these criteria. EPA encourages States and Tribes to use local or more site-specific exposure intake and concentration assumptions that they believe would appropriately protect the overall population, including highly exposed subgroups. The exposure assessment procedures used in this methodology, which includes the RSC Exposure Decision Tree recommendation, do not prohibit the use of Monte Carlo analysis. States and Tribes may consider using such probabilistic techniques when they have access to data that are adequate enough to provide meaningful results from such analyses. Again, the selection of a point off the overall distribution of exposures (which represents a combination of other distributions) is a decision that involves professional judgment.

2.3.4 Consideration of Non-Water Sources of Exposure When Setting AWQC

In the 1980 AWQC National Guidelines, different approaches for addressing non-water exposure pathways were used in setting AWQC for the protection of human health depending upon the toxicological endpoint of concern. For those substances for which the appropriate toxic endpoint was linear carcinogenicity, only the two water sources (i.e., drinking water consumption and freshwater/estuarine fish ingestion) were considered in the derivation of the AWQC. Non-water sources and marine fish ingestion were not considered explicitly. The rationale for this approach is that in the case of linear carcinogens the AWQC is being determined with respect to the incremental lifetime risk posed by a substance's presence in water, and is not being set with regard to an individual's total risk from all sources of exposure.

In the case of substances for which the AWQC is set on the basis of a nonlinear carcinogen or a noncancer endpoint where a threshold is assumed to exist, non-water exposures were considered when deriving the AWQC under the 1980 AWQC National Guidelines. In effect, the 1980 AWQC National Guidelines specified that the AWQC be calculated based on no more than that portion of the ADI that remains after contributions from other expected sources of exposure have been accounted for. The ADI is equivalent to the RfD, which is discussed in Section 2.2. The rationale

for this approach has been that for pollutants exhibiting threshold effects, the objective of the AWQC is to ensure that an individual's total exposure does not exceed that threshold level. It is useful to note that while the 1980 Guidelines recommended taking inhalation and nonfish dietary sources into account in setting the AWQC for threshold contaminants, in practice the data on these other sources were not available. Therefore, the AWQC usually were derived such that they accounted for all of the ADI (RfD).

EPA is proposing that only a portion of the RfD or Pdp/SF be used in setting AWQC in order to account for other sources of exposure for threshold toxicants, including both noncarcinogens and nonlinear carcinogens. Toxicological issues related to noncarcinogens and nonlinear carcinogens are discussed in detail in Sections 2.2 and 2.1, respectively. For carcinogens that act in a linear fashion, non-water sources would not be taken into account when setting AWQC. The rationale is the same as that given in the 1980 Guidelines, namely, that the AWQC is being determined for the incremental lifetime risk posed by a substance's presence in water and not for an individual's total risk from all exposure sources.

For noncarcinogens for which non-water exposures were considered, the 1980 methodology included the following general formula for setting the criterion:

$$AWQC = [70]\ [ADI - (DT + IN)] \div [2 + 0.0065R]$$

(Equation 2.3.1)

where AWQC is the criterion in units of mg/L; ADI is the Acceptable Daily Intake (now Reference Dose, RfD) in units of mg/kg-day; DT is non-freshwater and -estuarine fish dietary intake in mg/kg-day; IN is inhalation intake in mg/kg-day; 70 is human body weight in kg; 2 is the drinking water consumption in L/day; 0.0065 is fish ingestion in kg/day; and R is the bioconcentration factor in L/kg. As indicated by the above equation, the 1980 AWQC National Guidelines used a "subtraction" approach to account for non-water exposure sources when calculating AWQC for noncarcinogenic, threshold pollutants. That is, the amount of the ADI (RfD) "available" for water sources was determined by first subtracting out contributions from non-water sources. A similar subtraction approach was used, albeit inconsistently, in the derivation of drinking water MCLG values in the early and mid-1980s; more recently, however, the derivation of MCLGs has incorporated what has been termed the "percentage" approach.

EPA has considered several alternative approaches to account for non-water sources and to resolve past inconsistencies in its method. All approaches are discussed in detail in a separate document available in the public docket for this proposal (Borum, unpublished). The result of discussions on these approaches was a consensus by the Relative Source Contribution Policy Workgroup to recommend the Decision Tree Approach for internal Agency review. This was considered the best option of the alternatives presented. To account for exposures from other media when setting an AWQC, the exposure decision tree for determining proposed RfD or Pdp/SF allocations represents a method of comprehensively assessing a chemical for regulatory development.

This method considers the adequacy of available exposure data, levels of exposure, relevant sources/media of exposure, and regulatory agendas (i.e., multiple regulatory actions for the same chemical). The decision tree addresses most of the disadvantages associated with the exclusive use of either the percentage or subtraction approaches, because they are not arbitrarily chosen prior to determining the following: specific population(s) of concern, whether these populations are relevant to multiple-source exposures for the chemical in question (i.e., whether the population is actually or potentially experiencing exposure from multiple sources), and whether levels of exposure, regulatory agendas or other circumstances make allocation of the RfD or Pdp/SF desirable. Both subtraction and percentage methods are potentially utilized under different circumstances with the Decision Tree Approach, and the decision tree is recommended with the idea that there is enough flexibility to use other procedures if information on the contaminant in question suggests it is not appropriate to follow the decision tree (e.g., if multiple sources of exposure do not exist for the population of concern). EPA recognizes that there may be other valid approaches in addition to the exposure decision tree and the others identified in the *Federal Register* (FR) notice. EPA is specifically recommending the Exposure Decision Tree for use with this methodology.

As stated in the FR, current internal policy discussions include the application of this approach to all program offices to the extent practicable when conducting exposure assessments. As such, the broader goals are to ensure more comprehensive evaluations of exposure Agency-wide and consistent allocations of the RfD or Pdp/SF for criteria-setting purposes when appropriate.

2.3.4.1 Exposure Decision Tree Approach

Although the following discussion of the Exposure Decision Tree Approach is included in the *Federal Register* notice, it is repeated here for the benefit of the reader, and for use in evaluating the example below.

When data regarding exposure sources of a given chemical are adequate, the decision tree is designed to allow for accurate predictions of exposure for the population(s) of concern. When there are less data, there is an even greater need to make sure that public health protection is achieved. A series of qualitative alternatives is proposed. Specifically, the decision tree makes use of chemical information when actual monitoring data are inadequate. It considers information on the chemical/physical properties, uses of the chemical, and environmental fate and transformation, as well as the likelihood of occurrence in various media. Review of such information, when available, and concurrence on a reasonable exposure characterization for the chemical would result in a health-based criterion that is more accurate in predicting exposures than a default of 20 percent. Although the 20 percent default is still proposed when information is not adequate, the need for using a default is greatly reduced.

As stated above, the recommendation is made with the understanding that there may be situations where the decision tree procedure is not practicable or may be simply irrelevant after considering the properties, uses and sources of the chemical in question. It is important to have the flexibility to choose other procedures that are more appropriate for setting health-based criteria or,

perhaps, allocating the RfD or Pdp/SF, as long as reasons why the regulatory action should follow a different course are clearly presented. Often, however, the multiple source nature of chemicals is likely to merit a decision tree evaluation for the purpose of setting human health criteria or standards for a given chemical. The decision to perform, or not to perform, an allocation could actually be made at several points during the decision tree process. Working through the whole process may be most helpful for determining why another approach should be used. While combined exposures above the RfD (Pdp/SF) may or may not be an actual health risk, a combination of health standards exceeding the RfD (Pdp/SF) may not be sufficiently protective. Maintaining total exposure below the RfD (Pdp/SF) is a reasonable health goal and there are circumstances where health-based criteria for a chemical should not exceed the RfD (Pdp/SF), either alone (if only one criterion is relevant) or in combination. “Relevancy” here means determining whether more than one criterion, standard, or other guidance is being planned, performed or is in existence for the chemical in question.

It is clear that this will be an interactive process; input by exposure assessors will be provided to, and received from, risk managers throughout the process, given that there may be significant implications regarding control issues (i.e., cost/feasibility), environmental justice issues, etc. In cases where the decision tree is not chosen, communication and concurrence about the decision rationale and the alternatively proposed criteria are of great importance.

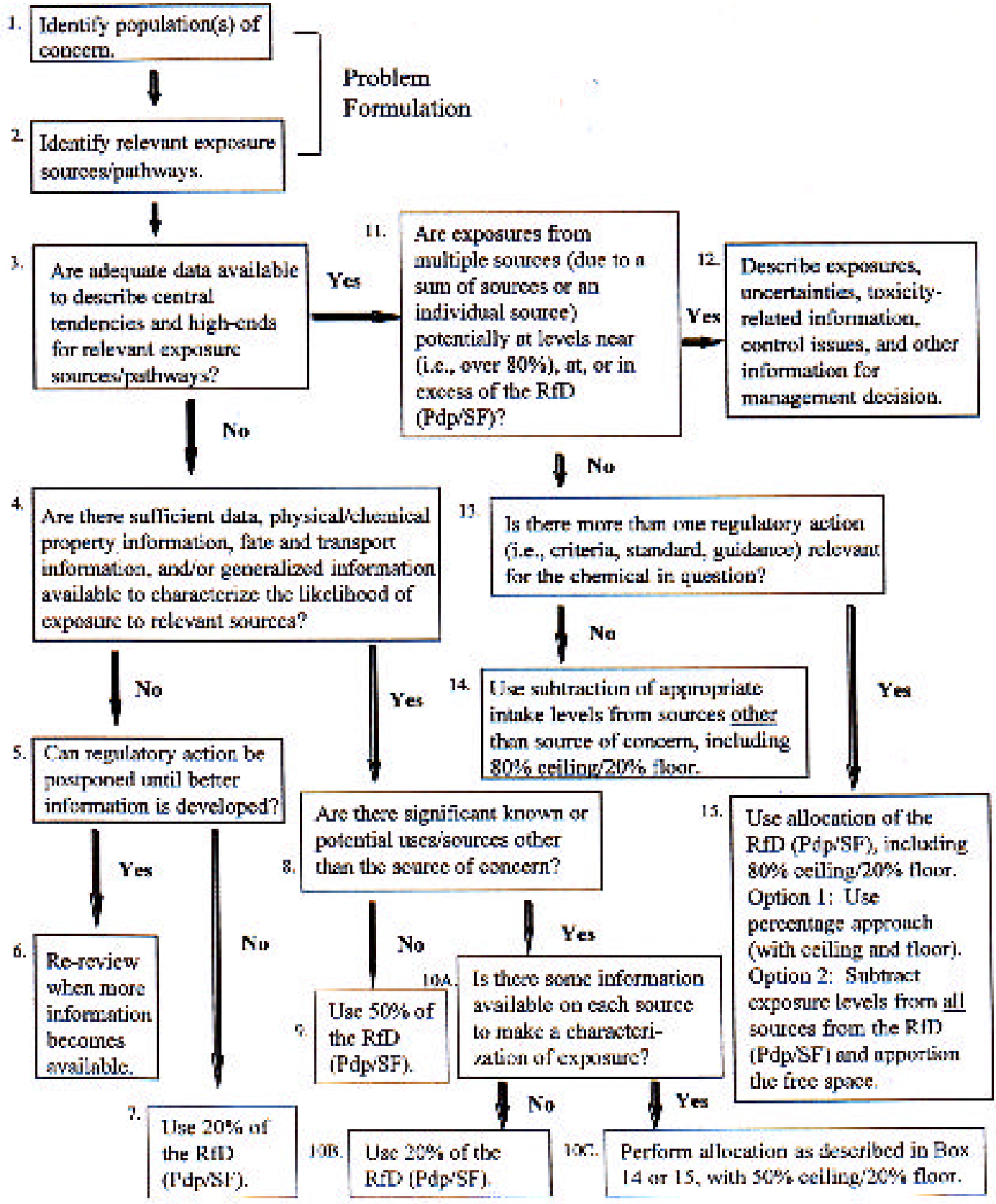
Exhibit 2.3.4 presents the Exposure Decision Tree. Descriptions of the boxes within the decision tree are separated by the following process headings to facilitate an understanding of the major considerations involved.

Problem Formulation

Initial decision tree discussion centers around the first two boxes: identification of population(s) of concern (Box 1) and identification of relevant exposure sources and pathways (Box 2). The term "problem formulation" refers to evaluating the population(s) and sources of exposure in the manner described above (i.e., the potential for the population of concern to experience exposures from multiple sources for the chemical in question), such that the data for the chemical in question consider each source/medium of exposure and its relevancy to the identified population(s). Evaluation includes determining whether the levels, multiple regulatory actions, or other circumstances make allocation of the RfD or Pdp/SF reasonable. The initial discussion has also included agreement on the exposure parameters chosen, intakes chosen for each route and any environmental justice or other social issues that aid in determining the population of concern. The term "data,” as used here and discussed throughout this section, refers to ambient sampling data (whether from Federal, regional, State or area-specific studies) and not internal human exposure measurements.

Exhibit 2.3.4

Alternate Exposure Decision Tree for Defining Proposed RfD (Pdp/SF) Allocation



Data Adequacy

In Box 3, it is necessary that adequate data exist for the relevant sources/pathways of exposure if one is to avoid using default procedures. In fact, distributional data may exist for some or most of the sources of exposure. At a minimum, the central tendency and high-end values are considered necessary to determine an appropriate estimate of exposure when using actual data. It is critically important to describe and provide guidance for the data adequacy issue, or the approach could be considered arbitrary.

There are numerous factors to consider in order to determine whether a dataset is adequate. These include: (1) sample size (i.e., the number of data points); (2) whether the dataset is a random sample representative of the target population (if not, estimates drawn from it may be biased no matter how large the sample); (3) the magnitude of the error that can be tolerated in the estimate (estimator precision); (4) the sample size needed to achieve a given precision for a given parameter (e.g., a larger sample is needed to precisely estimate an upper percentile than a mean or median); (5) an acceptable analytical method detection limit; and (6) the functional form and variability of the underlying distribution, which determines the estimator precision (e.g., whether the distribution is normal or lognormal and whether the standard deviation is 1 or 10). Lack of information may prevent assessment of each of these factors; monitoring study reports often fail to include background information or enough summary statistics (and rarely the raw data) to completely characterize data adequacy. Thus, a case-by-case determination of data adequacy is likely.

That being stated, there are some criteria, as proposed below, that lead to a rough rule-of-thumb on what constitutes an "adequate" sample size for exposure assessment. The primary objective is to estimate an upper percentile point (e.g., say the 90th) and a central tendency value of some exposure distribution based on a random sample from the distribution. Assuming that the distribution of exposure is unknown, a nonparametric estimate of the 90th percentile is required. The required estimate, based on a random sample of *n* observations from a target population, is obtained by ranking the data from smallest to largest and selecting the observation whose rank is 1 greater than the largest integer in the product of .9 times *n*. For example, in a data set of 25 points, the nonparametric estimate of the 90th percentile is the 23rd largest observation.

In addition to this point estimate, it is useful to have an upper confidence bound on the 90th percentile. To find the rank of the order statistic that gives an upper 95 percent confidence limit on the 90th percentile, the smallest value of *r* that satisfies the following formula is determined:

$$0.95 \approx \sum_{i=0}^{r-1} \binom{n}{i} 0.9^{i}\ 0.1^{n-i}$$

(Equation 2.3.2)

For relatively small data sets, the above formula will lead to selecting the largest observation as the upper confidence limit on the 90th percentile. However, the problem with using the maximum is that, in many environmental datasets, the largest observation is an outlier and would provide an unrealistic upper bound on the 90th percentile. It would, therefore, be preferable if the sample size *n* were large enough so that the formula yielded the second largest observation as the confidence limit.

This motivates establishing the following criterion for setting an "adequate" sample size: pick the smallest *n* such that the nonparametric upper 95 percent confidence limit on the 90th percentile is the second largest value. Application of the above formula with *r* set to *n*-1 yields *n* = 45 for this minimum sample size.

For the upper 95 percent confidence limit to be a useful indicator of a maximum exposure it must not be overly conservative (too large relative to the 90th percentile). It is, therefore, of interest to estimate the expected magnitude of the ratio of the upper 95 percent confidence limit to the 90th percentile. This quantity generally cannot be computed, since it is a function of the unknown distribution. However, to get a rough idea of its value, consider the particular case of a normal distribution. If the coefficient of variation is between 0.5 and 2.0 (i.e., the standard deviation divided by the mean) the expected value of the ratio in samples of 45 will be approximately 1.17 to 1.31; i.e., the upper 95 percent confidence limit will be only about 17 to 31 percent greater than the 90th percentile on the average.

It should be noted that the nonparametric estimate of the 95 percent upper confidence limit based on the second largest value can be obtained even if the data set has only two detects (it is assumed that the two detects are greater than the detection limit associated with all non-detects). This is an argument for using nonparametric rather than parametric estimation, since use of parametric methods would require more detected values. On the other hand, if non-detects were not a problem and the underlying distribution were known, a parametric estimate of the 90th percentile would generally be more precise.

As stated above, adequacy is also determined by determining whether the samples are relevant to and representative of the population at risk. Data may, therefore, be adequate for some decisions and inadequate for others; this determination requires some professional judgment.

If the answer to Box 3 is no, then the decision tree falls into Box 4. As suggested by the separate boxes, the available data that will be reviewed as part of Box 4 do not meet the requirements necessary for Box 3. In Box 4, any data that are available (information about the chemical/physical properties, uses, and environmental fate and transformation, as well as any other information that would characterize the likelihood of exposure from various media for the chemical) are evaluated to make a qualitative determination of the relation of one exposure source to another. Although this information will always be presented at the outset, it is proposed that this information also be used to estimate the health-based criteria. The estimate should be rather conservative, given that it is not based on actual monitoring data (or data that has been considered to be inadequate for a more

accurate quantitative estimate). Therefore, there are greater uncertainties, and accounting for variability is not really possible. With such information, a determination can be made as to whether there are significant known or potential uses/sources other than the source of concern (Box 8). If there are not, then it is recommended that 50 percent of the RfD or Pdp/SF can be safely allocated to the source of concern (Box 9). While this leaves half of the RfD or Pdp/SF unallocated, it is recommended as the maximum allocation due to the lack of data needed to more accurately quantify actual or potential exposures. If the answer to the question in Box 8 is yes, and some information is available on each source of exposure (Box 10A), apply the procedure in either Box 14 or Box 15 (depending on whether one or more criterion is relevant to the chemical), using a 50 percent ceiling (Box 10C), again due to the lack of adequate data. If the answer to the question in Box 10A is no, then use 20 percent of the RfD or Pdp/SF (Box 10B).

If the answer to the question in Box 4 is no; that is, there are not sufficient data/information to characterize exposure, it may be best to defer action on the chemical until better information becomes available (Boxes 5 & 6). If this is not possible, then the "default" assumption of 20 percent of the RfD or Pdp/SF (Box 7) should be used. Box 7 is not likely to be used very much, given that the information described in Box 4 should be available in most cases. However, EPA intends to use it as the default value that has also been used in past water program regulations.

Regulatory Actions

If there are adequate data available to describe the central tendencies and high ends from each exposure source/pathway, then the levels of exposure relative to the RfD or Pdp/SF are compared (Box 11). If the levels of exposure for the chemical in question are not near (currently defined as greater than 80 percent), at, or in excess of the RfD or Pdp/SF, then a subsequent determination is made (Box 13) as to whether there is more than one regulatory action relevant for the given chemical (i.e., more than one criteria, standard or other guidance being planned, performed or in existence for the chemical). The subtraction method is considered acceptable when only one criterion is relevant for a particular chemical. In these cases, other sources of exposure can be considered “background” and can be subtracted from the RfD (Pdp/SF). When more than one criterion is relevant to a particular chemical, apportioning the RfD (Pdp/SF) via the percentage method is considered appropriate to ensure that the combination of criteria, and thus the potential for resulting exposures, do not exceed the RfD (Pdp/SF).

Allocation Decisions

If the answer to this question (Box 13) is no, then the recommended method for setting a health-based criterion is to utilize a subtraction calculation (Box 14). Specifically, subtract out appropriate intake values for each exposure source <u>other</u> than the source of concern, based on the variability in occurrence levels for that source. This aspect implies that a case-by-case determination of the variability and the resulting intake chosen will be made, as each chemical evaluated can be expected to have different variabilities associated with each source of intake. As a default, high-end intakes (approximating the 90th to 98th percentiles of exposure) could be subtracted out. However,

there is concern that an estimate adding 98th percentile values for all sources could be above any actually exposed population or individual. Therefore, scientific judgment is needed in selecting intake values, including the appropriateness for the population of concern. The subtraction method would also include an 80 percent ceiling and a 20 percent floor.

If the answer to the question in Box 13 is yes, then the recommended method for setting health-based criteria is to allocate the RfD or Pdp/SF among those sources for which health-based criteria are being set (Box 15). Two main options for allocating the RfD or Pdp/SF are presented in this box. Option 1 is the percentage approach (with a ceiling and floor). This option simply refers to the percentage of overall exposure contributed by an individual exposure source. For example, if for a particular chemical, drinking water were to represent half of total exposure and diet were to represent the other half, then the drinking water contribution (known as the "relative source contribution" or RSC) would be 50 percent. The health-based criteria would, in turn, be set at 50 percent of the RfD or Pdp/SF. This option also utilizes an appropriate combination of intake values for each exposure source based on the variability in occurrence levels of each source. This will also be determined on a case-by-case basis. Option 2 would involve the subtraction of exposure levels from all sources of exposure from the RfD or Pdp/SF and apportioning the free space among those sources for which health-based criteria are being set. There are several ways to do this: 1) divide the free space among the sources with preference given to the source likely to need the most increase (e.g., because of intentional uses or because of physical/chemical properties like solubility in water); 2) divide the free space in proportion to the "base" amount used (e.g., the source accounting for 60 percent of exposure gets 60 percent of the free space - this is identical to the percentage method; the outcome is the same); and 3) divide the free space based on current variability of exposure from each source (i.e., such that more free space is allocated to the source that varies the most). The resulting criterion would then be equal to the amount of free space allocated plus the amount subtracted for that source. *Note: The allocation options continue to be discussed within EPA as part of an Agency-wide Pilot Study group. Although some preferences have been discussed, along with strengths and shortcomings of each option, it is still being deliberated. The Agency welcomes comments on these options.*

Finally, if the answer in Box 11 is yes, that is, if the levels of exposure for the chemical in question are near (currently defined as greater than 80 percent), at, or in excess of the RfD or Pdp/SF, then the estimates of exposures and related uncertainties, potential allocations, toxicity-related information, control issues, and other information are to be presented to managers for a decision (Box 12). The high levels referred to in Box 11 may be due to one source contributing that high level (while other sources contribute relatively little) or due to more than one source contributing levels that, in combination, approach or exceed the RfD or Pdp/SF. This presentation may inevitably be necessary due to the control issues (i.e., cost and feasibility concerns) that may be involved, especially when multiple criteria are at issue. In practice, risk managers are routinely a part of any decisions regarding regulatory actions and will be involved with any recommended outcome of the exposure decision tree or, for that matter, any alternative to the exposure decision tree. However, because exposures that approach or exceed the RfD or Pdp/SF and the feasibility of controlling different

sources of exposure are complicated issues, risk managers will need to be directly involved in formulating any allocation decisions.

Just as with the other outcomes in the exposure decision tree, a recommendation for setting a health-based value (or values, depending on the number of relevant sources) for chemicals that apply to Box 12 is also appropriate. It is likely that risk managers will want some input from the exposure assessors even if exposures are above the RfD or Pdp/SF and control issues apply. Therefore, in these cases, recommendations can still be offered and should be performed as with Boxes 13, 14, and 15. The recommendation should be made based on health-based considerations only, just as when the chemical in question was not a Box 12 situation. If the chemical is relevant to one regulatory action only, the other sources of exposure could be subtracted from the RfD or Pdp/SF to determine if there is any leftover amount for setting a criterion. If the chemical is a multiple criteria issue, then a recommended allocation could be made, even though it is possible that all sources would need to be reduced. Regardless of the outcome of Box 11, all allocations made (via the methods of Boxes 14 or 15) should include a presentation of the uncertainty in the estimate and in the RfD or Pdp/SF for a more complete characterization.

The process for a Box 12 situation, versus a situation that is not, differs in that the presentations for Boxes 14 and 15 are based on a concurrence of allocations (following the review of available information and a determination of appropriate exposure parameters) in the absence of control issues that would result in more selective reductions. With Box 12, one or several criteria possibilities ("scenarios") may be presented for comparison along with implications of the effects of various control options. It would be most appropriate to present the information in this manner to risk managers given the complexity of these additional issues, rather than the more definitive proposals that are not associated with Box 12 situations.

Results of both Boxes 14 and 15 rely on the 80 percent ceiling and 20 percent floor. The 80 percent ceiling was implemented to ensure that the health-based goal will be low enough to provide adequate protection for individuals whose total exposure to a contaminant is, due to any of the exposure sources, higher than currently indicated by the available data. This also increases the margin of safety to account for possible unknown sources of exposure. The 20 percent floor has been traditionally rationalized to prevent a situation where small fractional exposures are being controlled. That is, below a point it is more appropriate to reduce other sources of exposure, rather than promulgating standards for *de minimus* reductions in overall exposure. The idea of adding flexibility with the floor to go lower (perhaps to zero) if necessary in cases where total exposure exceeds the RfD or Pdp/SF and additional reductions are warranted has also been discussed. The Agency welcomes comments on this issue.

2.3.4.2 Notes on Use of the Exposure Decision Tree Approach for Setting AWQC

Because two different types of AWQC are proposed (based on either (1) fish ingestion only or (2) both fish and water ingestion), special circumstances arise under the decision tree approach

when accounting for the drinking water portion of exposure. These circumstances relate to whether it is a type (1) or (2), and whether one or more health-based criterion is being considered. These four instances are described below.

When a criterion is being set based on fish ingestion only, and when only one health-based criterion (i.e., AWQC) is relevant for the chemical, ingestion from drinking water would be considered a non-ambient water source and would be subtracted from the RfD (or subtracted out with nonlinear carcinogens; i.e., the Pdp/SF) in the numerator of the equation to determine the AWQC, as follows:

$$AWQC = \frac{[RfD - (DW + DT + IN)] \bullet BW}{FI \bullet BAF}$$

(Equation 2.3.3)

where:

RfD	=	Reference dose (mg/kg-day)
DW	=	Contaminant intake from drinking water (mg/kg-day)
IN	=	Contaminant intake from air (mg/kg-day)
DT	=	Contaminant intake from non-fresh/estuarine fish and other dietary intake (i.e., all other dietary sources) (mg/kg-day)
BW	=	Body weight (kg)
FI	=	Fish consumption rate (kg)
BAF	=	Bioaccumulation factor (L/kg)

The terms DW, DT, and IN represent the relative source contribution (RSC) and are indicated here as separate parameters to facilitate understanding of other common sources that could be subtracted out (when only one health-based criterion is relevant). In this case, the occurrence of the contaminant in treated drinking water would be the most relevant concentration data for determining intake from drinking water, because it is assumed that individuals get their drinking water from the tap.

When a criterion is being set based on fish ingestion only, and more than one health-based criterion is being set, then an appropriate RSC allocation procedure, using either Option 1 or Option 2 in Box 15 (Exhibit 2.3.4) would be performed. This calculation is expressed by the following equation:

$$AWQC = \frac{RfD \cdot RSC_{fish} \cdot BW}{FI \cdot BAF}$$

(Equation 2.3.4)

where:

RSC_{fish} = Relative source contribution for fish as determined by Option 1 or Option 2 in Box 15 (of Exhibit 2.3.4) and including only the portion of the intake ascribed to contaminated fish intake

All other parameters are the same as above.

As noted in the definition of RSC_{fish}, only the amount of contaminant intake from eating contaminated freshwater and estuarine finfish and shellfish would be included in the RSC allocation. Marine fish intake would normally be accounted for as part of the dietary intake component of the RSC calculation. Again, intake from treated drinking water would be considered separately as a non-ambient water source.

If a criterion is being set based on fish and water ingestion, and only one health standard is being set, then the following equation applies:

$$AWQC = \frac{[RfD - (DT+IN)] \cdot BW}{DI + (FI \cdot BAF)}$$

(Equation 2.3.5)

where:

DI = Drinking water consumption rate (in L/day)

All other parameters are the same as those in Equation 2.3.3.

In this case, drinking water consumption is not considered in the non-water sources of intake because the criterion is being set for both fish and water ingestion. Thus, only air and dietary intake are subtracted from the RfD or Pdp/SF (here, the parameters DT and IN represent the RSC to be subtracted out).

Finally, in a situation where a criterion is being set for both fish and water ingestion, and more than one health-based criterion is to be set, then the following equation is applicable:

$$AWQC = \frac{RfD \cdot RSC_{fish+water} \cdot BW}{DI + (FI \cdot BAF)}$$

(Equation 2.3.6)

where:

$RSC_{fish+water}$ = The relative source contribution for fish and water as determined by Option 1 or Option 2 in Box 15 (of Exhibit 2.3.4) and including the portion of the intake for contaminated fish and water intake

DI = Drinking water consumption rate (in L/day)

All other parameters are the same as Equation 2.3.3.

In this case, the concentration of a chemical in ambient water is the relevant exposure source to include in the $RSC_{fish+water}$, because use of this criterion assumes that an individual may ingest such concentrations of water daily.

Guidance has been provided on the type of studies that should be considered for estimating fish consumption (Preferences #1 through #4) and numerous studies have been summarized. Recommended values have also been presented for drinking water intakes and body weights. However, these are just some of the parameters that will be needed in order to perform estimates of overall exposure to a chemical. While it is not the intention of this document to provide an exhaustive list of sources of information, Table 2.3.1 does provide suggestions for sources of information on exposure intake parameters and contaminant data.

Although the consumption of marine species of fish is not a direct component of an ambient water quality criterion, there is certainly a reason to account for ingestion exposures to marine species, as they may significantly contribute to total human exposure. That is, although the AWQC derivation may be set for both fish and water ingestion, it is set to protect humans from exposure to the contaminant in fresh and estuarine species only. Therefore, to protect humans who additionally consume marine species of fish, the marine portion should be considered as part of the "other sources of exposure" when calculating an RSC value. Specifically, the DT parameter should account for all non-fresh/estuarine fish dietary intake, thus allowing the common consumption of marine species to be accounted for as well as all other ingested foods. Regarding the dietary information available from the Food and Drug Administration's (FDA) Total Diet Study Program (as cited in Table 2.3.1), EPA believes that the FDA estimates are acceptable to account for exposure to the major marine fish species in the typical U.S. diet (e.g., tuna, cod, haddock). However, States may utilize more comprehensive marine species estimates (e.g., using marine species intake estimates from the CSFII survey and marine fish contaminant concentration data) provided they ensure that marine fish intake is not double-counted with the other dietary intake estimate used (e.g., the FDA program).

In all four of the equations above (2.3.3 through 2.3.6), the proposed 80 percent ceiling and 20 percent floor apply. However, if exposures approach or exceed the RfD or Pdp/SF, then additional risk management decisions will be necessary regarding which exposure sources may most practically be further reduced (given control and feasibility limitations) beyond the decision tree approach to RSC.

2.3.4.3 Setting AWQC for Chemical X Using the Decision Tree Approach

This example describes the application of the Exposure Decision Tree Approach (described above and outlined in Exhibit 2.3.4) to account for sources of exposure to a generic Chemical X when setting AWQC. Two different criteria are evaluated: criteria that include fish intake only (and are applicable to recreational waters) and criteria that include both fish and drinking water intake (and are applicable to waters designated as public water supplies). As noted above, different exposure sources are used, depending on whether criteria are based on assumptions about consumption of both fish and water or of fish only. In the case of estimating a fish-only criterion, an incidental ingestion rate of water of 0.01 L/day from recreational activities is assumed and effectively replaces the DI intake assumption of 2 L/day.

The following sections describe the processes of accounting for sources of exposure and the data needed to apply these processes to the Exposure Decision Tree. Specifically, the sections describe the sources and uses of the chemical, the population of concern, the data available on contamination in exposure media and uptake from that media, the adequacy of exposure information, and the derivation of the AWQC using the decision tree approach. As stated previously, the underlying objective is to maintain total exposure below the RfD (Pdp/SF) by accounting for other sources of exposure and, therefore, using only a portion of either the RfD or Pdp/SF in setting AWQC.

Sources and Uses of Chemical X

There are no known natural sources of Chemical X in the environment. This chemical has been extensively used as a solvent in many industrial processes and has some uses as a pesticide. Current releases of Chemical X to the environment may occur from these numerous processes and from its pesticide use, and possibly from poorly maintained hazardous waste sites, illegal dumping, and disposal of Chemical X in municipal landfills rather than hazardous waste landfills. In addition, Chemical X may remain in the environment from past releases. Small amounts may be found in outdoor and indoor air, soil surfaces, and surface water. Chemical X in surface waters and sediments bioaccumulates in fish (the determined bioaccumulation factor for fish is 120,000).

Population of Concern

The first step in determining how to set AWQC for Chemical X when considering exposure contributions from all environmental media is to define the population of concern for the chemical (see Box 1 in Exhibit 2.3.4). The population of concern may be a group that is either more toxicologically sensitive or more highly exposed compared with the general population. For Chemical X, a particular population of concern is subsistence fishers who eat large quantities of self-caught fish. These fishers may eat fish for a large portion of the year, and may include such groups as Native Americans, immigrants who rely on fishing (particularly Asian-Americans), and poor populations (USEPA, 1994b). These individuals, who are highly exposed to self-caught fish, may have exposures

that are much higher than exposures to the general population. In addition to subsistence fishers, other individuals with higher than average exposures are those who engage in recreational fishing (i.e., sport-caught fish) and eat their catch. For this example, exposures are evaluated for more highly-exposed fish consumers within the population who may represent subsistence fishers. Subsistence fishers and sport fishers are compared with exposures of persons from the general U.S. population. However, use of the default assumptions discussed in Section 2.3.2.3 result in the same estimate for sport fishers and the general population.

Data Used to Assess Exposure to Chemical X

This section discusses data available for the relevant exposure sources and pathways for Chemical X (Box 2 of Exhibit 2.3.4). Exposure may occur from several environmental media, including ambient surface water, drinking water, commercial food products, and air. Human exposures are estimated by combining information on concentrations of Chemical X in environmental media with intake rates of these environmental media. The largest exposure for subsistence fishers, sport-fishers, and for the general population appears to be from ingestion of fish.

Exposures from Raw Surface Water

When setting AWQC for protection against intake of pollutants from both fish and water, ambient concentrations in surface waters (that have not been treated for drinking water) are used to assess exposure resulting from drinking the water directly from these sources. In addition to the need for assessing exposures from drinking water from surface water sources, available concentrations in fish may be used to assess intake from eating contaminated fish.

Exposure Resulting from Drinking Water Directly from Water Bodies. Information on concentrations in waters as well as intake rates of water are needed to assess exposure from surface waters. Several surveys have measured concentrations of Chemical X in ambient surface waters. A majority of these surveys have been conducted in U.S. lakes. In a study of chemical concentrations in surface water in one lake, average chemical concentrations in 1988, 1990, and 1992 were 0.33, 0.32, and 0.18 ng/L. These concentrations are based on both dissolved phase and particulate phase concentrations. These authors also show that, from 1980 to 1992, the total concentrations in the water column decreased with a first order rate constant of 0.20/yr. These authors note that the lake is relatively unimpacted by point sources of Chemical X and receives most of its loadings from the atmosphere.

Water samples were collected from another lake from June to October, 1989. In three periods throughout this time, samples were collected at four or five sites. Taking the arithmetic mean of these dissolved phase concentrations results in a value of 2.8 ng/L, and a 95th percentile value of ± 7.2 ng/L. Although the dissolved concentrations were reported at each site, the authors also give some composite information on Chemical X concentrations in the water. The average of total Chemical X for sites 18 and 21 was 1.7 ±0.6 ng/L, the average for site 14 was 5.5 ±2.4 ng/L, and the average

for sites 4 and 10 was 15.6 ±11.2 ng/L. Two sites were close to a heavily industrialized river which is an important source of Chemical X to the lake.

Other studies have been conducted in earlier years in several proximally located lakes. One collected samples in 1980 and reported the average concentration in the first lake to be 1.8 ng/L, with concentrations of 3.2 ng/L in near shore samples and 1.2 ng/L in open lake samples. Mean concentrations ranging from 0.63 to 3.3 ng/L were detected in another study of the second lake for the years 1978 to 1983. Another study reported a mean level of 0.49 ng/L in water columns of a third lake in 1981. From 1977 to 1981, 373 river samples from 9 locations near one of the lakes were collected. The overall mean concentration was 300 ng/L, with a detection limit of 50 ng/L. The authors did not specifically state the number of positives.

Surveys in other areas of the U.S. have also been conducted. Both surface water and subsurface water drainage were investigated in one area of California during 1977. No samples contained detectable levels of the chemical, and the detection limit was not reported. Chemical X was collected from a bay in Texas in an area of suspected contamination. Concentrations ranged from < 0.01 to 70 ng/L. The authors report an average of 3.1 ng/L but do not describe whether or how the average accounted for the non-detected values.

Because the first summarized U.S. lake study indicated a decrease in Chemical X concentrations throughout the period from 1980 to 1992, the most recent studies are the most useful to this analysis, especially where older studies were conducted in areas of suspected contamination. The information from the studies that measured concentrations in the late 1980s and early 1990s (from the first two summarized studies) were used to estimate average and high-end values for Chemical X. The first study reports a value of 0.18 ng/L for 1992, based on the concentration of the total chemical in the water column; this value is used as an average value for this analysis. As indicated above, the data came from an uncontaminated lake. We assume that these values are appropriate, assuming that most water bodies in the United States have not been impacted by point sources of contamination. However, using this mean value may underestimate the true mean of concentrations in ambient waters throughout the United States. For the high-end estimate, the value of 15.6 ng/L from the second study is used. This value was not the highest value seen from this study, because it is an average using data from two sites, but it was taken from the most contaminated area within the lake. Although the data are reported for both dissolved and total chemical fractions, data on the total chemical is used to match the data from the first study, which is based on the total chemical. These estimates are only crude estimates of central and high-end concentrations in water, because they are based only on information from these lakes.

Combining the above values with the drinking water intake of 2 liters/day yields a central tendency intake rate of 5.1×10^{-9} mg/kg-day and a high-end value of 4.4×10^{-7} mg/kg-day.

Exposure from Eating Contaminated Fish: Concentrations in Fish. Measurements of chemical concentration in fish in U.S. waters are available from several surveys. One national study, begun in 1986, measured Chemical X in fish at nearly 400 sites. A majority of these locations (314)

were affected by a variety of point and nonpoint sources of pollution, 39 locations were from the United States Geological Survey sites, and 35 areas represented background contaminant levels. Game fish for human consumption were analyzed as fillets, and bottom feeders were analyzed as whole-body samples. The mean concentration of Chemical X found in samples of this study was 1.89 µg/g (wet weight). The median value determined was 0.21 µg/g and the maximum value found was 124.0 µg/g.

National distributions of Chemical X in fish are also available from an ongoing study. The purpose of this study is to determine differences in concentrations of organochlorines at different geographic locations, and to estimate changes in these concentrations over time. The most recent information available is for 1984, in which 112 sites were sampled. These sites were selected to represent all major river basins in the United States. Eleven sites were common to both national studies. Composite samples from the ongoing study consisted of five fish and were collected at each site for two bottom feeder species and one predator species; the whole bodies of these fish were collected for analysis. The geometric mean value determined from the 1984 survey is 0.39 µg/g, and the maximum value is 6.7 µg/g. Earlier data from this survey, collected between 1980 and 1981, shows a geometric mean chemical residue of 0.53 µg/g, and a maximum value of 11.3 µg/g.

Concentrations in marine fish have been measured in a nationwide shellfish study. Total chemical concentrations in whole tissue of bivalves (mussels and oysters) collected during 1986 ranged from 0.009 to 6.8 µg/g (dry weight).

Regional studies of chemical contamination in fish have also been conducted. In New York, chemical concentrations in standard fillets of striped bass were measured, and were shown to decline between 1984 and 1990. In 1990, the arithmetic mean was 1.3 µg/g measured on a wet weight basis. In 1983, levels of 0.6 to 72 µg/g, measured on a lipid basis, were found in fish from major tributaries and embayments of the Great Lakes. In cooked fish from one, median concentrations ranged from 0.17 to 3.0 µg/g.

Exposure from Eating Contaminated Fish: Consumption Rates of Fish. Consumption rates of sport-caught fish vary, depending on whether the rate is determined for the general population or for individuals who receive a large portion of their dietary intake from sport-caught fish. For the general U.S. population, the proposed default national non-marine fish consumption rate for adults of 17.80 grams/day has been estimated from information using three years of data from the nationally-based Continuing Survey of Food Intake for Individuals (CSFII) conducted by USDA. The CSFII is conducted annually, and dietary intake data from the 48 conterminous states are collected over 3-day survey periods (USEPA, 1998). The estimates based on CSFII used information for both adult consumers and non-consumers of fish, and represent intake of all fish whether store-bought or sport-caught. This survey is described in more detail under Preference #3 (page 103).

Data on national distributions of fish intake by sportfishers are not available. Although several surveys have measured consumption of fish by sportfishers in particular areas, these studies are limited to particular geographic regions and do not approximate a national distribution. Because of

the lack of information specific to national estimates for sportfishers, 17.80 grams/day, which approximates the 90th percentile from the CSFII, is used here to represent the average consumption rate of the sportfisher population. This value is used to estimate intake for derivation of national criteria.

Data on national distributions of intake by subsistence fishers are also not available. Some studies that have specifically targeted subsistence fishers have been conducted in certain geographic areas. In addition, sportfisher surveys have included information on specific subpopulations who have high consumption rates and may subsist on fish for a large part of the year. Because of the lack of national distributions, this example, which is conducted to represent an average intake estimate of subsistence fishers, uses the default value of 86.30 grams/day, based on the 95th percentile from the CSFII.[17]

Combining data on consumption rates with concentration data from the ongoing national study to estimate exposure from Chemical X yields central tendency and high-end intake estimates from consumption of fish for an average individual from the general, sportfisher, and subsistence fisher populations, as indicated in Table 2.3.24. Because the high-end values in each case use the maximum contaminant value from the national study, this high-end intake of Chemical X represents a value higher than the 90th percentile intake from the chemical in contaminated fish.

Consumption of sport-caught fish may replace consumption of other commercial meats and fish. Thus, Chemical X intake resulting from consumption of commercial foods was adjusted to account for this replacement. This adjustment is described below, under the section describing dietary intake of commercial foods.

Exposure from Treated Drinking Water

In cases where AWQC are set based on fish intake only, drinking water intake is accounted for as a separate exposure. In these instances, information on treated drinking water, if available, is the relevant information to use when accounting for other sources of exposure. National and regional studies have measured Chemical X contamination in both ground-water and surface water sources of drinking water. Information from these studies can be combined with information on intake rates of water to estimate total intake of Chemical X from this source.

In a regional study of contamination of drinking water, Chemical X was measured from the mid-1970s to early 1985 in tap water, raw water, and finished water. Chemical X concentrations were either not detected, or they were found at levels close to the limit of detection.

[17] For simplicity, the example uses the 86.30 g/day subsistence fisher assumption only. The alternative default subsistence fisher intake value of 39.04 g/day would result in lower estimates of Chemical X intake from fresh/estuarine fish and lower (less stringent) AWQC. These differences are footnoted in Tables 2.3.24 and 2.3.28.

Table 2.3.24: Chemical X Intakes from Eating Fresh/Estuarine Fish for Three Types of Individuals

	Central Tendency Estimate (mg/kg-day)	High-End Estimate (mg/kg-day)
General Population	9.9×10^{-5}	1.7×10^{-3}
General Sportfishers	9.9×10^{-5}	1.7×10^{-3}
Subsistence Fishers[18]	4.8×10^{-4}	8.3×10^{-3}

A discussion of the adequacy of these data for determining exposure estimates follows this section. Although data on surface water are limited, the detection limit from the first subset of the first national study summarized is used as a crude estimate of average human exposure. A high-end estimate may be about 1.4 µg/L, the highest value seen in this study. Concentrations may have decreased since these data were collected. Because of this possible decrease and because 1.4 µg/L was the highest value seen, the value may represent a value higher than the 98th percentile, if such concentrations are still seen.

Ground Water. National studies of Chemical X in ground water showed either no detectable levels of the chemical, or very few positive values. In the same three-sampling national study, 18 ground-water supplies sampled in the first subset found no positive Chemical X concentrations. Only one finished ground-water sample out of 18 in each of the other samplings contained detectable chemical levels, at 0.1 µg/L. The second national study found no detectable chemical levels in ground water.

Two state studies found detectable chemical concentrations in ground water. One study measured Chemical X concentrations in 163 wells across the state, including public and private drinking water wells. Many of the wells sampled were from highly-populated, industrialized areas. Chemical X concentrations were found in 32 wells, and ranged from 0.06 to 1.27 µg/L. The other study, a pesticide hazard assessment survey, was conducted from 1983 to 1984. They found Chemical X in 2 out of 143 samples from 10 counties. The two detectable concentrations were 0.269 and 2.3 µg/L, and the detection limit was 0.25 µg/L.

Other regional ground-water studies either found no detectable levels of Chemical X, or did not report the Chemical X concentrations in the detected samples. In one, drinking water wells in 12 towns were sampled for Chemical X in 1984 and 1985. With a detection limit of 3.3 µg/L, no concentrations of the chemical were found in 42 well locations. In another, a survey of ground-water supplies found positive chemical concentrations at less than 8 percent of the 96 locations sampled.

[18] If the alternate default intake assumption of 39.04 g/day was used instead, the subsistence fisher central tendency and high-end estimates would be approximately 2.2×10^{-4} mg/kg-day and 3.7×10^{-3} mg/kg-day, respectively.

Data on positive samples from the three-sampling national study are very limited. Information from the first state ground-water study was used to estimate central tendency and high-end values for Chemical X in ground water. By assuming that the detected concentration values are equally distributed between 0.06 to 1.27 µg/L and that the non-detected samples had concentrations of 0.03 µg/L, an average of 0.16 µg/L was determined from this study. To provide a crude estimate of high exposure, the high value of 1.27 µg/L from the same study may be used. Because these data come from only one state, the values are not representative of national distributions of Chemical X in ground-water sources. Thus, these data do not adequately represent a national estimate of risk.

Estimating Exposure from Surface Water and Ground-Water Concentrations. To estimate exposures from drinking water sources, these chemical concentrations in surface water and ground water sources are averaged to determine estimates of exposure to Chemical X in drinking water. To do this, we used the percent of the U.S. population served by systems using surface water and ground water and determined a weighted average concentration in drinking water by using the following equation:

$$DWConc = (0.67) * (SWConc) + (0.33) * (GWConc)$$

(Equation 2.3.27)

where:

DWConc	=	Average or high-end drinking water concentration from both surface water and ground water
0.67	=	The fraction of the U.S. population served by public surface water supplies
SWConc	=	Average or high-end Chemical X concentration in surface waters
0.33	=	The fraction of the U.S. population served by public ground water supplies
GWConc	=	Average or high-end Chemical X concentration in ground waters

The weighted average value determined above was multiplied by an estimate of daily drinking water intake of 2 liters/day and divided by adult body weight of 70 kilograms to estimate exposure in units of mg/kg-day. The resulting estimates of intake from drinking water are 3.4×10^{-6} mg/kg-day as a central tendency value, and 3.9×10^{-5} mg/kg-day as a high-end estimate.

It should be noted that these estimates are larger than the estimates from ambient surface water sources (by about three orders of magnitude for the central tendency estimate and two orders

of magnitude for high-end estimates). This may be because the drinking water samples were collected a significant number of years prior to the collection of the raw surface water samples. In addition, the lack of data for both raw surface water and for treated drinking water may also be a factor in the differences between the intake estimates.

Dietary Intake from Commercial Foods

Estimates of dietary intake of Chemical X from commercial foods combine measurements of Chemical X concentrations in store-bought foods and daily intake rates of various food items. Data available on exposure estimates and concentrations in foods are described below.

Two sources of information on dietary intakes of Chemical X from commercial foods and concentrations of Chemical X in commercial food are available. The estimates of intake used in this analysis and presented in Table 2.3.25 use the second source of information described here. The first source of information is an estimate by FDA of the adult dietary intakes, which was determined by combining Chemical X concentrations detected in 12 Total Diet Studies (TDS) conducted over the time period between April 1982 and April 1985 with intake rates of different food items. The TDS measure concentrations of various contaminants in 234 foods purchased from supermarkets or grocery stores throughout the United States and are collected four or five times a year. Using these 12 TDS samplings, the FDA determined mean daily intakes ranging from 0.038 to 0.054 µg/day for males and 0.026 to 0.040 µg/day for females. In addition to the FDA estimates of exposure using information from the 12 TDS samplings, the second source of information includes food concentrations of Chemical X available from 44 TDS samplings conducted from April, 1982 to November 1993, including the 12 described above. From the sampling conducted over this full range of years (1982 to 1993), Chemical X concentrations have been found in 30 of the 234 food items sampled. For each of the 30 food items, Chemical X was detected in one to three of the 44 TDS sampling collections. However, some of these reported values are trace amounts of Chemical X, which represent the best estimates of those who analyzed the data, but are below quantifiable limits. Thus, only eleven samples are above quantifiable limits. These concentrations can be combined with information on age- and sex-specific intake rates of different food items found in Pennington (1983) to determine overall exposure.

For this analysis, as noted above, concentration data from the full range of years (1982 to 1993) was used to estimate exposures. For each food item, the detected Chemical X levels were averaged with the samples in which Chemical X was not detected to estimate an average Chemical X concentration for a given food item. The nondetected levels were given a value of zero. To estimate a high-end Chemical X concentration, the highest values seen from each food item were used.

These concentration data were then combined with information on age- and sex-specific dietary intakes of different food items to estimate total adult intake of Chemical X from commercial foods. The daily intake of individual food items was taken from Pennington (1983), which reports daily intake rates of individual food items for four population groups (males aged 25-30 and 60-65

years old and females aged 25-30 and 60-65 years old). To represent the full range of adult ages, we assumed that the dietary intake of 25-30 year-olds represents dietary habits of individuals aged 18 to 54 years old, and that the consumption rate of 60-65 year-olds represents the consumption rate for adults aged 55 years and older. The percent of these wider age ranges (18 to 54 years; 55 years and older) in the United States population and information that half of each age group consists of males and half consists of females (US DOC, 1992) were then used to determine an age- and sex-weighted overall average consumption rate for each food item.

Table 2.3.25: Intake of Chemical X from Commercial Food Items by Three Types of Individuals

	Central Tendency Estimate (mg/kg-day)	High-End Estimate (mg/kg-day)
General Population	1.13×10^{-6}	4.10×10^{-5}
General Sportfishers	1.13×10^{-6}	4.10×10^{-5}
Subsistence Fishers	1.06×10^{-6}	3.86×10^{-5}

Source: Based on FDA data.

To estimate total exposure from food, the Chemical X concentrations in the food items (mg/g) were then multiplied by the consumption rate of each food item (g/day) and then divided by 70 kilograms to determine intake of Chemical X expressed in mg/kg-day. These values for each food item were then summed, resulting in total mean and high-end intake of Chemical X from the diet. These total intakes were then further adjusted for average individuals from the general population, sportfishers, and subsistence fishers to exclude the amount of a chemical that is ingested through freshwater/estuarine fish intake. For the general population, it was assumed that the amount of freshwater/estuarine fish intake (17.8 g) that was introduced earlier may replace 17.8 grams of commercial meat consumed in the diet. Thus, the Chemical X intake from commercial meat was adjusted by the ratio of freshwater/estuarine fish consumption to total consumption of commercial meat (17.8g/205g = 0.087). In other words, the Chemical X contribution from commercial meat was decreased by 8.7 percent for the average individual. Similar adjustments were made for sportfishers and for subsistence fishers. For sportfishers, the amount of Chemical X intake from commercial meat was also decreased by 8.7 percent, and for subsistence fishers, the amount was decreased by 19 percent. These assumptions were made with the idea that the "typical" dietary composition based on the FDA analysis should be adjusted to reflect a fish consumer's diet. It is included in this example as a reasonable adjustment for exposure assessors to consider. EPA acknowledges that, with some fish consumer groups, a much more significant adjustment may be more appropriate and States and Tribes are encouraged to consider the dietary choices of their target population, if information is available. The resulting intake rates of Chemical X from commercial foods are included in Table 2.3.25. These intake estimates assume concentrations of Chemical X only in the food items described above, which equate to approximately six percent of the diet (i.e., assumed contamination of 161.50 grams of food). These assumptions are presented in Appendix G, which lists the individual food

items and Chemical X concentrations. The assumed total daily intake of foods discussed above, and based on Pennington (1983), is 2,582 g/day.

Intake from Air

Outdoor Air. National data on Chemical X concentration distributions in air are not available. Monitoring data from EPA, however, are available for several states. From six sites in one state, the average value is determined to be 2.14 ppb by volume, with a maximum value of 3.9 ppb. Converting from values in ppb to ug/m^3 results in an average value of 0.028 µg/m^3, and a maximum of 0.05 µg/m^3. Additional studies have reported ambient concentrations in several regions of the United States. One report summarized ambient air data collected from several studies conducted in various regions of the United States. These studies, all published in the 1970s, show

a range of concentrations from a low 2.1-9.4 µg/m^3 in one state to a high value of 100 µg/m^3, which is an average value using data from three other states. In a separate report, concentrations of 0.007 µg/m^3 in one state and 0.004 µg/m^3 in another state were seen during the summer of 1978. Another state study showed that during the summer of 1985, the ambient concentration was 0.002 µg/m^3. One other state study conducted from 1979 to 1980, showed average atmospheric concentration of Chemical X as 0.0003 µg/m^3. Data from an EPA urban air data base shows a mean value from about 0.002 to 0.007 µg/m^3, with a minimum value of 0.0005 µg/m^3 and a maximum value of greater than 0.03 µg/m^3.

Data from the more recent studies cited above are combined to estimate exposure. Averaging the average values from recent studies yields a central tendency air concentration value of 0.008 µg/m^3. The high-end value may be more than 0.03 µg/m^3 and may be 0.05 µg/m^3. These data are from limited geographic regions and are not indicative of areas in which Chemical X concentrations have not been detected. Therefore, the average values are likely to be overestimates of the actual national average estimates. However, because data are not readily available on the number of areas where air concentrations have been measured but are below detection, these values are used as crude estimates of central and high-end values of intake of 2.3 x 10^{-6} mg/kg-day and 1.4 x 10^{-5} mg/kg-day, respectively.[19]

Indoor Air. Research also suggests that indoor air concentrations may be significantly higher than outdoor air. One study measured Chemical X levels in seven buildings. All types of buildings examined had concentrations that were significantly higher than outdoor concentrations. A second study measured the magnitude of the difference between indoor and outdoor air. This study found that normal indoor air concentrations of Chemical X were at least one order of magnitude higher than outdoor concentrations. Although these data suggest that indoor air may have higher concentrations than outdoor air, the study which measured the difference between indoor and outdoor levels was done in only three buildings. Indoor levels are likely to have decreased via a reduction in indoor uses

[19]These values were determined by multiplying the air concentrations by a daily air intake of 20 m^3 and dividing by the average adult body weight of 70 kg.

of Chemical X. In addition, because this study measured the differences for only three buildings, the estimate is fairly uncertain. Thus, we have not included separate indoor air exposures in the current analysis. Instead, the analysis models only outdoor ambient air concentrations. A more recent study of one building, however, does give an indication of levels of indoor air. This study indicated levels of 0.018 and 0.017 $\mu g/m^3$ at two locations were found during 1989-1991.

Adequacy of Exposure Data

The exposure data must be evaluated as to whether they are adequate to estimate central tendencies and high-end values for each particular exposure medium (see Box 3 of Exhibit 2.3.4). Although crude exposure estimates have been presented in the previous section, the use of these data for estimating reliable central and high-end values of exposure are limited. This section outlines the problems with these data, and indicates why these data are considered inadequate in terms of Box 3 for estimating the total dose from Chemical X in the population of concern to compare with the RfD for Chemical X. Because data are determined to be inadequate to describe central and high-end values well for the relevant exposure sources, one of two processes are used to set standards in the environmental media of concern. Depending on the process, either default values are used as the allowable dose from a given exposure medium or the available data are used to determine media-specific allowable doses via a more conservative allocation (starting with Box 4 of Exhibit 2.3.4).

As noted earlier under the description of the Exposure Decision Tree, several factors must be considered when evaluating data adequacy for allocating the RfD among media. One of the main factors to consider is the number of samples in the data set being used to describe a particular exposure medium. Although there are no universal rules about adequate sample sizes, the proposed rules of thumb discussed earlier on page 146 are used here. For estimating a 90th percentile value using a non-parametric method, 45 samples are needed, of which at least five must be above detection limits to determine the 90th percentile value. Fewer samples are usually adequate for estimating mean and median values. In addition to evaluation of sample size, the other aforementioned factors should be assessed for a full evaluation of data adequacy [i.e., representativeness of the sample, the accuracy in the analytical procedures, and the sensitivity of the measurement relative to the environmental levels of concern (i.e., whether detection limits are low enough such that concentrations can be detected in most samples within a data set)].

Intake of Drinking Water from Raw Surface Water Sources

For this analysis, the two most recent studies were used to represent central and high-end estimates of concentrations. The central tendency estimate was determined using the most recent data previously indicated. The number of data points that made up this value was five. Because the high-end estimate of 15.6 ng/L was not determined as a 90th percentile value, the sample size used to determine the value was not evaluated in the context of the number needed to determine a 90th percentile.

It is important to consider several factors in determining whether the data are adequate. First, both samples are current and thus more representative of Chemical X concentrations than older data. However, the data are from two lakes only, and thus, do not represent a national distribution of data. In addition, the data used for the average and the high-end values are taken from two surveys, and thus, differences exist between these studies such as the number of chemical analogues generally detected. Neither study reports the detection limits, or whether any of the values were below detection.

Based on the lack of information regarding detection limits, limited geographic representation of the data, and low sample sizes, it was determined that data are inadequate to obtain central tendency and high-end estimates of exposure. Although such estimates are presented, they represent only crude numbers.

Freshwater/Estuarine Fish Intake

The most recent data appear adequate to use in estimating typical and high-end exposures from contaminants in fish. The purpose of the national study used was to determine the geographical extent of chemical contamination. Thus, data were collected from all watersheds in the United States and were collected in 1984. The sample size of this study seems large enough to adequately represent the geometric mean value. As noted above, the minimum number of samples needed to adequately represent the 90th percentile of a given exposure (using non-parametric methods to estimate acceptable sample size) was determined to be 45. The sample size needed to adequately determine the median value would be smaller than the size needed to determine the 90th percentile. Because the geometric mean may be assumed to be equivalent to the median, it is assumed that the number of samples used in the study is adequate to estimate the geometric mean. In addition to a minimum sample size needed to estimate the geometric mean, a minimum number of positive values is also needed to determine the median (or geometric mean). Although it is not known how many samples are above detection, 91 percent of the stations sampled had Chemical X concentrations above detection. Thus, for purposes of this example, it was assumed that a majority of samples had Chemical X concentrations above detection.

For the estimates of fish consumption rates, the large sample size and national representation of the CSFII survey make it a useful survey for measurement of fish consumption, if the assumption is made that the consumption rates from the CSFII study (which measured consumption of both sport-caught and commercial fish) apply to consumption of freshwater/estuarine fish.

Intake of Treated Drinking Water from Surface Water Sources

None of the studies of Chemical X concentrations in drinking water from surface water sources is ideal for estimating exposure through drinking water from surface water sources. The first national study reviewed may offer the best information to use in estimating exposure because Chemical X concentrations from surface water sources were taken from many cities across the country and because the survey reported detection limits. However, because of the large number of

nondetected samples, central exposure values cannot be determined without making assumptions about the concentrations in the undetected values. In addition, the data are older and, therefore, may not represent current concentrations. The more recent national study did not detect any Chemical X concentrations and did not report the detection limits. Without knowing the detection limit, it is impossible to make any assumption about the concentrations in the undetected samples, unless it is assumed that the concentrations are zero. Because of these problems, these data are considered inadequate for estimating exposure from surface water supplies of drinking water.

Intake of Treated Drinking Water from Ground Water Sources

Data on exposures from ground water sources of drinking water are difficult to use because few detected samples have been found. As with the surface water sources, it is impossible to make assumptions about undetected samples measured in the study chosen. For data from the first national study, the number of undetected samples and the time period during which the study was conducted make it difficult to estimate central estimates of exposure from this study with any level of confidence. The state study chosen collected about 160 samples, of which 30 had concentrations above the detection limit. However, this study was done at the time that uses of Chemical X stopped and the concentrations were measured in industrialized settings within this one state. Because some studies reported so many nondetected values, and others used only regional data, these data are considered inadequate for estimating reliable central estimates of exposure to Chemical X in ground water sources of drinking water.

Sources of Food Intake

The limited number of positive samples found in the 44 diet collections make estimating exposure using these data difficult. Without knowing exact detection limits, it is difficult to make assumptions about concentrations for the undetected samples. In addition, for any given food item, generally only one value was above the quantifiable limit for Chemical X. (Two positive samples were found for one food item.) Thus, neither adequate central or high-end concentrations could be estimated. Because of these problems, it was determined that the data are not adequate for estimating national distributions of Chemical X concentrations in food.

Sources of Air Intake

These data are too limited for adequately estimating national exposure to Chemical X from air. Several of the studies were performed in the 1970s when companies still manufactured Chemical X. In addition, more recent nationally representative exposure estimates are not available. Finally, sample size was not available for many of these studies. Thus, it was determined that these data are inadequate to estimate exposure from air sources of Chemical X.

Setting AWQC

Under the Exposure Decision Tree Approach, either the available exposure data or default values are evaluated against the toxicological dose that should result in no adverse health effects from exposure to Chemical X. The toxicological dose used to evaluate the exposure and the method of allocation are described below.

The toxicological dose is determined first, as it is the parameter to which the other factors are applied. Chemical X has been shown to cause more than one type of toxicity. Two chronic RfDs have been established for Chemical X, based on the oral route. The lowest value is 2.0×10^{-5} mg/kg-day and is based on clinical and immunological studies performed on monkeys. The adverse health effects found in this study include decreased antibody response to injected sheep red blood cells by three principal cells of the immune system, exudate from the eye, inflammation of eyelid glands, and changes in finger and toe nails. Because non-water exposures are considered for cases in which pollutants cause threshold effects, this example uses the chronic RfD value of 2.0×10^{-5} mg/kg-day to evaluate chronic toxicity effects.

In addition to these chronic effects, Chemical X has been shown to result in adverse health effects based on results from short duration studies. EPA recommends that where such effects have been identified, these should be considered and compared with exposure estimates which use intake rates that may plausibly be ingested within a short time. A literature review shows an acute study with a LOAEL of 244 mg/kg-day for developmental (fetal) effects. Assuming uncertainty factors of 10 for animal-to-human, intrahuman, and LOAEL to NOAELs results in a value of 0.244 mg/kg-day. To determine whether to evaluate the chronic or developmental effects, the differences between short-term exposures and the "RfD_{DT}" were compared with differences between chronic exposure and the chronic RfD.

Specifically, health effects and relevant intake assumptions for a target population of pregnant women were considered for this example due to the fetal developmental effects indicated above. It was assumed that a pregnant woman might ingest a one-time high dose or multiple high doses of fish within a short time period. Data show that such doses may be much higher than average fish ingestion. However, it is unlikely that high-end intakes from other media would occur simultaneously. Thus, the comparison used high intake assumptions for fish intake only. The information on "acute" fish intake rates (as defined in Section 2.3.2.3, Preference #3) available from the CSFII includes assumptions for women of childbearing age (ages 15-44 years old). The 90th percentile value of "acute" intake (see Section 2.3.2.3 for a discussion of these intake values determined in the CSFII) is 148.8 g/day, which was used in the comparison. The body weight value of 65 kilograms from Ershow and Cantor (1989) was used and is applicable to pregnant women.

Comparing differences between this shorter-term exposure and the developmental effect RfD "RfD_{DT}" with the differences between chronic exposure and the chronic RfD indicated that shorter-term exposure compared with the developmental RfD is lower than the chronic exposure versus the chronic RfD. Chronic exposures using intake from public drinking waters rather than ambient water

(1.1×10^{-4} mg/kg-day) are about five and a half times higher than the chronic RfD (2×10^{-5} mg/kg-day), whereas the shorter-term exposures (1.6×10^{-3} mg/kg-day) are much lower than the developmental "RfD_{DT}" (0.244 mg/kg-day). Thus, only chronic exposures are considered in this example.

Using the process to set AWQC outlined in Exhibit 2.3.4, the available exposure data (although limited) are used to determine allowable doses for each medium. This allocation is performed because there is more than one source/use of the chemical (Box 8) and because there is some information available to characterize all sources of exposure (Box 10A). Because the exposure estimates are determined not to be adequate enough to represent central and high-end estimates, the allowable dose for any one source can only be as high as 50 percent of the total allowable dose. The allowable dose is also limited by the floor 20 percent of the allowable dose (Box 10C). Total exposures compared with the RfD are included in Table 2.3.26. Each exposure source as a percent of total exposure, as well as the default values (also as percentages) of these exposures used in criteria allocation, are included in Table 2.3.27. These allowable doses from each medium are determined for three types of individuals discussed earlier (average individuals from the general population, sportfishers, and subsistence fishers). Crude contaminant concentration values are available for high exposure estimates and for central tendency estimates. Thus, a decision must be made about whether to use the high-end or central value when setting standards for a given environmental medium. Guidance is currently being developed to address the use of central tendency versus high-end values. For this example, central estimates of contaminant concentrations are used for the general population, and high-end concentration estimates of fish are used for sport and subsistence fishers. [Because the variability in the exposure estimates is based predominantly on the variability of concentrations in the exposure media, the high-end values do not reflect use of high-end versus central tendency consumption rates. Rather, differences in consumption rates (which apply only to fish consumption) are reflective of the defaults used for the different populations of fishers.] States may wish to use different percentile values for the general population and other fishers based on concentrations of contaminants in their area.

For the three groups of fish consumers being evaluated (subsistence fishers, sportfishers, and individuals from the general population), two criteria are relevant: the AWQC and health tolerances set for pesticide use. Thus, an allocation based on the percentage approach (and allocating the free space) is done. Because total exposure is greater than the RfD, there is no free space to be allocated. Thus, the percentage approach was used without allocating free space.

Table 2.3.26: Total Exposure Compared with the RfD

	Total Exposures with Ambient water (mg/kg-day)	Total Exposures with Drinking water (mg/kg-day)
General population	1.0×10^{-4}	1.1×10^{-4}
Sportfisher[20]	1.7×10^{-3}	1.7×10^{-3}
Subsistence fisher[20]	8.3×10^{-3}	8.3×10^{-3}
RfD	2.0×10^{-5}	2.0×10^{-5}

Table 2.3.27: Exposure Information -- Percent of Total Exposures and Default Exposure Percentages for Three Types of Individuals

	Fish and Water Criterion				Fish-Only Criterion			
	Exposure as a Percent of Total Exposure			Default Value	Exposure as a Percent of Total Exposure			Default Value
	Subsist.	Sport	Gen.		Subsist.	Sport	Gen.	
Fish	99.9	99.8	96.6	50%	99.9	99.6	93.5	50%
Water					0.04	0.2	3.2	20%
Diet	0.01	0.07	1.1	20%	0.01	0.07	1.1	20%
Air	0.03	0.1	2.2	20%	0.03	0.1	2.2	20%

Total exposure compared with the RfD is included in Table 2.3.26. All exposures are greater than the RfD. For both criteria and all three types of individuals, the percent of exposure from eating either (1) fish and water or (2) fish-only is very high (>90 percent of the fisher's total exposure). The ceiling of 50 percent is used for the RSC allocation for the ambient water quality criterion.

The value of 50 percent is then multiplied by the total allowable dose (2.0×10^{-5} mg/kg-day) to determine allowable doses for all three types of individuals, as noted in Table 2.3.28. For each of the criteria, the allowable dose of 1×10^{-5} mg/kg-day is used to determine the AWQC. Criteria based on (1) fish and water intake, and (2) fish intake only are calculated and presented in this table. For

[20] These estimates were made using high-end values of fish exposure (i.e., the reported high-end contaminant concentration, along with the default consumption rates) for these populations. High-end values were also assumed for the estimates made with ambient water data (i.e., high-end contaminant concentrations). If central tendency contaminant concentrations had been used, the subsistence fisher percent of total exposure attributable to fish and water, and fish-only would be 99.3% and 98.6%, respectively. If central tendency contaminant concentrations had been used for the sportfisher, the estimates would equal those for the general population.

each type of fisher, the fish and water criterion values do not differ from the fish only criterion values. Other exposure factors from the equation used in the calculation are: body weight=70 kg; drinking water intake=2 L/day (or incidental ingestion of 0.01 L/day); fish intake rates of 0.01780 kg/day for the general and sportfisher populations and 0.08630 kg/day for subsistence fishers; and a bioaccumulation factor of 120,000.

Table 2.3.28: AWQC for Three Types of Individuals

	Fish and Water Criterion	Fish Only Criterion
Default Allowable Dose (50% of RfD)	1.0×10^{-5} mg/kg-day	1.0×10^{-5} mg/kg-day
AWQC:		
Subsistence Fisher[21]	6.8×10^{-8} mg/L	6.8×10^{-8} mg/L
Sportfisher	3.3×10^{-7} mg/L	3.3×10^{-7} mg/L
General Population	3.3×10^{-7} mg/L	3.3×10^{-7} mg/L

Presenting Information to Risk Managers

Although the above example utilizes the 20 percent floor for the other sources of exposure, it is clear that a combination of allocations of the RfD, if used, would exceed the 80 percent ceiling and in the case of the fish-only criterion, would exceed 100 percent of the RfD. This example also illustrates the potential need for flexibility to lower the floor (perhaps to zero?) due to exposures in exceedance of the RfD.

Because total exposures from all environmental media are greater than the dose without an appreciable risk of toxicological effects, several pieces of information can be presented to risk managers for their review in deciding how to apportion the dose of 2.0×10^{-5} mg/kg-day among exposure sources. These data include information about the toxicity of the chemical (including uncertainty in the estimate), information about exposures, and issues involving control of Chemical X. Because exposures and uncertainties in these estimates were discussed in previous sections, they will not be discussed again here. Additionally, control technology issues will not be discussed here, as they are not directly related to estimating exposure via the Exposure Decision Tree Approach. However, additional toxicity information is presented below.

[21] If the alternate default intake assumption of 86.3 g/day was used instead, the subsistence fisher AWQC estimates for fish and water, and fish only, would be 1.5×10^{-7} mg/L

The toxicity data supporting the RfD of 2.0 x 10^{-5} mg/kg-day should be described in order to give risk managers an idea about the confidence in the value. Some evaluative information is available from the Integrated Risk Information System. As noted above, the critical endpoints upon which the RfD is based include decreased antibody response to injected sheep red blood cells, exudate from the eye, inflammation of eyelid glands, and changes in finger and toe nails. A total uncertainty factor of 300 is applied to the Lowest Observed Adverse Effect Level (LOAEL) from the critical study. The total number of uncertainty factors account for: sensitive individuals within the population (a 10-fold factor); extrapolation from monkeys to humans (a 3-fold factor); use of a LOAEL instead of a NOAEL (a partial factor); and use of a subchronic rather than a chronic study (a 3-fold factor). The overall confidence in the RfD is medium because the confidence in the principal study based, in turn, on the confidence in the data base are also considered medium.

In addition to toxicity data, information on ways to control exposure in different environmental media can be presented to risk managers to aid them in determining the relative ease of controlling exposure from different environmental media. Ideally, this information would include expected incremental costs of treatment needed per unit decrease of Chemical X and other feasibility issues associated with controlling Chemical X in different environmental media.

Exposure from consuming freshwater/estuarine fish represents the single largest exposure to Chemical X. Other sources of exposure represent smaller percentages of total exposure, but all high-end exposures except air exposures also exceed the RfD individually.

2.3.4.4 Bioavailability of Substances from Different Routes of Exposure

For many chemicals, the rate of absorption can differ substantially from ingestion compared to inhalation. There is also available information for some chemicals which demonstrates appreciable differences in gastrointestinal absorption depending on whether the chemical is ingested from water, soil, or food. For some contaminants, plant and animal food products may also have appreciably different absorption rates. Regardless of the allocation approach used, EPA proposes using existing data on differences in bioavailability between water, air, soils, and different foods for estimating total exposure and in allocating the RfD. The Agency has developed such exposure estimates for cadmium (USEPA, 1994b). In the absence of data, EPA will assume equal rates of absorption from different routes and sources of exposure.

Information on absorption rates for Chemical X is not available. Available studies only generally describe varying fractions of the chemical in different media due to varying rates of volatilization, solubility, and adsorption. Discussions about chemical transformations in the environment and by human metabolism are similarly vague. In the absence of such data, it is assumed for this example that Chemical X is fully absorbed and that the rates of absorption from different routes and sources of exposure are equal.

2.3.5 References

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2.4. Use of BAFs in the Derivation of AWQC

2.4.1 Introduction

Aquatic organisms are known to accumulate certain types of chemicals in their bodies. Uptake of these chemicals may occur from exposure to contaminated water, consumption of contaminated food, and exposure to other sources such as contaminated bottom sediment. This chemical uptake process is called bioaccumulation. For some chemicals, such as certain highly hydrophobic chemicals, uptake through the food chain can be the most important route of exposure. As organisms in higher trophic levels feed on organisms in lower trophic levels, tissue concentrations of these chemicals increase through the trophic levels so that the concentrations in the highest trophic level organisms may be many orders of magnitude higher than levels in the environment. The trophic-level increase in contaminated concentrations is called biomagnification, and may result in serious adverse health effects for consumers of the highest trophic levels of fish.

To protect humans from harmful exposures to bioaccumulative chemicals, EPA proposes to use bioaccumulation factors (BAFs) in deriving AWQC. These BAFs are ratios of the contaminant concentration in tissue to the concentration in water, taking into account uptake through contaminated food, sediment, and water. Chemicals with larger BAFs reflect greater accumulation in fish tissues compared to chemicals with lower BAFs. The BAFs may be of such large magnitude that the resulting ambient water quality criterion will be strongly influenced by the BAF.

In contrast to the current guidelines, the 1980 AWQC National Guidelines for deriving human health criteria relied on an alternate type of ratio, the biconcentration factor (BCF), to derive AWQC.[22] In contrast to the BAF, the BCF measures uptake of chemicals into fish that have been exposed only through water (not through food or sediment). Because BAFs account for uptake from all sources of waterborne exposure of a chemical to an organism (through food, water, and sediment), EPA believes the use of the BAF to be superior to the BCF for deriving human health AWQC.

[22]According to the 1980 AWQC National Guidelines, laboratory-measured or predicted bioconcentration factors were used when field-measured bioconcentration factors (equivalent to what are now called field-measured BAFs) were not available.

2.4.1.1 Bioaccumulation and Bioconcentration Concepts

Bioaccumulation reflects the uptake and retention of a chemical by an aquatic organism from all surrounding media (e.g., water, food, sediment). Bioconcentration refers to the uptake and retention of a chemical by an aquatic organism from water only. Both bioaccumulation and bioconcentration can be viewed simply as the result of competing rates of chemical uptake and depuration (chemical loss) by an aquatic organism. However, the rates of uptake and depuration can be affected by numerous factors including the physical and chemical properties of the chemical, the physiology and biology of the organism, environmental conditions, ecological factors such as food web structure, and the amount and source of the chemical. When the rates of chemical uptake and depuration are equal, the distribution of the chemical between the organism and its source(s) is said to be at equilibrium or at steady state. For a constant chemical exposure, the time required to achieve steady state conditions varies according to the properties of the chemical and other factors. For example, some chemicals require a long time to reach steady state conditions between environmental compartments (e.g., many months for certain highly hydrophobic chemicals) while others reach steady state relatively quickly (e.g., hours to days for certain hydrophilic chemicals).

The concept of steady state or equilibrium conditions is very important when assessing or evaluating bioaccumulation or bioconcentration and applying these principles in real world situations, such as the derivation of ambient water quality criteria. For some chemicals and organisms that require relatively long time periods to reach steady state, changes in water column chemical concentrations may occur on a much more rapid time scale compared to the corresponding changes in an organism's tissue concentrations. Thus, if the system departs substantially from steady state conditions, the ratio of the tissue concentration to the water concentration may have little resemblance to the steady-state ratio and have little predictive value of long-term bioaccumulation potential.

For highly bioaccumulative pollutants in dynamic systems, reliable BAFs can be determined only if, among other factors, water column concentrations are averaged over a sufficient period of time (e.g., a duration approximating the amount of time predicted for the pollutant to reach steady-state). In addition, adequate spatial averaging of both tissue and water column concentrations is required to develop reliable BAFs for use in deriving human health ambient water quality criteria.

For this reason, a bioaccumulation factor is defined in this guidance as representing the ratio (in L/kg) of a concentration of a substance in tissue to its concentration in the surrounding water in situations where the organism and its food are exposed and the ratio does not change substantially over time. A bioconcentration factor is considered to represent the uptake and retention of a substance by an aquatic organism from the surrounding water only, through gill membranes or other external body surfaces, in situations where the tissue-to-water ratio does not change substantially over time.

This chapter provides the technical basis and rationale for EPA's proposed procedures for determining BAFs for toxic substances. Section 2.4.2 lists pertinent definitions used throughout the

chapter, Sections 2.4.3 through 2.4.5 describe issues and procedures relevant to estimating BAFs for nonpolar organic chemicals, Section 2.4.6 describes procedures relevant to the derivation of BAFs for inorganic chemicals, and Section 2.4.7 discusses the derivation of BAFs for two example chemicals. Issues associated with applying fish consumption rate information to trophic level-specific BAFs are discussed in Section 2.4.8.

2.4.2 Definitions

Baseline BAF (BAF^{fd}). For organic chemicals, a BAF (in L/kg-lipid) that is based on the concentration of freely dissolved chemical in the ambient water and the lipid normalized concentration in tissue; for inorganic chemicals, a BAF that is based on the wet weight of the tissue.

Baseline BCF (BCF^{fd}). For organic chemicals, a BCF (in L/kg-lipid) that is based on the concentration of freely dissolved chemical in the ambient water and the lipid normalized concentration in tissue; for inorganic chemicals, a BCF that is based on the wet weight of the tissue.

Bioaccumulation. The net accumulation of a substance by an organism as a result of uptake from all environmental sources.

Bioaccumulation Factor (BAF). The ratio (in L/kg-tissue) of the concentration of a substance in tissue to its concentration in the ambient water, in situations where both the organism and its food are exposed and the ratio does not change substantially over time. The BAF is calculated as:

$$BAF = \frac{C_t}{C_w}$$

(Equation 2.4.1)

where:

C_t = Concentration of the chemical in the wet tissue (either whole organism or specified tissue)

C_w = Concentration of chemical in water

Bioconcentration. The net accumulation of a substance by an aquatic organism as a result of uptake directly from the ambient water, through gill membranes or other external body surfaces.

Bioconcentration Factor (BCF). The ratio (in L/kg-tissue) of the concentration of a substance in tissue of an aquatic organism to its concentration in the ambient water, in situations where the organism is exposed through the water only and the ratio does not change substantially over time. The BCF is calculated as:

$$BCF = \frac{C_t}{C_w}$$

(Equation 2.4.2)

where:

C_t = Concentration of the chemical in the wet tissue (either whole organism or specified tissue)

C_w = Concentration of chemical in water

Biota-Sediment Accumulation Factor (BSAF). The ratio (kg of sediment organic carbon per kg of lipid) of the lipid-normalized concentration of a substance in tissue of an aquatic organism to its organic carbon-normalized concentration in surface sediment, in situations where the ratio does not change substantially over time, both the organism and its food are exposed, and the surface sediment is representative of average surface sediment in the vicinity of the organism. The BSAF is defined as:

$$BSAF = \frac{C}{C_{soc}}$$

(Equation 2.4.3)

where:

C = The lipid-normalized concentration of the chemical in tissues of the biota (g/g lipid)

C_{soc} = The organic carbon-normalized concentration of the chemical in the surface sediment (g/g sediment organic carbon)

Biomagnification. The increase in tissue concentration of poorly depurated materials in organisms along a series of predator-prey associations, primarily through the mechanism of dietary accumulation.

Biomagnification Factor (BMF). The ratio (unitless) of the tissue concentration of a predator organism at a particular trophic level to the tissue concentration in its prey organism at the next lowest trophic level, for a given waterbody and chemical exposure. For organic chemicals, a BMF can be calculated using lipid-normalized concentrations in the tissue of organisms at two successive trophic levels as:

$$BMF_{(TL,\ n)} = \frac{C_{(TL,\ n)}}{C_{(TL,\ n-1)}}$$

where:

$C_{(TL, n)}$ = Lipid-normalized concentration in appropriate tissue of predator organism at trophic level "n"

$C_{(TL, n-1)}$ = Lipid-normalized concentration in appropriate tissue of prey organism at the next lowest trophic level from the predator.

For inorganic chemicals, a BMF can be calculated using chemical concentrations in the tissue of organisms at two successive trophic levels as:

$$BMF_{(TL,\ n)} = \frac{C_{t\ (TL,\ n)}}{C_{t\ (TL,\ n-1)}}$$

where:

$C_{t\ (TL, n)}$ = Concentration in appropriate tissue of predator organism at trophic level "n" (may be either wet weight or dry weight concentration so long as both the predator and prey concentrations are expressed in the same manner)

$C_{t\ (TL, n-1)}$ = Concentration in appropriate tissue of prey organism at the next lowest trophic level from the predator (may be either wet weight or dry weight concentration so long as both the predator and prey concentrations are expressed in the same manner)

As explained in the TSD, BMFs can also be related to (and calculated from) FCMs and baseline BAFs.

Depuration. The loss of a substance from an organism as a result of any active or passive process.

Food-Chain Multiplier (FCM). The ratio of a baseline BAF for an organism of a particular trophic level to the baseline BCF (usually determined for organisms in trophic level one).

Freely Dissolved Concentration. For hydrophobic organic chemicals, the concentration of the chemical that is dissolved in ambient water, excluding the portion sorbed onto particulate or dissolved organic carbon. The freely dissolved concentration is considered to represent the most bioavailable form of an organic chemical in water and, thus, is the form that best predicts bioaccumulation. The freely dissolved concentration can be determined as:

$$C_w^{fd} = (f_{fd}) \cdot (C_w^t)$$

(Equation 2.4.4)

where:

C_w^{fd} = Freely dissolved concentration of the organic chemical in ambient water

C_w^t = Total concentration of the organic chemical in ambient water

f_{fd} = Fraction of the total chemical in ambient water that is freely dissolved

Lipid-normalized Bioaccumulation Factor (BAF). The ratio (in L/kg-lipid) of a substance's lipid-normalized concentration in tissue to its concentration in the ambient water, in situations where both the organism and its food are exposed and the ratio does not change substantially over time. The lipid-normalized BAF is calculated as:

$$BAF = \frac{C}{C_w}$$

(Equation 2.4.5)

where:

C = Lipid-normalized concentration of the chemical in whole organism or specified tissue

C_w = Concentration of chemical in water

Lipid-normalized Bioconcentration Factor (BCF). The ratio (in L/kg-lipid) of a substance's lipid-normalized concentration in tissue of an aquatic organism to its concentration in the ambient water, in situations where the organism is exposed through the water only and the ratio does not change substantially over time. The lipid-normalized BCF is calculated as:

$$BCF = \frac{C}{C_w}$$

(Equation 2.4.6)

where:

C = Lipid-normalized concentration of the chemical in whole organism or specified tissue

C_w = Concentration of chemical in water

Lipid-normalized Concentration (C). The total concentration of a contaminant in a tissue or whole organism divided by the lipid fraction in that tissue or whole organism. The lipid-normalized concentration can be calculated as:

$$C = \frac{C_t}{f}$$

(Equation 2.4.7)

where:

C_t = Concentration of the chemical in the wet tissue (either whole organism or specified tissue)

f = Fraction lipid content in the organism or specified tissue

Octanol-water Partition Coefficient (K_{ow}). The ratio of the concentration of a substance in the n-octanol phase to its concentration in the aqueous phase in an equilibrated two-phase octanol-water system. For log K_{ow}, the log of the octanol-water partition coefficient is a base 10 logarithm.

Organic Carbon-normalized Concentration (C_{soc}). For sediments, the total concentration of a contaminant in sediment divided by the fraction of organic carbon in sediment. The organic carbon-normalized concentration can be calculated as:

$$C_{soc} = \frac{C_s}{f_{oc}}$$

(Equation 2.4.8)

where:

C_s = Concentration of chemical in sediment

f_{oc} = Fraction organic carbon in sediment

Uptake. Acquisition by an organism of a substance from the environment as a result of any active or passive process.

2.4.3 Determining BAFs for Nonpolar Organics

The calculation of a BAF for a nonpolar organic chemical (chemicals that do not readily dissolve in water) used in the derivation of AWQC is a two-step process. The first step is to calculate a baseline BAF for the chemical of interest using information from the field site or laboratory where the original data were collected (i.e., the lipid content of the species collected and the freely dissolved fraction of the chemical in water at the site where the data were collected). If information used to estimate fish consumption rates indicates that organisms are being consumed from different trophic levels, then baseline BAFs need to be determined for each of the relevant trophic levels.

The second step is to calculate a BAF (or BAFs) for the chemical that will be used in the derivation of AWQC, using information from the location where the aquatic species of interest are consumed (i.e., the lipid content of the aquatic species consumed by humans and the freely dissolved fraction of the chemical in water at the site where the aquatic species are being consumed). The difference between a baseline BAF and a BAF used in the derivation of a AWQC is that baseline BAFs can be used for extrapolating from one species to another and from one water body to another. This is the case because baseline BAFs are lipid-normalized, enabling extrapolation for organic chemicals from one species to another; and because they are based on the freely dissolved concentration of organic chemicals, enabling extrapolation from one water body to another (the importance of these concepts is discussed below). Baseline BAFs, however, cannot be used directly in the derivation of AWQC because they may not reflect the conditions in the area of interest (e.g., the lipid content of the aquatic species consumed in the area of interest and the freely dissolved fraction of the chemical in the area of concern).

Depending on the type of information available for a given chemical, different procedures may be used to determine the baseline BAF. The most preferred BAFs are those derived using appropriate field data. Field-measured BAFs, however, have not been determined for all chemicals. Thus, EPA proposes a hierarchy of procedures to determine BAF values. The data preference for derivation of baseline BAFs for nonpolar organic substances is as follows (in order of priority):

1. A field-measured baseline BAF derived from a field study of acceptable quality.

2. A predicted baseline BAF derived from a field-measured BSAFs of acceptable quality.

3. A predicted baseline BAF derived from a laboratory-measured BCF of acceptable quality and a food-chain multiplier (FCM).

4. A predicted baseline BAF derived from an acceptable K_{ow} and a food-chain multiplier.

While EPA recommends the above hierarchy for determining final baseline BAF values, for comparative purposes, baseline BAFs should be determined for each chemical by as many of the four methods as available data allow. Comparing baseline BAFs derived using the different methods recommended above can provide insight for identifying and evaluating any discrepancies in the BAF determinations that might occur. The information needed to derive a baseline BAF using each of the four methods is discussed in Section 2.4.4. Section 2.4.5 discusses the information needed to derive a BAF for use in the calculation of AWQC.

2.4.4 Estimating Baseline BAFs for Nonpolar Organics

All the baseline BAFs for nonpolar organic chemicals should be expressed on a freely-dissolved and lipid-normalized basis. The procedures for adjusting a field-measured BAF, field-

measured BSAF, or laboratory-measured BCF to a freely-dissolved and lipid-normalized basis are discussed below.

2.4.4.1 Field-Measured Baseline BAF

EPA's first preference for deriving a BAF for nonpolar organic substances is the use of a valid field-measured BAF. Field-measured BAFs are preferred to other procedures because they inherently account for the effects of metabolism, biomagnification, and other factors affecting bioaccumulation.

The calculation of a field-measured baseline BAF requires information on: (1) a field-measured BAF based on the total concentration of a chemical in the tissue of the aquatic organism sampled and the total concentration of the chemical in the ambient water; (2) the fraction of tissue that is lipid in the aquatic organism of interest; and (3) either the measured or estimated freely dissolved fraction of the total chemical in the ambient water where the aquatic species were collected (estimating the freely dissolved fraction for a chemical requires information on the particulate and dissolved organic carbon content in the ambient water and the K_{ow} of the chemical of interest). The equation for deriving a field-measured baseline BAF expressed on a freely-dissolved and lipid-normalized basis is:

$$\text{Baseline BAF}^{fd} = \left[\frac{\text{Measured BAF}_T^t}{f_{fd}} - 1 \right] \left(\frac{1}{f} \right)$$

(Equation 2.4.9)

where:

Baseline BAF^{fd}	=	BAF expressed on a freely-dissolved and lipid-normalized basis
Measured BAF_T^t	=	BAF based on total concentration in tissue (wet weight basis) and water
f	=	Fraction of the tissue that is lipid
f_{fd}	=	Fraction of the total chemical that is freely dissolved in the ambient water

For the derivation of Equation 2.4.9, see Appendix C.

For each trophic level, a species mean baseline BAF is calculated as the geometric mean if more than one acceptable, measured baseline BAF is available for a given species. For each trophic level, a trophic level-specific BAF is calculated as the geometric mean of the species mean measured baseline BAFs. Each of the three components for deriving the baseline BAF are described in further detail below.

Measured BAF_T^t

To estimate a measured BAF_T^t, information is needed on the total concentration of the pollutant in the tissue of the organism and the total concentration of the chemical in ambient water at the site of sampling. The equation to derive a measured BAF_T^t is:

$$\text{Measured } BAF_T^t = \frac{\text{Total concentration of chemical in tissue (ug/Kg wet weight)}}{\text{Total concentration of chemical in the ambient water (ug/L)}}$$

(Equation 2.4.10)

Guidance for Measuring Field-Based BAFs

Application of data quality assurance procedures when measuring, estimating, and applying BAFs is of primary importance. The following procedural and quality assurance requirements should be met for field-measured BAFs:

- The field studies used should be limited to those that include fish at or near the top of the aquatic food chain (i.e., in trophic levels 3 and/or 4). In situations where consumption of lower trophic level organisms represents an important exposure route, such as certain types of shellfish at trophic level 2, the field study should also include appropriate target species at this trophic level.

- The trophic level of the fish species should be determined, taking into account the life stage(s) consumed and food web structure at the location(s) of interest.

- Collection of bioaccumulation field data at a specific site for which criteria are to be applied and with the species of concern are preferred.

- If data cannot be collected from every site for which criteria are to be derived, the site of the field study should not be so unique that the BAF cannot be extrapolated to other locations where the criteria and values will be applied.

- Samples of the appropriate resident species and the water in which they reside should be collected and analyzed using appropriate, sensitive, accurate, and precise methods to determine the concentrations of bioaccumulative chemicals present.

- For organic chemicals, the percent lipid should be either measured or reliably estimated for the tissue used in the determination of the BAF to permit the measured concentration of chemical in the organism's edible tissues to be lipid-normalized.

- The concentration of the chemical in the water should be measured in a way that can be related to particulate organic carbon (POC) and dissolved organic carbon (DOC), as further described in the forthcoming section on POC and DOC concentrations (page 14).

- For organic chemicals with log K_{ow} greater than four, the concentrations of POC and DOC in the ambient water should be either measured or reliably estimated.

- For inorganic chemicals where lipid normalization does not apply, BAFs should be used only if they are expressed on a wet weight basis; BAFs reported on a dry weight basis can be used only if they are converted to a wet weight basis using a conversion factor that is measured or reliably estimated for the tissue used in the determination of the BAF.

EPA recommends the use of field-measured BAFs as the first preferred method for determining BAFs because they incorporate numerous site-specific factors that can affect bioaccumulation (food web structure, temporal and spatial variation in contaminant levels, and metabolism of the contaminant). However, in order to ensure that the resulting BAFs accurately reflect contaminant bioaccumulation and subsequent exposure to the target human population, the measurement of field-based BAFs must be performed carefully and should consider several factors that can lead to variability and uncertainty in BAF estimates. Several of these factors are summarized below. Further discussion of these and other factors is provided in USEPA (1995a; 1995b). EPA is developing additional guidance on performing field studies for determining BAFs and will provide this guidance for review upon its completion.

Selection of Target Species. The choice of the target species for contaminant analysis is one critical aspect in determining a valid and representative field-measured BAF for establishing AWQC designed to protect human health. Selection of the target species should be made with knowledge of the key exposure route(s) involved in bioaccumulation of the contaminant of interest (e.g., uptake from water, food, sediment/pore water). Several important factors to consider when selecting target species for contaminant monitoring have been summarized by EPA in their document: *Fish Sampling and Analysis: A Guidance Document for Issuing Fish Consumption Advisories* (USEPA, 1993), and are recommended for consideration when identifying target species in BAF studies. While the objectives of fish consumption advisory studies and BAF studies are not entirely identical, many of the principles described in USEPA (1993) also apply to the determination of BAFs from field studies.

It is of primary importance that the target species selected be among those species commonly consumed in the study area and those of commercial, recreational or sustenance fishing value. In addition, the potential for bioaccumulation of the contaminant(s) of interest should be considered. Knowledge of the food web structure, likely exposure routes, and contaminant properties (e.g., K_{ow} for organics) is important for evaluating a species' bioaccumulation potential. Species occupying

trophic level three (e.g., forage fish) or four (e.g., predator fish) are recommended for selection in BAF studies because they have consistently been among the highest bioaccumulators in the aquatic food web, particularly for highly hydrophobic chemicals. If possible, the target finfish species should include at least one species of bottom feeding fish species (trophic level three) and one top predator species (trophic level four). Including species with different dietary preferences will help account for the effect of food web structure on bioaccumulation, the effect of which can vary with the properties of the chemical (i.e., in some cases, bottom feeders can have higher BAFs and in other cases lower BAFs compared to top predator (piscivorous) species). Organisms occupying trophic level two (e.g., clams, oysters) should also be sampled if information indicates that consumption of such organisms is likely to be an important exposure route to contaminants. In addition, the geographic distribution of the species should be considered in relation to the target human population intended for protection. Further information pertaining to the selection of target aquatic species for contaminant analysis for fish advisories is provided in USEPA (1993).

Choice of Sampling Sites. Selection of sampling sites and the frequency at which they are sampled should take into account numerous factors, many of which relate to the spatial and temporal variability in the contaminant concentrations in the target aquatic species and environmental media. If the proper temporal and spatial intervals are not selected, such measurements can lead to erroneous estimates of bioaccumulation. The sites should be representative of those from which the target human population are expected to be exposed. In addition, the sampling sites need to be representative of the area of movement of the target species. This is particularly important for migratory species which may only spend a portion of the time in the study area of interest.

Temporal and spatial variability can be particularly high for water concentrations of contaminants. Thus, individual water samples taken at one point in time may not adequately reflect average exposure to the target species. Water concentrations should be averaged over the approximate time it takes for the target species to reach steady state, which varies depending on the toxicokinetics of the contaminants in relation to the target organism. For example, chemicals with high K_{ow} values are expected to reach steady-state in top trophic level organisms much slower than chemicals with low K_{ow} values, and thus, require greater temporal averaging of water column concentrations for estimating BAFs. Other factors to consider when determining the frequency of sampling include the home range of the target species, its life history, and the pattern of contaminant release (episodic vs. continuous releases). Selection of sampling sites should also consider temporal and spatial variations in food web structure that may occur across the study area. The desired level of statistical power should also be considered when determining the number of sampling sites and replicates.

Biological Considerations. When sampling target species for BAF determinations used in deriving human health criteria, several biological attributes of the target species should also be considered. For example, the size/age of the organism can affect the extent of bioaccumulation in the organism. Young fish can exhibit lower accumulation of some contaminants due to growth dilution. In addition, the reproductive status (e.g., pre/post spawning) can alter the body burden of contaminants, with significant contaminant loss observed due to maturation and release of sperm or

eggs. Seasonal variations in lipid content can also lead to differences in accumulation of contaminants. In general, the size of the target species should be representative of the size being consumed by the target human population. If this size range is broad, stratifying sampling strategies by size class is necessary, particularly when taking composite samples. The timing of sampling should include the period of most frequent harvesting of the species. Additional discussion of these and other attributes to consider when sampling finfish and shellfish for contaminant monitoring is provided in USEPA (1993).

Measurement of Other Important Parameters. For nonpolar organic chemicals, lipid content of the target species should be measured in the same tissue in which the contaminant was measured to permit lipid normalization. This will usually be fillet for finfish and edible tissue for shellfish. In addition, POC and DOC should be measured in the water samples in order to estimate the freely dissolved fraction. For inorganic chemicals, the bioavailability of various forms of the chemical should be considered when deciding upon the analyte being measured for the BAF determination. Where appropriate, BAFs should be expressed for specific forms of the contaminant. For example, methylmercury is known to be more bioavailable than inorganic forms of mercury, and the relative proportions of each can vary significantly over space and time. Thus, BAFs determined for total mercury without knowledge of the relative proportion of various organic and inorganic forms of mercury are more uncertain in their applicability to other sites and times than BAFs measured for specific forms of mercury. Other parameters such as temperature, pH, dissolved oxygen, conductivity/salinity, total suspended sediments, and sediment grain size should also be measured, as they may alter the bioavailability and subsequent bioaccumulation of contaminants by aquatic organisms. EPA will provide additional guidance on the design and conduct of field BAF studies in its forthcoming guidance document, which is expected to undergo external review in the fall of 1998.

Freely Dissolved Fraction of the Chemical in Water (f_{fd})

Nonpolar organic chemicals can exist in water in several different forms, including freely dissolved chemicals in the water column, chemicals bound to particulate matter, and chemicals bound to dissolved organic matter in the water. The form of the chemical has been shown to affect bioaccumulation, with the freely dissolved form of a chemical considered to be the best expression of the bioavailable form to aquatic organisms. Because the amount of chemical that is freely dissolved may differ among water bodies due to differences in the total organic carbon in the water, BAFs based on the concentration of freely dissolved chemical will provide the most universal BAF for organic chemicals when averaging BAFs from different studies. However, BAFs based on the total concentration of the chemical in water (i.e., the freely dissolved plus that sorbed to particulate organic carbon and dissolved organic carbon) can often be measured more accurately than BAFs based on freely dissolved concentrations in water. Therefore, if BAFs based on total water concentrations are reported in a BAF study, information on the organic carbon content of water (at the site from which the BAF was measured, if available) is required to predict freely dissolved concentrations used to determine the baseline BAF. Specifically, the fraction freely dissolved (f_{fd}) in Equation 2.4.9 must be estimated, using information on the chemical's K_{ow} and both dissolved and

particulate organic carbon contents (DOC and POC) of the water. The equation used to estimate f_{fd} is:

$$f_{fd} = \frac{1}{[1 + (POC \cdot K_{ow}) + (DOC \cdot \frac{K_{ow}}{10})]}$$

(Equation 2.4.11)

where:

POC	=	Concentration of particulate organic carbon (kg/L) in the ambient water
DOC	=	Concentration of dissolved organic carbon (kg/L) in the ambient water
K_{ow}	=	N-octanol water partition coefficient for the chemical

In this equation, the terms "K_{ow}" and "$K_{ow}/10$" are used to estimate the partition coefficients to POC and DOC, respectively, which have units of L/kg. The scientific basis supporting the derivation of this equation for estimating the freely dissolved fraction is provided in Appendix D.

POC and DOC Concentrations. As noted above, when converting from the total concentration of a chemical to a freely dissolved concentration, the POC and DOC should be obtained from the original study that reports BAFs based on total concentrations of a chemical in water. However, if the POC and DOC concentrations are not reported in the BAF study, then reliable estimates of POC and DOC might be available from other studies of the same site used in the BAF study or closely related sites within the same water body. When using POC/DOC data from other studies of the same water body for the same or very similar sites, care must be taken to ensure that environmental conditions that may affect POC or DOC concentrations are similar to those in the BAF study. Information on the spatial and temporal variability of POC and DOC at the site of interest (and factors influencing this variability) should be used in evaluating the applicability of any surrogate POC or DOC data for estimating the freely dissolved fraction. For example, differences in hydrological conditions between the BAF study and the surrogate study (e.g., high vs. low flow events, mixed vs. stratified water column, tidal cycle differences) and the degree to which such conditions influence POC and DOC concentrations should be evaluated in deciding whether surrogate data provide reliable estimates of POC and DOC for the BAF study. Similarly, differences in other factors which may influence POC and DOC concentrations, such as the sampling season, sampling depth, proximity to areas of high DOC inputs including wetlands, should be evaluated in determining the reliability of surrogate data. Additional factors besides the examples listed here may also be important in determining the reliability of surrogate POC and DOC data for estimating the baseline BAF.

Guidance on Selecting Appropriate K_{ow} Values

The conversion of total chemical concentrations in water to freely dissolved chemical concentrations, as well as other procedures discussed in this chapter (including the BSAF method and

use of the food chain model) rely on the K_{ow} for chemicals. A variety of techniques are available to estimate or predict K_{ow} values, some of which are more or less reliable depending on the K_{ow} of the chemical.

As discussed in USEPA 1998a, EPA is proposing and taking comment on two options on how to select a reliable K_{ow} value. The first option is EPA's existing guidance published in the Great Lakes Water Quality Initiative (60 FR 15366, March 23, 1995). A second option is more detailed, draft guidance on selecting K_{ow} values which EPA has developed and is currently undergoing external scientific peer review. The salient features of both the GLWQI K_{ow} selection guidance (option 1) and EPA's new, draft guidance (option 2) are presented below. Additional details of the new draft K_{ow} selection guidance (option 2) are provided in Appendix F.

Guidance on selecting reliable values of K_{ow} based on the GLWQI approach (option 1) is as follows:

For chemicals with log $K_{ow} < 4$:

Priority	Technique
1	Slow-stir Shake-flask Generator-column
2	Measured value from the CLOGP program
3	Reverse-phase liquid chromatography on C_{18} with extrapolation to zero percent solvent
4	Reverse-phase liquid chromatography on C_{18} without extrapolation to zero percent solvent
5	Calculated by the CLOGP program

For chemicals with log $K_{ow} > 4$:

Priority	Technique
1	Slow-stir Generator-column
2	Reverse-phase liquid chromatography on C_{18} with extrapolation to zero percent solvent

3 Reverse-phase liquid chromatography on C_{18} without extrapolation to zero percent solvent

4 Shake-flask

5 Measured value from the CLOGP program

6 Calculated by the CLOGP program

If no measured K_{ow} is available, the K_{ow} must be estimated using the CLOGP program. Several general points should be kept in mind when using K_{ow} values. Values should be used only if they were obtained from the original authors or from a critical review that supplied sufficient information. If more than one "best" K_{ow} value is available for a chemical (i.e., the highest priority value available), the arithmetic mean of the available log K_{ow}s or the geometric mean of the available K_{ow}s may be used. Because of potential interference due to radioactivity associated with impurities, values determined by measuring radioactivity in water and/or octanol should be considered less reliable than values determined by a K_{ow} method of the same priority that employ non-radioactive techniques except when measurements of parent chemical are done. The values determined using radioactive methods should be moved down one step in the priority below the values determined using the non-radioactive technique except when measurements of parent chemical are done. Because the K_{ow} is an intermediate value in the derivation of a BAF, the value used for the K_{ow} of a chemical should not be rounded to less than three significant digits. K_{ow} values that are outliers compared with other values for a chemical should not be used.

The salient features of EPA's new draft methodology (option 2) for selecting reliable values of K_{ow} is described below.

I. Assemble/evaluate experimental and calculated data (e.g.,CLOGP, LOGKOW, SPARC)

II. If calculated log K_{ow}'s > 8,
   A. Develop independent estimates of K_{ow} using:
      1. Liquid Chromatography (LC) methods with "appropriate" standards. (See Appendix F for guidelines for LC application).
      2. Structure Activity Relationship (SAR) estimates extrapolated from similar chemicals where "high quality" measurements are available. "High quality" SARs are defined in Appendix F of the TSD.
      3. Property Reactivity Correlation (PRC) estimates based on other measured properties (solubility, etc.).
   B. If calculated data are in reasonable agreement and are supported by independent estimates described above, report the average calculated value. Guidance on determining whether K_{ow} values are in "reasonable agreement" are presented in Appendix F of the TSD.

C. If calculated/estimated data do not agree, use professional judgement to evaluate/blend/weight the calculated and estimated data to assign a K_{ow} value.
D. Document rationale including relevant statistics.

III. If calculated log K_{ow}'s range from 6 - 8,
A. Look for "high quality" measurements. These will generally be slow stir measurements, the exception being certain classes of compounds where micro emulsions tend to be less of a problem (i.e., PNA's, shake flask measurements are good to log K_{ow} of 6.5).
B. If measured data are available and are in reasonable agreement (both measurements and calculations), report average measured value.
C. If measured data are in reasonable agreement, but differ from calculated values, develop independent estimates and apply professional judgement to evaluate/blend/weight the measured, calculated and estimated data to assign K_{ow} value.
D. If measured data are not in reasonable agreement (or if only one measurement is available), use II A, B, and C to produce a 'best estimate;' use this value to evaluate/screen the measured K_{ow} data. Report the average value of screened data. If no measurements reasonably agree with 'best estimate,' apply professional judgement to evaluate/blend/weight the measured, calculated and estimated data to assign K_{ow}.
E. If measured data are unavailable, proceed through II A, B, C and report the 'best estimate.'
F. Document rationale including relevant statistics.

IV. If calculated log K_{ow}'s < 6,
A. Proceed as in III. Slow stir is the preferred method but shake flask data can be considered for all chemicals if sufficient attention has been given to emulsion problems in the measurement.

The general operational guidelines for EPA's new draft methodology for selecting K_{ow} values are as follows:

1. For chemicals with log K_{ow} > 5, it is highly unlikely to find multiple "high quality" measurements. (Note: "high quality" is data judged to be reliable based on the guidelines presented in Appendix F of the TSD).

2. "High Quality" measured data are preferred over estimates, but due to the scarcity of 'high quality' data, the use of estimates is important in assigning K_{ow}'s.

3. K_{ow} measurements by slow stir are extendable to 10^8. Shake flask K_{ow} measurements are extendable to 10^6 with sufficient attention to micro emulsion effects; for classes

of chemicals that are not highly sensitive to emulsion effects (i.e., PNA's) this range may extend to $10^{6.5}$.

4. What is to be considered reasonable agreement in log K_{ow} data (measured or estimated) depends primarily on the log K_{ow} magnitude. The following standards for data agreement have been set for this guidance: 0.5 for log $K_{ow} > 7$; 0.4 for $6 \leq \log K_{ow} \leq 7$; 0.3 for log $K_{ow} < 6$.

5. Statistical methods should be applied to data as appropriate but application is limited due to the scarcity of data, and the determinate/methodic nature of most measurement error(s).

The various techniques are summarized as follows:

- The *slow-stir method* requires adding the test chemical to a reaction flask which contains a water and octanol phase. The chemical partitions to these two phases under conditions of slow stirring the flask. After the phases are allowed to separate, the concentration of the test chemical in each phase is determined (Brooke et al., 1986). This method is easy to use and can be replicated with a high degree of confidence. Emulsions, which can contaminate the aqueous phase and influence the observed K_{ow} values, can be prevented, and high K_{ow} values can be obtained easily (de Bruijn et al., 1989). In general, there is reasonable agreement between the slow stir method and literature data obtained using the generator-column method. For log K_{ow} values less than 4.5, data agree well with K_{ow}s determined based on the shake-flask method (de Bruijn et al., 1989).

- The *shake-flask method* also involves adding the chemical to a reaction flask with a mixture of octanol and water. In this method, however, the flask is shaken to obtain partitioning of the chemical between the octanol and water phases (OECD, 1981). Several researchers have found that the shake-flask technique is acceptable only for chemicals with log K_{ow}s less than certain values. Some researchers found that the shake-flask technique has been reported to be acceptable only for chemicals which have log K_{ow}s less than 4 (Karickhoff et al., 1979; Konemann et al., 1979; Braumann and Grimme, 1981; Harnisch et al., 1983; Brooke et al., 1990). Others have found that the technique is acceptable for chemicals with slightly higher log K_{ow} values. Brooke et al. (1986) compared techniques and decided that the shake-flask technique is acceptable for chemicals with log K_{ow}s up to 5, whereas Chessells et al. (1991) stated that this technique is acceptable for log K_{ow} values up to about 5.5.

- The *generator-column method* involves filling a column with an inert material (silanized Chromosorb W or glass beads) that is coated with water-saturated octanol and contains the test chemical. Pumping water through the column results in an aqueous solution in equilibrium with the octanol phase. The water that leaves the

column is extracted with specifically either an organic solvent or a C_{18} column that is then eluted with hexane or methanol (DeVoe et al., 1981; Woodburn et al., 1984; Miller et al., 1984).

- The *reverse-phase liquid chromatography method* involves adding the test chemical in a polar mobile phase (such as water or water-methanol) to a hydrophobic porous stationary phase (the C_{18} *n*-alkanes covalently bound to a silica support). The chemical partitions between the column and the polar aqueous phase. K_{ow} values are estimated from linear equations between the K_{ow} and retention indices that are derived for reference chemicals (Konemann et al., 1979; Veith et al., 1979; McDuffie, 1981; Garst and Wilson, 1984).

- The *CLOGP program* is a computer program that contains measured K_{ow} values for some chemicals and can calculate K_{ow} values for additional chemicals based on similarities in chemical structure between chemicals with measured K_{ow} values and chemicals for which K_{ow}s are to be determined. The method used to calculate the K_{ow} values is described in Hansch and Leo (1979).

- *SPARC* (SPARC Performs Automated Reasoning in Chemistry) is a mechanistic model developed at the Ecosystems Research Division of the National Exposure Research Laboratory of the Office of Research and Development of the U.S. Environmental Protection Agency by Sam Karickhoff, Lionel Carreira, and co-workers.

In some situations, available data may require determination of a single K_{ow} value for a class of chemicals or a or mixture of closely related chemicals (e.g., when toxicity data are class- or mixture-specific). However, it is not possible to determine experimentally a valid K_{ow} for a substance that is a mixture of chemicals (e.g., PCBs, toxaphene, chlordane). For calculating the composite freely dissolved fraction used to adjust a composite field-measured BAF to a composite baseline BAF, a composite K_{ow} value of the mixture can be calculated based on the sum of the total concentration of the mixture components in water (e.g., individual congeners for PCBs), the sum of the dissolved mixture components in water, and the DOC and POC from the site for which the BAF was measured. The equation used to derive the composite K_{ow} for use in determining a composite baseline BAF is:

$$\text{Composite } K_{ow} = \left(\frac{1}{\frac{DOC}{10} + POC} \right) \left(\frac{\sum_{i=1}^{n} C_w^t}{\sum_{i=1}^{n} C_w^{fd}} - 1 \right)$$

where:

i	=	1, 2, … n individual mixture components (e.g., congeners for PCBs).
C_w^t	=	total concentration of the mixture component in water.
C_w^{fd}	=	freely dissolved concentration of the mixture component in water.

Notably, calculation of a composite K_{ow} is just one of a series of steps involved in deriving composite baseline BAFs and AWQC BAFs for chemical mixtures for which single toxicity values apply. These steps include: (1) first determining a composite initial total BAF (analogous to the total field-measured BAF for individual chemicals), (2) determining a composite baseline BAF, using the composite freely dissolved fraction and composite K_{ow} derived using the equation above, (3) calculating a composite AWQC BAF from the composite baseline BAF based on the composite freely dissolved fraction at the AWQC site(s). This last step requires calculation of a second composite K_{ow} which is used to determine the composite freely dissolved fraction at the AWQC site(s) using POC and DOC data from the AWQC site(s). Additional details of the steps required in determining a composite K_{ow} for deriving composite baseline BAFs and composite AWQC BAFs (including example calculations for PCBs) are provided in 62 FR 117250 (March 12, 1997).

Lipid Normalization of Data

Partitioning of organic chemicals into aquatic organisms has been shown to be a function of the lipid content of the organism (Mackay, 1982; Connolly and Pederson, 1988; Thomann, 1989). For this reason, EPA assumes that BAFs and BCFs for lipophilic organic chemicals are directly proportional to the percent lipid in the tissue or whole body of the organism of interest. For example, an organism with two percent lipid content would accumulate twice the amount of a chemical as an organism with one percent lipid content, all else being equal. This assumption has been extensively evaluated in the literature and is generally accepted. To account for the influence of the lipid content on the BAF or BCF, EPA recommends normalizing the BAF or BCF to the percent lipid in the fish. This procedure is consistent with other EPA guidance on bioaccumulation (Stephan et al., 1985; USEPA, 1991).

To compare BAFs and BCFs that have been measured in fish that have different lipid contents, EPA recommends that BAFs and BCFs be normalized by dividing by the mean lipid fraction of the aquatic organism. Whole body and edible tissue BAFs and BCFs are normalized using the respective whole body and edible tissue fraction lipid values. Since lipid content is known to vary from one tissue to another and from one aquatic species to another, EPA recommends the percent lipid used to normalize the BAF or BCF (whole body or edible tissue) be obtained from the BAF or BCF study. Unless comparability can be determined across organisms, the fraction lipid should be determined for the test organism. Lipid content of the fish tissue is affected by the age, sex and diet of the fish, by the season the fish are sampled, and by differing environmental conditions. Therefore, it is generally necessary to determine an average percent lipid value for the test organisms.

EPA recommends using a gravimetric method for determining the percent lipid value (USEPA, 1995a). The method is easy to use and is employed by many laboratories. It should be noted that the solvent used to determine lipid content has been shown to affect the percent lipid values measured in some studies because different solvent systems extract differing fractions of total lipids (Lapin and Chernova, 1969; Randall et al., 1991; and Cabrini et al., 1992). These authors note that percent lipid values can vary by as much as a factor of four depending on the solvent system used. To ensure consistency among States, EPA recommends for lipid analyses that the method of Bligh and Dyer (1959) which uses chloroform/methanol as an extraction solvent or the lower toxicity solvent modification of this the method by Hara and Radin (1978) which uses hexane/isopropanol as an extraction solvent. Other extraction solvents for lipid analyses, e.g., hexane/acetone and dichloromethane, might provide equivalent results when used with appropriate sample sizes and extraction times (Honeycutt et al., 1995, de Boer, J., 1988).

In addition to the effect of the solvent on lipid analysis, additional factors may affect variability of results if they are not adequately controlled (USEPA, 1995a). Use of alcohol as a solvent may overestimate total lipids because non-lipid material may also be extracted. Several factors, including solvent contaminants, lipid decomposition from exposure to oxygen or light, and lipid degradation from changes in pH during cleanup can lead to underestimation of total lipids. Finally, high temperature may decompose lipid material. Laboratories should consider these sources of error when conducting and evaluating results of lipid analyses (USEPA, 1995a).

2.4.4.2 Baseline BAF Derived from Biota-Sediment Accumulation Factors (BSAFs)

When acceptable field-measured values of the BAF are not available for a nonpolar organic chemical, EPA recommends the use of a BSAF to predict the BAF as the second procedure in the BAF data preference hierarchy. Although BSAFs may be used for measuring and predicting bioaccumulation directly from concentrations of chemicals in surface sediment, they also can be useful in estimating a BAF as noted by Cook et al. (1993). Because BSAFs are based on field data and incorporate effects of metabolism, biomagnification, growth, and other factors, BAFs estimated from BSAFs will incorporate the net effect of all these factors. The BSAF approach is particularly beneficial for developing water quality criteria for chemicals such as polychlorinated dibenzo-p-dioxins, dibenzofurans, and certain biphenyl congeners. These chemicals are detectable in fish tissues and sediments but are difficult to measure in the water column and are subject to metabolism.

Predicting BAFs from BSAFs requires several steps. First, BSAFs must be measured for the chemical of interest and for one or more reference chemicals for which measured BAFs are also available. Second, the relationship between the BSAFs for the chemical of interest and the reference chemical and the relationship between the chemicals' K_{ow} values must be determined. Finally, information on the BSAF and K_{ow} relationships and the BAF of the reference chemical(s) should be used to determine the BAF for the chemical of interest. The following sections describe the methodology for determining BAFs from BSAFs, the data requirements, and the application and validation of this procedure for estimating BAFs using data from Lake Ontario.

Determination of BSAF Values

As shown in the following equation, the BSAF is determined by relating lipid-normalized concentrations of chemicals in an organism to organic carbon-normalized concentrations of the chemicals in surface sediment samples associated with the average exposure environment of the organism.

$$BSAF = \frac{C}{C_{soc}}$$

(Equation 2.4.12)

where:

C = Lipid-normalized concentration of the chemical in tissues of biota (g/g lipid)

C_{soc} = Organic carbon-normalized concentration of the chemical in the surface sediment (g/g sediment organic carbon)

The lipid-normalized concentration of a chemical in an organism (C) is determined by:

$$C = \frac{C_t}{f}$$

(Equation 2.4.13)

where:

C_t = Concentration of the chemical in the wet tissue (either whole organism or specified tissue) (g/g)

f = Fraction lipid content in the organism

The organic carbon-normalized concentration of a chemical in sediment (C_{soc}) is determined by:

$$C_{soc} = \frac{C_{sed}}{f_{oc}}$$

(Equation 2.4.14)

where:

C_{sed} = Concentration of chemical in sediment (g/g sediment)

f_{oc} = Fraction organic carbon in sediment

BSAFs are most useful when measured under steady state or near steady-state conditions in which chemical concentrations in water are linked to slowly changing concentrations in sediment. However, because BSAFs are rarely measured for ecosystems which are at equilibrium, the BSAF inherently includes a measure of the "disequilibrium" of the ecosystem. This disequilibrium can be assessed for chemicals with log $K_{ow} > 3$ with the following relationship:

$$BSAF \approx \frac{C_b^{fd} \bullet K}{C_s^{fd} \bullet K_{soc}} = D_{bs} \bullet \frac{K}{K_{soc}} \approx D_{bs} \bullet 2$$

(Equation 2.4.15)

where:

C_b^{fd} = Concentration of freely dissolved chemical (associated with water) in the tissues of biota (g/g wet tissue)

C_s^{fd} = Concentration of freely dissolved chemical (associated with pore water) in the sediment (g/g sediment organic carbon)

K = Lipid-water equilibrium partition coefficient (C / C_b^{fd})

K_{soc} = Sediment organic carbon-water equilibrium partition coefficient (C_{soc}/C_s^{fd})

D_{bs} = Disequilibrium (fugacity) ratio between biota and sediment (C_b^{fd}/C_s^{fd})

Measured BSAFs may range widely for different chemicals depending on K , K_{soc}, and the actual ratio of C_b^{fd} to C_s^{fd}. However, at equilibrium, the ratio between the freely dissolved chemical in the tissue water to sediment pore water (D_{bs}) is one. Thus, the BSAF under equilibrium conditions is equal to the ratio K / K_{soc} (which is thought to range from 1-4)[23]. When chemical equilibrium between sediment and biota does not exist, the BSAF will equal the disequilibrium (fugacity) ratio between biota and sediment ($D_{bs} = C_b^{fd}/C_s^{fd}$) times the ratio of the equilibrium partition coefficients (approximately 2).

[23]Because K and K_{soc} are of similar magnitude and vary in proportion to one another, the BSAF at equilibrium is expected to be at or near unity.

The deviation of D_{bs} from the equilibrium value of 1.0 is determined by the net effect of all factors which contribute to the disequilibrium between sediment and aquatic organisms. A disequilibrium ratio (D_{bs}) greater than one can occur due to biomagnification or when surface sediment has not reached steady-state with water. A disequilibrium ratio (D_{bs}) less than one can occur as a result of kinetic limitations for chemical transfer from sediment to water, water to food chain, and biological processes (such as growth or biotransformation of the chemical in the animal and its food chain). BSAFs are most useful when measured under steady-state conditions. BSAFs measured for systems with new chemical loadings or rapid increases in loadings may be unreliable due to underestimation of steady-state C_{soc}s.

Relationship of BAFs to BSAFs

Differences between BSAFs for different organic chemicals are good measures of the relative bioaccumulation potentials of the chemicals. When calculated from a common organism-sediment sample set, chemical-specific differences in BSAFs primarily reflect the net effect of biomagnification, metabolism, bioenergetics, and bioavailability factors on each chemical's disequilibrium ratio between biota and sediment. Thus, the relationship between the BSAF for the test chemical *i* and the BSAF for the reference chemical *r* can be used with additional information (K_{ow} values for all chemicals and the BAF for the reference chemicals) to predict a BAF for chemical *i*. This approach is consistent with previously proposed guidance, in which ratios of BSAFs for PCDDs and PCDFs to TCDD were proposed for evaluation of TCDD toxic equivalency associated with complex mixtures of the dioxin and furan congeners (see 60 FR 15366 for discussion of bioequivalency factors).

The calculation of the BAF from the BSAF is as follows:

$$(\text{Baseline BAF}^{fd})_i = (\text{Baseline BAF}^{fd})_r \cdot \frac{(BSAF)_i \cdot (K_{ow})_i}{(BSAF)_r \cdot (K_{ow})_r}$$

(Equation 2.4.16)

where:

$(\text{Baseline BAF}^{fd})i$	=	BAF expressed on a freely-dissolved and lipid-normalized basis for chemical of interest “i”
$(\text{Baseline BAF}^{fd})r$	=	BAF expressed on a freely-dissolved and lipid-normalized basis for reference chemical “r”
$(BSAF)_i$	=	BSAF for chemical “i”
$(BSAF)_r$	=	BSAF for the reference chemical “r”
$(K_{ow})_i$	=	octanol-water partition coefficient for chemical “i”

$(K_{ow})_r$ = octanol-water partition coefficient for the reference chemical "r"

Appendix E presents the derivation of this equation using the general BAF equation relating concentration in tissue to concentration in water, a relationship between concentrations in sediment organic carbon and water, and assumptions about equilibrium between water and sediment.

Note that BAF^{fd}s calculated from BSAFs will incorporate any errors associated with measurement of the BAF^{fd} for the reference chemical and the K_{ow}s for both the reference and unknown chemicals. Such errors can be minimized by comparing results from several reference chemicals and assuring consistent use of freely dissolved water concentration (C_w^{fd}) values which are adjusted for dissolved organic carbon binding effects on the fraction of each chemical that is freely dissolved (f_{fd}) in unfiltered, filtered, or centrifuged water samples. Other errors may be introduced by using values based on non-steady state external loading rates or chemicals with strongly reduced C_w^{fd} due to rapid volatilization from water. When selecting K_{ow} values for use in estimating BAFs from BSAFs, consideration should be given to the similarity of K_{ow} measurement techniques between the reference and target chemicals, in addition to the guidance previously described for selecting representative K_{ow} values.

The trophic level to which the baseline BAF applies is the same as the trophic level of the organisms used in the determination of the BSAF. For each trophic level, a species mean baseline BAF is calculated as the geometric mean if more than one acceptable baseline BAF is predicted from BSAFs for a given species. For each trophic level, a trophic level-specific BAF is calculated as the geometric mean of the acceptable species mean baseline BAFs derived using BSAFs.

Procedural and Quality Assurance Requirements

EPA recommends certain requirements for measuring the data needed for this procedure. These requirements, described below, apply to BAF values for the reference chemicals, the measured BSAFs for all chemicals, and the K_{ow} values used in this procedure.

The data requirements for measuring BAF values that were noted in Section 2.4.4.1 (*Field-Measured BAFs*) are also applicable to the measurement of BAF^{fd} values to assure reliable values for the reference chemicals. Data on several reference chemicals should be obtained for use in the analysis to ensure that predictions are more robust than those that would be obtained using only one reference chemical. The water sample analyses should approximate the average exposure of the organism and its food chain over a time period that is most appropriate for the chemical, organism, and ecosystem. It is preferable to choose at least some reference chemicals that have similar log K_{ow}s and chemical class characteristics as the test chemicals for which the BAF is to be determined. In addition, for consistency among reference chemicals, each freely dissolved water concentration used to calculate a BAF^{fd} should be based on a consistent adjustment of the concentration of total chemical in water for DOC and POC using the relationship described in the section titled "Freely Dissolved Fraction of Chemical in Water."

For measured BSAFs, chemical concentrations in surface sediment and in biota and data on the percent organic carbon in surface sediment samples are needed. The following procedural and quality assurance requirements should be met for determining the field-measured BSAFs:

- The field studies used should be limited to those conducted with fish at or near the top of the aquatic food chain (i.e., in trophic levels 3 and/or 4). In situations where consumption of lower trophic level organisms represents an important exposure route, such as certain types of shellfish at trophic level 2, the field study should also include appropriate target species at this trophic level.

- Samples of surface sediments (0-1 cm is ideal) should be from locations in which sediment is regularly deposited and is representative of average surface sediment in the vicinity of the organism.

- The K_{ow}s used should be of acceptable quality as described in Section 2.4.4.1 above.

- The site of the field study should not be so unique that the resulting BAF cannot be extrapolated to other locations where the criteria and values will be applied.

- The percent lipid should be either measured or reliably estimated for the tissue used in the determination of the BAF.

Application of BSAF Procedure for Predicting Lake Ontario and Green Bay BAF_{ℓ}^{fd}s

To demonstrate the use of the BSAF procedure to predict BAFs, EPA has calculated BAF^{fd}s from BSAFs using two independent data sets from Lake Ontario and one from Green Bay. These data sets come from Oliver and Niimi (1988), the EPA Lake Ontario TCDD Bioaccumulation Study (USEPA, 1990), and the EPA Green Bay/Fox River Mass Balance Study.

The first data set (Oliver and Niimi, 1988) has been used extensively for construction of food chain models of bioaccumulation and calculation of food chain multipliers, biomagnification factors and BAF^{fd}s from chemical concentrations determined in organisms and water. Oliver and Niimi (1988) also collected surface sediment data which allows calculation of lakewide average BSAFs. These data were collected from 1981 to 1984 for PCB congeners and other chlorinated organics.

The second data set (from the TCDD Bioaccumulation Study) includes extensive samples of fish and sediment collected in 1987 from Lake Ontario. Samples from this study were later analyzed for PCDD, PCDF, PCB congeners, and some organochlorine pesticides at EPA. Although data from the TCDD Bioaccumulation Study have not been published, they are useful to show a comparison with BAF^{fd}s calculated from Oliver and Niimi samples and to provide BAF^{fd}s for additional organic chemicals not measured by Oliver and Niimi (1988).

Four reference chemicals (the PCB congeners 52, 105 and 118 and DDT) were used for evaluating chemicals from both Oliver and Niimi (1988) and the TCDD Bioaccumulation Study in order to examine the variability introduced by the choice of reference chemical.

The third study, the Green Bay/Fox River Mass Balance Study, involved extensive sampling of water, sediment, and fish in Green Bay in 1989. Brown trout BAF^{fd}s were calculated from PCB BSAFs measured in the mid-bay region using PCB congeners 52 and 118 as reference chemicals. The reference chemical BAF^{fd}s were determined using water and brown trout data from the same region.

Tables 2.4.1a and 2.4.1b present the predicted BAF^{fd}s from all three data sets as well as measured BAF^{fd}s from Oliver and Niimi (1988) and the TCDD Bioaccumulation Study. The geometric means of the BAF^{fd} predicted using the Lake Ontario data (Oliver and Niimi, 1988; TCDD Bioaccumulation Study) are reported in Table 2.4.2.

There are several assumptions and additional data used for these evaluations. First, the water analyses of Oliver and Niimi (1988) were adjusted for an estimated 2 mg/L residual dissolved organic carbon concentration in the centrifuged water (assuming no residual particulate organic carbon after centrifuging) and an estimated $K_{doc} = K_{ow}/10$ in order to calculate a freely dissolved water concentration from f_{fd} (see Section 2.4.4.1 on total vs. freely dissolved concentrations and Appendix D for calculation of water concentrations). Concentrations of freely dissolved PCBs from Green Bay were also calculated on the basis of dissolved organic carbon in the water samples and an assumed $K_{doc} = K_{ow}/10$. Log K_{ow} values were taken from a variety of sources. Log K_{ow}s for PCBs are those reported by Hawker and Connell (1988). Log K_{ow}s for PCDDs and PCDFs are those estimated by Burkhard and Kuehl (1986) except for the penta-, hexa-, and hepta-chlorinated dibenzofurans which were estimated on the basis of assumed similarity to the trends reported for the PCDDs by Burkhard and Kuehl (1986).

Evaluation of BAF_{ℓ}^{fd}s Calculated from Lake Ontario and Green Bay BSAFs

The validity of the BSAF method for predicting BAFs is evaluated in this section using several approaches: (1) correlating measured vs. predicted log BAF^{fd}s from the same lake and same study (i.e., Lake Ontario, Oliver and Niimi, 1988), (2) correlating measured vs. predicted log BAF^{fd}s from the same lake (Ontario) but separate studies (Oliver and Niimi, 1988, U.S. EPA, 1990), (3) comparisons of predicted BAF^{fd}s with K_{ow} values, and (4) comparisons of predicted and measured BAF^{fd}s from different lakes (i.e., Lake Ontario and Green Bay, Lake Michigan). These comparisons were based on data presented in Tables 2.4.1a and 2.4.1b.

Exhibit 2.4.1 illustrates that measured log BAF^{fd}s calculated using water data from Oliver and Niimi (1988) generally agree with log BAF^{fd}s predicted from BSAFs determined using sediment data from the same study. The correlation coefficient (r) for the correlation of BAFs using data from Tables 2.4.1a and 2.4.1b is 0.92 and indicates that the data are well correlated. One deviation of predicted BAFs from measured BAFs should be noted, however. For chlorinated benzenes and

toluenes, BAF^{fd}s predicted from BSAFs are underestimated compared with measured BAF^{fd}s. This underestimation may be due to altered water-sediment fugacity gradient in response to rapid volatilization from water. The better agreement between measured and predicted BAF^{fd}s for PCBs, on the other hand, is facilitated by the lower volatilization of PCBs from water. In addition to the correlation shown in Exhibit 2.4.1, the ratios between the BAFs (which indicates the magnitude of difference between the values) were plotted as a frequency distribution, as shown in Exhibit 2.4.2. The magnitude of difference between these two BAFs is within a factor of four in the majority of cases.

Exhibit 2.4.3 demonstrates the predictability of BAFs for the same chemical but based on BSAF from different studies. The predicted log BAF^{fd}s using data from the EPA TCDD Bioaccumulation Study (U.S. EPA, 1990) (collected several years after the Oliver and Niimi samples were collected) correlate equally well with the predicted log BAF^{fd}s calculated from Oliver and Niimi (1988) data. An r value of 0.94 was obtained for the correlation of BAFs using data from Tables 2.4.1a and 2.4.1b. Exhibit 2.4.4 shows that for the majority of chemicals, predicted BAFs from the TCDD Bioaccumulation Study are within a factor of two of predicted BAFs from Oliver and Niimi (1988); measured and predicted BAFs for all chemicals are within a factor of ten of each other.

Exhibit 2.4.5 shows the relationship of log BAF^{fd}s calculated from EPA BSAFs using lake trout data from the TCDD Bioaccumulation Study (Cook et al., 1994) to log K_{ow}s. The bioaccumulative PCDDs and PCDFs (2,3,7,8-chlorinated) have BAF^{fd}s 10- to 1,000-fold less than PCBs with similar K_{ow}s, which is expected due to PCDD and PCDF metabolism in fish. It should be noted, however, that some of the chlordane and nonachlor BAF^{fd}s do not have the expected correlations with K_{ow}. This is shown in Exhibit 2.4.5 by the BAF^{fd}s for five of six chlordanes and nonachlors that are much greater than those for PCBs with the same estimated log K_{ow}. This finding is unexpected because PCBs are not metabolized in fish and would be expected to have higher BAFs than other chemicals with the same K_{ow} values. Therefore, the log K_{ow} values chosen here for the chlordanes and nonachlors may be significantly underestimated.

All of the above correlations were based on the BSAF procedure using the Oliver and Niimi (1988) Lake Ontario salmonid BAF^{fd} for PCB congener 52 as a reference chemical. As noted earlier, the BSAF procedure is strengthened through use of several reference chemicals with both a range of K_{ow}s and ability to be accurately measured in water. Using additional reference chemicals (PCB congeners 105 and 118 and DDT) results in correlations with other measured and predicted BAF^{fd}s from Tables 2.4.1a and 2.4.1b that are very similar to comparisons seen using PCB congener 52 as a reference chemical.

A good test for robustness of the BSAF procedure for predicting BAF^{fd}s is comparison of two independent data sets based on different ecosystems and conditions. Such a comparison can be made for bioaccumulation of PCBs in Lake Ontario fish and Green Bay fish. Although both ecosystems are specific to the Great Lakes area, Green Bay is a shallower, smaller, and more eutrophic body of water than Lake Ontario. The correlation between the PCB log BAF^{fd}s for brown trout predicted from BSAFs using Green Bay data and measured log BAF^{fd}s based on Oliver and Niimi (1988) data

is shown in Exhibit 2.4.6. An r value of 0.91 was obtained for the correlation of these log BAFs (using data from Tables 2.4.1a and 2.4.1b), showing that the values are well correlated. Exhibit 2.4.7 shows that, most frequently, the BAFs differ from each other by less than a factor of two, and all chemical BAFs are within a factor of ten of each other. The correlation between predicted log BAF^{fd}s from Green Bay (for brown trout) and predicted lake trout log BAFs using Oliver and Niimi (1988) salmonid and water measurements and lake trout BSAFs from the EPA TCDD Bioaccumulation Study is shown in Exhibit 2.4.8. The r value for the relationship between these log BAFs using data from Tables 2.4.1a and 2.4.1b is 0.90. As shown in Exhibit 2.4.9, the most frequent difference in these BAFs is less than or equal to a factor of two. However, for PCB congener 198, the difference between BAFs is 85, as indicated by the value farthest to the right in the exhibit.

Despite the complex exposures of Green Bay fish (which result from movement and interaction of biota through gradients of decreasing PCBs, nutrients and suspended organic carbon extending from the Fox River to the outer bay and Lake Michigan), good agreement exists between Green Bay brown trout predicted log BAFs and both field-measured log BAF^{fd}s and predicted log BAF^{fd}s from BSAFs from Lake Ontario, using PCB 52 as a reference chemical. Although not shown, good agreement also exists for the predicted BAFs using PCB 118 as the reference chemical. In addition to the above comparisons, correlations of predicted log BAFs with log K_{ow} values from Green Bay show relationships that are similar to the log BAF -log K_{ow} relationship for predicted BAF^{fd}s from Lake Ontario data.

Based on the above correlations and ratios, the BSAF method appears to work well not only for predicting BAFs using data from the same system (Lake Ontario) but also for predicting BAFs between systems (Green Bay vs. Lake Ontario). These evaluations support the use of the BSAF method for predicting BAFs.

Table 2.4.1a: Great Lakes Trout BAF^{fd}s Calculated from Measured BSAFs/BAFs

		Measured Values			Predicted BAF^{fd}			
Chemical	**Log K_{ow}**	**BSAF Ol. & Niimi (1988)**	**log BAF Ol. & Niimi (1988)**	**BSAF EPA (1990)**	**log BAF Ol. & Niimi ref PCB 52**	**log BAF EPA ref PCB 52**	**log BAF Ol. & Niimi ref PCB 105**	**log BAF EPA ref PCB 105**
dieldrin	5.3			6.65		7.67		6.95
ddt	6.45	1.09	7.78	1.67	7.87	8.22	7.54	7.5
dde	6.76	4.14	8.35	7.7	8.76	9.19	8.43	8.47
ddd	6.06	0.28	7.00		6.90		6.56	
mirex	6.89	1.43	8.13	1.31	8.43	8.55	8.09	7.84
photomirex	6.89	5.48	8.07		9.01		8.68	
g-chlordane	6.0	2.22	6.79		7.73		7.40	
t-chlordane	6.0			2.00		7.85		7.13
c-chlordane	6.0			4.77		8.23		7.51
t-nonachlor	6.0			10.5		8.57		7.85
c-nonachlor	6.0			0.51		7.25		6.54
alpha-hch	3.78	2.45	4.69		5.55		5.22	
gamma-hch	3.67	0.69	4.93		4.89		4.56	
hcbd	4.84							
ocs	6.29	0.98	8.07		7.67		7.33	
hcb	5.6	0.09	6.40		5.95		5.62	
pcb	5.11	0.04	5.81		5.07		4.73	
1235tcb	4.56							
1245tcb	4.56							
1234tcb	4.59	0.01	5.07		4.11		3.78	
135tcb	4.17							
124tcb	3.99							
123tcb	4.1							
245tct	4.93							
236tct	4.93							
pct	6.36							
Total-PCB	6.14	1.85	7.81		7.79		7.46	
PCB 5	4.97							
PCB 6	5.06			0.36		6.16		5.44
PCB 8	5.07							

Table 2.4.1a: Great Lakes Trout BAF^{fd}s Calculated from Measured BSAFs/BAFs								
		Measured Values			Predicted BAF^{fd}			
Chemical	**Log K_{ow}**	**BSAF Ol. & Niimi (1988)**	**log BAF Ol. & Niimi (1988)**	**BSAF EPA (1990)**	**log BAF Ol. & Niimi ref PCB 52**	**log BAF EPA ref PCB 52**	**log BAF Ol. & Niimi ref PCB 105**	**log BAF EPA ref PCB 105**
PCB 12	5.22			0.44		6.41		5.69
PCB 13	5.29							
PCB 16	5.16		5.92					
PCB 17	5.25	0.15	5.52	0.99	5.80	6.79	5.47	6.07
PCB 18	5.24	0.26	5.75	0.1	6.05	5.79	5.71	5.07
PCB 22	5.58	0.21	6.39	0.27	6.28	6.56	5.95	5.84
PCB 25	5.67	0.25		0.33	6.44	6.74	6.11	6.02
PCB 26	5.66	1.72		0.44	7.28	6.85	6.94	6.13
PCB 32	5.44	0.18	6.76		6.09		5.75	
PCB 33	5.60	0.15	5.32	0.49	6.15	6.84	5.82	6.12
PCB 40	5.66	0.10	6.55	0.18	6.06	6.46	5.72	5.74
PCB 42	5.76	0.52	7.49		6.86		6.53	
PCB 44	5.75	0.48	6.96	0.4	6.82	6.90	6.48	6.18
PCB 45	5.53			0.22		6.42		5.70
PCB 46	5.53	0.57		0.02	6.67	5.38	6.34	4.66
PCB 49	5.85	0.69	7.13		7.07		6.74	
PCB 52	5.84	0.61	7.01	0.42	7.01	7.01	6.67	6.29
PCB 53	5.62	1.84	6.51		7.27		6.93	
PCB 63	6.17			0.82		7.63		6.91
PCB 64	5.95	0.73	7.51		7.20		6.86	
PCB 66	6.20	0.85	7.79		7.52		7.18	
PCB 74	6.20	3.45	7.66	0.61	8.12	7.53	7.79	6.81
PCB 77	6.36			0.29		7.37		6.65
PCB 81	6.36			0.67		7.73		7.01
PCB 82	6.20	2.45	8.13	0.18	7.97	7.00	7.64	6.28
PCB 83	6.26			1.33		7.93		7.21
PCB 84	6.04	3.04	8.28		7.91		7.57	
PCB 85	6.30	1.45	7.89	1.29	7.85	7.96	7.51	7.24
PCB 87	6.29			1.37		7.97		7.25
PCB 91	6.13	1.25	6.92	0.64	7.61	7.48	7.28	6.76
PCB 92	6.35	1.43	8.11		7.89		7.55	

Table 2.4.1a: Great Lakes Trout BAF^{fd}s Calculated from Measured BSAFs/BAFs								
		Measured Values			Predicted BAF^{fd}			
Chemical	**Log K_{ow}**	**BSAF Ol. & Niimi (1988)**	**log BAF Ol. & Niimi (1988)**	**BSAF EPA (1990)**	**log BAF Ol. & Niimi ref PCB 52**	**log BAF EPA ref PCB 52**	**log BAF Ol. & Niimi ref PCB 105**	**log BAF EPA ref PCB 105**
PCB 95	6.13	1.40	7.25		7.66		7.33	
PCB 97	6.29			0.28		7.28		6.56
PCB 99	6.39	0.68	7.39	1.51	7.61	8.12	7.27	7.40
PCB 100	6.23			1.78		8.03		7.31
PCB 101	6.38	2.45	7.45	1.06	8.15	7.95	7.82	7.23
PCB 105	6.65	2.70	8.13	4.49	8.47	8.85	8.13	8.13
PCB 110	6.48	1.53	7.79	0.82	8.05	7.94	7.71	7.22
PCB 118	6.74	4.09	8.15	1.72	8.74	8.52	8.40	7.80
PCB 119	6.58			3.83		8.71		7.99
PCB 126	6.89			3.21		8.94		8.22
PCB 128	6.74	3.61		2.78	8.68	8.73	8.35	8.01
PCB 129	6.73	1.75		1.13	8.36	8.33	8.02	7.61
PCB 130	6.8			2.15		8.68		7.96
PCB 132	6.58	0.87	7.56		7.90		7.57	
PCB 136	6.22	10.87	7.37		8.64		8.30	
PCB 138	6.83	4.25	8.30		8.84		8.51	
PCB 141	6.82	2.75	8.32	1.74	8.64	8.61	8.31	7.89
PCB 146	6.89	3.22	8.73	1.25	8.78	8.53	8.45	7.81
PCB 149	6.67	2.33	7.99	0.93	8.42	8.19	8.09	7.47
PCB 151	6.64	3.38	8.51	1.65	8.55	8.40	8.22	7.69
PCB 153	6.92	4.22	8.32	1.91	8.93	8.75	8.59	8.03
PCB 156	7.18	3.97			9.16		8.83	
PCB 158	7.02			1.52		8.75		8.03
PCB 167	7.27			0.69		8.66		7.94
PCB 171	7.11	2.71			8.93		8.59	
PCB 172	7.33			1.36		9.01		8.29
PCB 174	7.11	1.54	8.74	1.25	8.68	8.75	8.35	8.03
PCB 177	7.08	3.53	9.01	1.91	9.01	8.91	8.68	8.19
PCB 178	7.14	4.48		2.76	9.18	9.13	8.84	8.41
PCB 180	7.36	3.78	8.58	3.26	9.32	9.42	8.99	8.70
PCB 183	7.20	5.62	9.03	2.68	9.33	9.17	9.00	8.46

Table 2.4.1a: Great Lakes Trout BAF^{fd}s Calculated from Measured BSAFs/BAFs								
		Measured Values			Predicted BAF^{fd}			
Chemical	**Log K_{ow}**	**BSAF Ol. & Niimi (1988)**	**log BAF Ol. & Niimi (1988)**	**BSAF EPA (1990)**	**log BAF Ol. & Niimi ref PCB 52**	**log BAF EPA ref PCB 52**	**log BAF Ol. & Niimi ref PCB 105**	**log BAF EPA ref PCB 105**
PCB 185	7.11	1.55		2.24	8.68	9.01	8.35	8.29
PCB 189	7.71			0.71		9.11		8.39
PCB 194	7.80	1.53	8.56	2.47	9.37	9.74	9.03	9.02
PCB 195	7.56	1.90			9.22		8.89	
PCB 197	7.3			1.1		8.89		8.17
PCB 198	7.62			6.55		9.98		9.26
PCB 201	7.62	1.53		1.13	9.19	9.22	8.85	8.50
PCB 205	8.00	0.34		0.48	8.91	9.23	8.58	8.51
PCB 206	8.09	0.47		0.34	9.15	9.17	8.81	8.45
PCB 207	7.74	0.66		0.89	8.95	9.24	8.61	8.52
PCB 209	8.18	0.14		0.03	8.70	8.20	8.36	7.48
PCB 24+27	5.40	0.25		0.12	6.17	6.02	5.83	5.30
PCB 28+31	5.67	0.52	6.89	0.19	6.77	6.50	6.43	5.78
PCB 37+42	5.8			0.62		7.14		6.42
PCB 47+48	5.82	1.23	7.18	0.65	7.29	7.17	6.95	6.46
PCB 41+64+71	5.87			0.46		7.08		6.36
PCB 56+60	6.11			0.31		7.15		6.43
PCB 70+76	6.17	1.49	7.56	0.61	7.72	7.50	7.39	6.78
PCB 66+95	6.17			0.53		7.44		6.72
PCB 56+60+81	6.19	0.55	7.96		7.32		6.98	
PCB 84+92	6.2			1.22		7.83		7.11
PCB 87+97	6.29	2.45	8.08		8.06		7.73	
PCB 137+176	6.8			1.16		8.41		7.69
PCB 138+163	6.91			2.23		8.81		8.09
PCB 156+171+202	7.18			1.25		8.82		8.10
PCB 182+187	7.19	3.80	8.43		9.15		8.81	
PCB 157+200	7.23			1.56		8.97		8.25
PCB 170+190	7.37	2.06	9.20	4.17	9.06	9.53	8.73	8.81
PCB 195+208	7.64			0.72		9.04		8.33
PCB 196+203	7.65	1.56	9.26	1.12	9.23	9.25	8.89	8.53
2378-TCDD	7.02			0.059		7.34		6.62

Table 2.4.1a: Great Lakes Trout BAF^{fd}s Calculated from Measured BSAFs/BAFs

		Measured Values			Predicted BAF^{fd}			
Chemical	**Log K_{ow}**	**BSAF Ol. & Niimi (1988)**	**log BAF Ol. & Niimi (1988)**	**BSAF EPA (1990)**	**log BAF Ol. & Niimi ref PCB 52**	**log BAF EPA ref PCB 52**	**log BAF Ol. & Niimi ref PCB 105**	**log BAF EPA ref PCB 105**
12378-PeCDD	7.5			0.054		7.78		7.06
123478-HxCDD	7.8			0.018		7.60		6.88
123678-HxCDD	7.8			0.0073		7.21		6.49
123789-HxCDD	7.8			0.0081		7.26		6.54
1234678-HpCDD	8.2			0.0031		7.24		6.52
OCDD	8.6			0.00074		7.02		6.30
2378-TCDF	6.5			0.047		6.72		6.00
12378-PeCDF	7.0			0.013		6.66		5.94
23478-PeCDF	7.0			0.095		7.52		6.81
123478-HxCDF	7.5			0.0045		6.70		5.98
123678-HxCDF	7.5			0.011		7.09		6.37
123789-HxCDF	7.5			0.037		7.61		6.90
234678-HxCDF	7.5			0.04		7.65		6.93
1234678-HpCDD	8.0			0.00065		6.36		5.64
1234789-HpCDD	8.0			0.023		7.91		7.19
OCDF	8.8			0.00099		7.34		6.62

a. Oliver and Niimi (1988). BAF^{fd} calculated from measured BAFs using freely dissolved equation 2.4.11, DOC=2.0 mg/L, POC=0.0 mg/L, $K_{doc}=K_{ow}/10$, $K_{poc}=K_{ow}$. Predicted BAFs based on equation 2.4.16.
b. U.S. EPA 1990. (TCDD Bioaccumulation Study). Predicted BAFs based on equation 2.4.16.
c. Green Bay/Fox River Mass Balance Study (As described in Great Lakes Water Quality Initiative Technical Support Document for the Procedure to Determine Bioaccumulation Factors. EPA-820-B-95-005. March 1995.)

Table 2.4.1b: Great Lakes Trout BAF[d]s Calculated from Measured BSAFs/BAFs								
		Predicted Values						
Chemical	**Log K_{ow}**	**log BAF Ol. & Niimi[a] ref DDT**	**log BAF EPA[b] ref DDT**	**log BAF Ol. & Niimi[a] ref PCB 118**	**log BAF EPA[b] ref PCB 118**	**BT-BSAF EPA-G Bay[c]**	**log BAF EPA-G Bay[c] ref PCB 52**	**log BAF EPA-G Bay[c] ref PCB 118**
dieldrin	5.3		7.23		7.30			
ddt	6.45	7.78	7.78	7.29	7.85			
dde	6.76	8.67	8.75	8.18	8.82			
ddd	6.06	6.80		6.31				
mirex	6.89	8.33	8.11	7.84	8.18			
photomirex	6.89	8.92		8.43				
g-chlordane	6	7.64		7.14				
t-chlordane	6		7.41		7.48			
c-chlordane	6		7.78		7.85			
t-nonachlor	6		8.13		8.20			
c-nonachlor	6		6.81		6.88			
alpha-hch	3.78	5.46		4.97				
gamma-hch	3.67	4.80		4.31				
hcbd	4.84							
ocs	6.29	7.57		7.08				
hcb	5.6	5.86		5.37				
pcb	5.11	4.97		4.48				
1235tcb	4.56							
1245tcb	4.56							
1234tcb	4.59	4.02		3.53				
135tcb	4.17							
124tcb	3.99							
123tcb	4.1							
245tct	4.93							
236tct	4.93							
pct	6.36							
Total-PCB	6.14	7.70		7.21				
PCB 5	4.97					0.14	4.88	5.12
PCB 6	5.06		5.72		5.79	1.7	6.05	6.29
PCB 8	5.07					0.14	4.98	5.22

Table 2.4.1b: Great Lakes Trout BAF[d]s Calculated from Measured BSAFs/BAFs								
		Predicted Values						
Chemical	**Log K_{ow}**	**log BAF Ol. & Niimi[a] ref DDT**	**log BAF EPA[b] ref DDT**	**log BAF Ol. & Niimi[a] ref PCB 118**	**log BAF EPA[b] ref PCB 118**	**BT-BSAF EPA-G Bay[c]**	**log BAF EPA-G Bay[c] ref PCB 52**	**log BAF EPA-G Bay[c] ref PCB 118**
PCB 12	5.22		5.97		6.04			
PCB 13	5.29							
PCB 16	5.16							
PCB 17	5.25	5.71	6.35	5.22	6.42	0.75	5.89	6.13
PCB 18	5.24	5.95	5.34	5.46	5.41	0.64	5.81	6.05
PCB 22	5.58	6.19	6.12	5.70	6.19	0.39	5.94	6.18
PCB 25	5.67	6.35	6.29	5.86	6.36	0.73	6.30	6.54
PCB 26	5.66	7.18	6.41	6.69	6.48	0.95	6.40	6.64
PCB 32	5.44	5.99		5.50				
PCB 33	5.60	6.06	6.39	5.57	6.46	0.29	5.83	6.07
PCB 40	5.66	5.96	6.02	5.47	6.09	0.69	6.26	6.50
PCB 42	5.76	6.77		6.28				
PCB 44	5.75	6.72	6.46	6.23	6.53			
PCB 45	5.53		5.98		6.05	1.16	6.36	6.60
PCB 46	5.53	6.58	4.94	6.09	5.01	0.61	6.08	6.32
PCB 49	5.85	6.98		6.49		3.34	7.14	7.38
PCB 52	5.84	6.91	6.57	6.42	6.64	4.74	7.28	7.52
PCB 53	5.62	7.17		6.68		2.12	6.71	6.95
PCB 63	6.17		7.19		7.26	4.37	7.57	7.81
PCB 64	5.95	7.10		6.61				
PCB 66	6.20	7.42		6.93		3.1	7.46	7.70
PCB 74	6.20	8.03	7.09	7.54	7.16	2.46	7.36	7.60
PCB 77	6.36		6.93		7.00	4.12	7.74	7.98
PCB 81	6.36		7.29		7.36	11.6	8.19	8.43
PCB 82	6.20	7.88	6.56	7.39	6.63	4.05	7.57	7.81
PCB 83	6.26		7.49		7.56	5.67	7.78	8.02
PCB 84	6.04	7.81		7.32		7.2	7.66	7.90
PCB 85	6.30	7.75	7.51	7.26	7.59	7.25	7.92	8.16
PCB 87	6.29		7.53		7.60	6.13	7.84	8.08
PCB 91	6.13	7.52	7.04	7.02	7.11	8.44	7.82	8.06
PCB 92	6.35	7.79		7.30				

Table 2.4.1b: Great Lakes Trout BAF[d]s Calculated from Measured BSAFs/BAFs								
		Predicted Values						
Chemical	**Log K_{ow}**	**log BAF Ol. & Niimi[a] ref DDT**	**log BAF EPA[b] ref DDT**	**log BAF Ol. & Niimi[a] ref PCB 118**	**log BAF EPA[b] ref PCB 118**	**BT-BSAF EPA-G Bay[c]**	**log BAF EPA-G Bay[c] ref PCB 52**	**log BAF EPA-G Bay[c] ref PCB 118**
PCB 95	6.13	7.57		7.08				
PCB 97	6.29		6.84		6.91	6.42	7.86	8.10
PCB 99	6.39	7.51	7.67	7.02	7.74	7.18	8.01	8.25
PCB 100	6.23		7.58		7.65	1.71	7.23	7.47
PCB 101	6.38	8.06	7.51	7.57	7.58	10.01	8.14	8.38
PCB 105	6.65	8.37	8.41	7.88	8.48	5.35	8.14	8.38
PCB 110	6.48	7.95	7.50	7.46	7.57	4.15	7.86	8.10
PCB 118	6.74	8.64	8.08	8.15	8.15	4.96	8.20	8.44
PCB 119	6.58		8.27		8.34	3.03	7.83	8.07
PCB 126	6.89		8.50		8.57			
PCB 128	6.74	8.59	8.29	8.10	8.36	10.21	8.51	8.75
PCB 129	6.73	8.26	7.89	7.77	7.96			
PCB 130	6.8		8.24		8.31	11.21	8.61	8.85
PCB 132	6.58	7.81		7.32				
PCB 136	6.22	8.55		8.05				
PCB 138	6.83	8.75		8.26				
PCB 141	6.82	8.55	8.16	8.06	8.24	9.30	8.55	8.79
PCB 146	6.89	8.69	8.09	8.20	8.16	10.0	8.66	8.90
PCB 149	6.67	8.33	7.74	7.84	7.81	8.7	8.37	8.61
PCB 151	6.64	8.46	7.96	7.97	8.03	9.7	8.39	8.63
PCB 153	6.92	8.84	8.31	8.34	8.38	5.35	8.41	8.65
PCB 156	7.18	9.07		8.58				
PCB 158	7.02		8.31		8.38			
PCB 167	7.27		8.21		8.28	16.0	9.24	9.48
PCB 171	7.11	8.83		8.34				
PCB 172	7.33		8.57		8.64			
PCB 174	7.11	8.59	8.31	8.10	8.38	4.46	8.52	8.76
PCB 177	7.08	8.92	8.47	8.43	8.54	8.04	8.75	8.99
PCB 178	7.14	9.08	8.69	8.59	8.76			
PCB 180	7.36	9.23	8.98	8.74	9.05	10.96	9.16	9.40
PCB 183	7.20	9.24	8.73	8.75	8.80	6.5	8.78	9.02

Table 2.4.1b: Great Lakes Trout BAF[d]s Calculated from Measured BSAFs/BAFs								
		Predicted Values						
Chemical	**Log K_{ow}**	**log BAF Ol. & Niimi[a] ref DDT**	**log BAF EPA[b] ref DDT**	**log BAF Ol. & Niimi[a] ref PCB 118**	**log BAF EPA[b] ref PCB 118**	**BT-BSAF EPA-G Bay[c]**	**log BAF EPA-G Bay[c] ref PCB 52**	**log BAF EPA-G Bay[c] ref PCB 118**
PCB 185	7.11	8.59	8.56	8.10	8.63	3.23	8.38	8.62
PCB 189	7.71		8.67		8.74	3.45	9.01	9.25
PCB 194	7.80	9.27	9.30	8.78	9.37	3.29	9.08	9.32
PCB 195	7.56	9.13		8.64				
PCB 197	7.3		8.45		8.52			
PCB 198	7.62		9.54		9.61	0.46	8.05	8.29
PCB 201	7.62	9.10	8.78	8.60	8.85	4.79	9.06	9.30
PCB 205	8.00	8.82	8.79	8.33	8.86	3.09	9.25	9.49
PCB 206	8.09	9.05	8.73	8.56	8.80	0.95	8.83	9.07
PCB 207	7.74	8.85	8.79	8.36	8.86	1.3	8.62	8.86
PCB 209	8.18	8.60	7.76	8.11	7.83	0.19	8.22	8.46
PCB 24+27	5.40	6.07	5.58	5.58	5.65	1.55	6.35	6.59
PCB 28+31	5.67	6.68	6.05	6.18	6.12	0.67	6.26	6.50
PCB 37+42	5.8		6.70		6.77	6.75	7.39	7.63
PCB 47+48	5.82	7.19	6.73	6.70	6.80	7.86	7.47	7.71
PCB 41+64+71	5.87		6.64		6.71	2.55	7.04	7.28
PCB 56+60	6.11		6.71		6.78	1.14	6.93	7.17
PCB 70+76	6.17	7.63	7.05	7.14	7.12	1.2	7.01	7.25
PCB 66+95	6.17		7.00		7.07	3.1	7.43	7.67
PCB 56+60+81	6.19	7.22		6.73		1.15	7.02	7.26
PCB 84+92	6.2		7.39		7.46	7.25	7.82	8.06
PCB 87+97	6.29	7.97		7.48		6.3	7.85	8.09
PCB 137+176	6.8		7.97		8.04	1.43	7.72	7.96
PCB 138+163	6.91		8.36		8.43	11.94	8.75	8.99
PCB 156+171+202	7.18		8.38		8.45	10.70	8.97	9.21
PCB 182+187	7.19	9.05		8.56		9.38	8.92	9.16
PCB 157+200	7.23		8.53		8.60	8.66	8.93	9.17
PCB 170+190	7.37	8.97	9.09	8.48	9.16	4.10	8.74	8.98
PCB 195+208	7.64		8.60		8.67	1.01	8.41	8.65
PCB 196+203	7.65	9.13	8.80	8.64	8.87	4.24	9.04	9.28
2378-TCDD	7.02		6.90		6.97			

Table 2.4.1b: Great Lakes Trout BAF[d]s Calculated from Measured BSAFs/BAFs								
		Predicted Values						
Chemical	**Log K_{ow}**	**log BAF Ol. & Niimi[a] ref DDT**	**log BAF EPA[b] ref DDT**	**log BAF Ol. & Niimi[a] ref PCB 118**	**log BAF EPA[b] ref PCB 118**	**BT-BSAF EPA-G Bay[c]**	**log BAF EPA-G Bay[c] ref PCB 52**	**log BAF EPA-G Bay[c] ref PCB 118**
12378-PeCDD	7.5		7.34		7.41			
123478-HxCDD	7.8		7.16		7.23			
123678-HxCDD	7.8		6.77		6.84			
123789-HxCDD	7.8		6.81		6.88			
123334678-Hp	8.2		6.80		6.87			
OCDD	8.6		6.57		6.64			
2378-TCDF	6.5		6.28		6.35			
12378-PeCDF	7.0		6.22		6.29			
23478-PeCDF	7.0		7.08		7.15			
123478-HxCDF	7.5		6.26		6.33			
123678-HxCDF	7.5		6.65		6.72			
123789-HxCDF	7.5		7.17		7.24			
234678-HxCDF	7.5		7.21		7.28			

Table 2.4.1b: Great Lakes Trout BAF[d]s Calculated from Measured BSAFs/BAFs								
		Predicted Values						
Chemical	**Log K_{ow}**	**log BAF Ol. & Niimi[a] ref DDT**	**log BAF EPA[b] ref DDT**	**log BAF Ol. & Niimi[a] ref PCB 118**	**log BAF EPA[b] ref PCB 118**	**BT-BSAF EPA-G Bay[c]**	**log BAF EPA-G Bay[c] ref PCB 52**	**log BAF EPA-G Bay[c] ref PCB 118**
1234678-HpCD	8.0		5.92		5.99			
1234789-HpCD	8.0		7.47		7.54			
OCDF	8.8		6.90		6.97			

a. Oliver and Niimi (1988). BAF^{fd} calculated from measured BAFs using freely dissolved equation 2.4.11, DOC=2.0 mg/L, POC=0.0 mg/L, $K_{doc}=K_{ow}/10$, $K_{poc}=K_{ow}$. Predicted BAFs based on equation 2.4.16.

b. U.S. EPA 1990. (TCDD Bioaccumulation Study). Predicted BAFs based on equation 2.4.16.

c. Green Bay/Fox River Mass Balance Study (As described in Great Lakes Water Quality Initiative Technical Support Document for the Procedure to Determine Bioaccumulation Factors. EPA-820-B-95-005. March 1995.)

Table 2.4.2: Mean BAF^{fd}s from Lake Ontario BSAFs for Salmonids

Chemical	log K_{ow}	Number BAFs	Mean log BAF^{fd}	Mean BAF^{fd}
dieldrin	5.30	4	7.29	1.93e+07
ddt	6.45	8	7.73	5.33e+07
dde	6.76	8	8.66	4.56e+08
ddd	6.06	4	6.64	4.39e+06
mirex	6.89	8	8.17	1.49e+08
photomirex	6.89	4	8.76	5.74e+08
g-chlordane	6.00	4	7.48	3.00e+07
t-chlordane	6.00	4	7.46	2.91e+07
c-chlordane	6.00	4	7.84	6.95e+07
t-nonachlor	6.00	4	8.18	1.53e+08
c-nonachlor	6.00	4	6.87	7.43e+06
alpha-hch	3.78	4	5.30	2.00e+05
gamma-hch	3.67	4	4.64	4.34e+04
hcbd	4.84			
ocs	6.29	4	7.41	2.58e+07
hcb	5.60	4	5.70	5.01e+05
pcb	5.11	4	4.81	6.47e+04
1235tcb	4.56			
1245tcb	4.50			
1234tcb	4.59	4	3.86	7.25e+03
135tcb	4.17			
124tcb	3.99			
123tcb	4.10			
245tct	4.93			
236tct	4.93			
pct	6.36			
PCBs				
5	4.97			
6	5.06	4	5.78	6.02e+05
8	5.07			
12	5.22	4	6.03	1.06e+06
13	5.29			
16	5.16			
17	5.25	8	5.98	9.52e+05
18	5.24	8	5.60	3.96e+05
22	5.58	8	6.10	1.27e+06
25	5.67	8	6.27	1.87e+06
26	5.66	8	6.75	5.57e+06

Table 2.4.2: Mean BAF^{fd}s from Lake Ontario BSAFs for Salmonids (continued)

Chemical	log K_{ow}	Number BAFs	Mean log BAF^{fd}	Mean BAF^{fd}
PCBs				
32	5.44	4	5.84	6.84e+05
33	5.60	8	6.18	1.50e+06
40	5.66	8	5.94	8.72e+05
42	5.76	4	6.61	4.06e+06
44	5.75	8	6.54	3.46e+06
45	5.53	4	6.04	1.09e+06
46	5.53	8	5.71	5.08e+05
49	5.85	4	6.82	6.61e+06
52	5.84	8	6.69	4.90e+06
53	5.62	4	7.02	1.04e+07
63	6.17	4	7.25	1.77e+07
64	5.95	4	6.94	8.80e+06
66	6.20	4	7.26	1.83e+07
74	6.20	8	7.51	3.23e+07
77	6.36	4	6.99	9.68e+06
81	6.36	4	7.35	2.24e+07
82	6.20	8	7.17	1.48e+07
83	6.26	4	7.55	3.53e+07
84	6.04	4	7.65	4.50e+07
85	6.30	8	7.58	3.83e+07
87	6.29	4	7.59	3.89e+07
91	6.13	8	7.23	1.69e+07
92	6.35	4	7.64	4.32e+07
95	6.13	4	7.41	2.55e+07
97	6.29	4	6.90	7.95e+06
99	6.39	8	7.54	3.49e+07
100	6.23	4	7.64	4.40e+07
101	6.38	8	7.73	5.43e+07
105	6.65	8	8.34	2.18e+08
110	6.48	8	7.68	4.74e+07
118	6.74	8	8.31	2.04e+08
119	6.58	4	8.33	2.12e+08
126	6.89	4	8.56	3.63e+08
128	6.74	8	8.39	2.44e+08
129	6.73	8	8.03	1.06e+07
130	6.80	4	8.30	1.98e+08
132	6.58	4	7.65	4.47e+07

Table 2.4.2: Mean BAF[d]s from Lake Ontario BSAFs for Salmonids (continued)

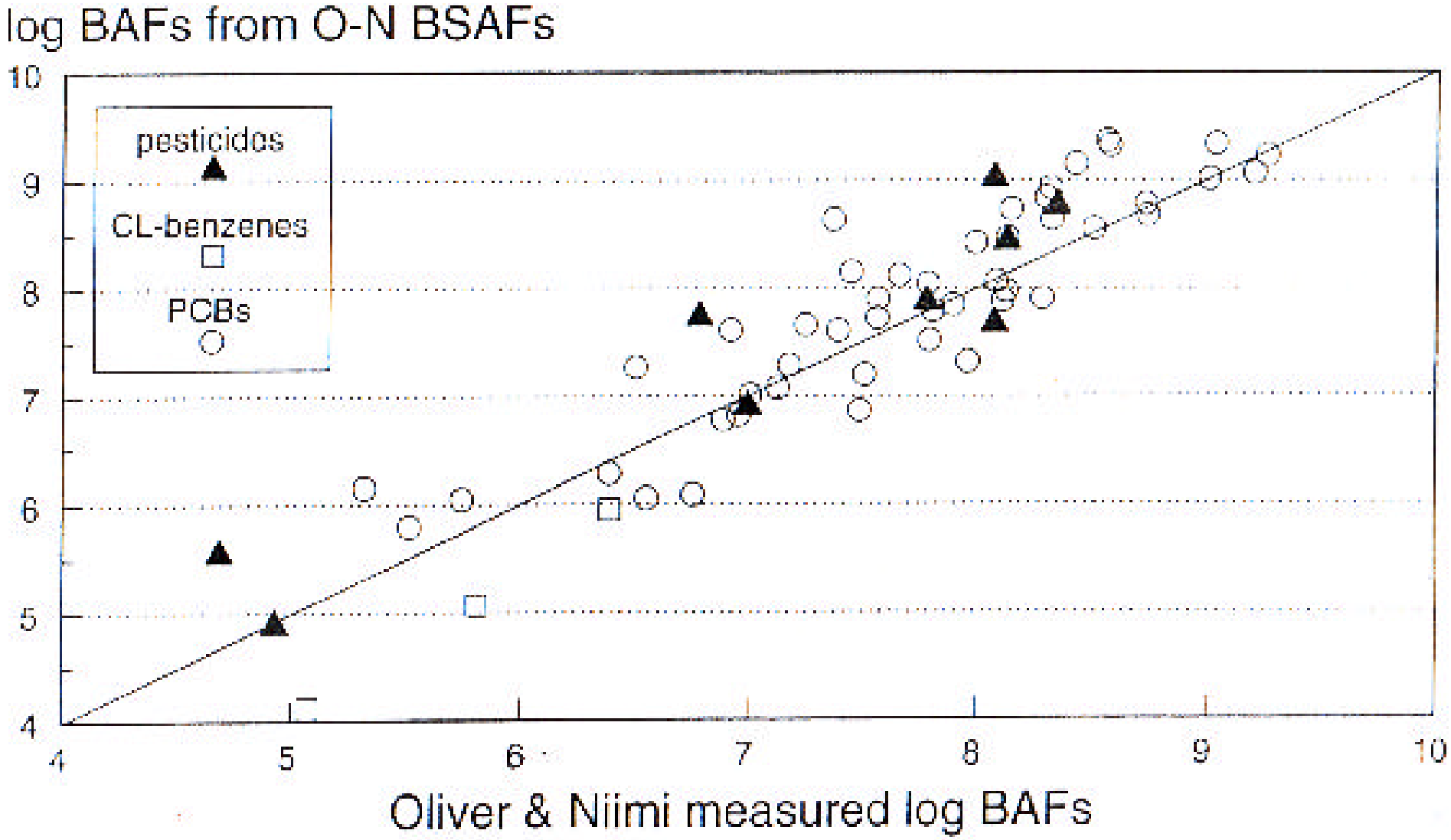
Chemical	log K_{ow}	Number BAFs	Mean log BAF[d]	Mean BAF[d]
PCBs				
136	6.22	4	8.39	2.44e+08
138	6.83	4	8.59	3.88e+08
141	6.82	8	8.31	2.03e+08
146	6.89	8	8.34	2.18e+08
149	6.67	8	7.98	9.66e+07
151	6.64	8	8.16	1.45e+08
153	6.92	8	8.52	3.31e+08
156	7.18	4	8.91	8.12e+08
158	7.02	4	8.37	2.32e+08
167	7.27	4	8.27	1.87e+08
171	7.11	4	8.67	4.72e+08
172	7.33	4	8.63	4.24e+08
174	7.11	8	8.40	2.51e+08
177	7.08	8	8.64	4.38e+08
178	7.14	8	8.83	6.80e+08
180	7.36	8	9.05	1.13e+09
183	7.20	8	8.94	8.63e+08
185	7.11	8	8.53	3.36e+08
189	7.71	4	8.72	5.30e+08
194	7.80	8	9.23	1.72e+09
195	7.56	4	8.97	9.32e+08
197	7.30	4	8.50	3.20e+08
198	7.62	4	9.60	3.98e+09
201	7.62	8	8.89	7.70e+08
205	8.00	8	8.75	5.64e+08
206	8.09	8	8.84	6.90e+08
207	7.74	8	8.77	5.92e+08
209	8.18	8	8.13	1.35e+08
24+27	5.40	8	5.78	5.98e+07
28+31	5.67	8	6.31	2.06e+06
37+42	5.80	4	6.76	5.70e+06
47+48	5.82	8	6.91	8.18e+06
41+64+71	5.87	4	6.70	4.97e+06
56+60	6.11	4	6.76	5.82e+06
70+76	6.17	8	7.29	1.96e+07
66+95	6.17	4	7.06	1.14e+07
56+60+81	6.19	4	7.06	1.16e+07
84+92	6.20	4	7.45	2.82e+07

Table 2.4.2: Mean BAF[d]s from Lake Ontario BSAFs for Salmonids (continued)

Chemical	log K_{ow}	Number BAFs	Mean log BAF[d]	Mean BAF[d]
PCBs				
87+97	6.29	4	7.81	6.46e+07
137+176	6.80	4	8.03	1.07e+08
138+163	6.91	4	8.42	2.64e+08
156+171+202	7.18	4	8.44	2.76e+08
182+187	7.19	4	8.89	7.85e+08
157+200	7.23	4	8.59	3.86e+08
170+190	7.37	8	8.98	9.53e+08
195+208	7.64	4	8.66	4.58e+08
196+203	7.65	8	8.92	8.27e+08
PCDDs				
2378-TCDD	7.02	4	6.95	9.00e+06
12378-PeCDD	7.50	4	7.40	2.49e+07
123478-HxCDD	7.80	4	7.22	1.65e+07
123678-HxCDD	7.80	4	6.83	6.71e+06
123789-HxCDD	7.80	4	6.87	7.44e+06
1234678-HpCDD	8.20	4	6.85	7.16e+06
OCDD	8.60	4	6.63	4.29e+06
PCDFs				
2378-TCDF	6.50	4	6.34	2.16e+06
12378-PeCDF	7.00	4	6.28	1.89e+06
23478-PeCDF	7.00	4	7.14	1.38e+07
123478-HxCDF	7.50	4	6.32	2.07e+06
123678-HxCDF	7.50	4	6.70	5.07e+06
123789-HxCDF	7.50	4	7.23	1.70e+07
234678-HxCDF	7.50	4	7.27	1.84e+07
1234678-HpCDF	8.00	4	5.98	9.47e+05
1234789-HpCDF	8.00	4	7.53	3.35e+07
OCDF	8.80	4	6.96	9.10e+06

Exhibit 2.4.1: Lake Ontario Salmonid BAFs

Correlation of Measured BAFs to BSAF Predicted



Oliver & Niimi - Referenced to BAF for PCB 52

Doc=2mg/L & Kdoc=Kow/10

Exhibit 2.4.2:
Ratios between Oliver and Niimi (1988) measured BAFs and BAFs predicted from Oliver and Niimi (1988)

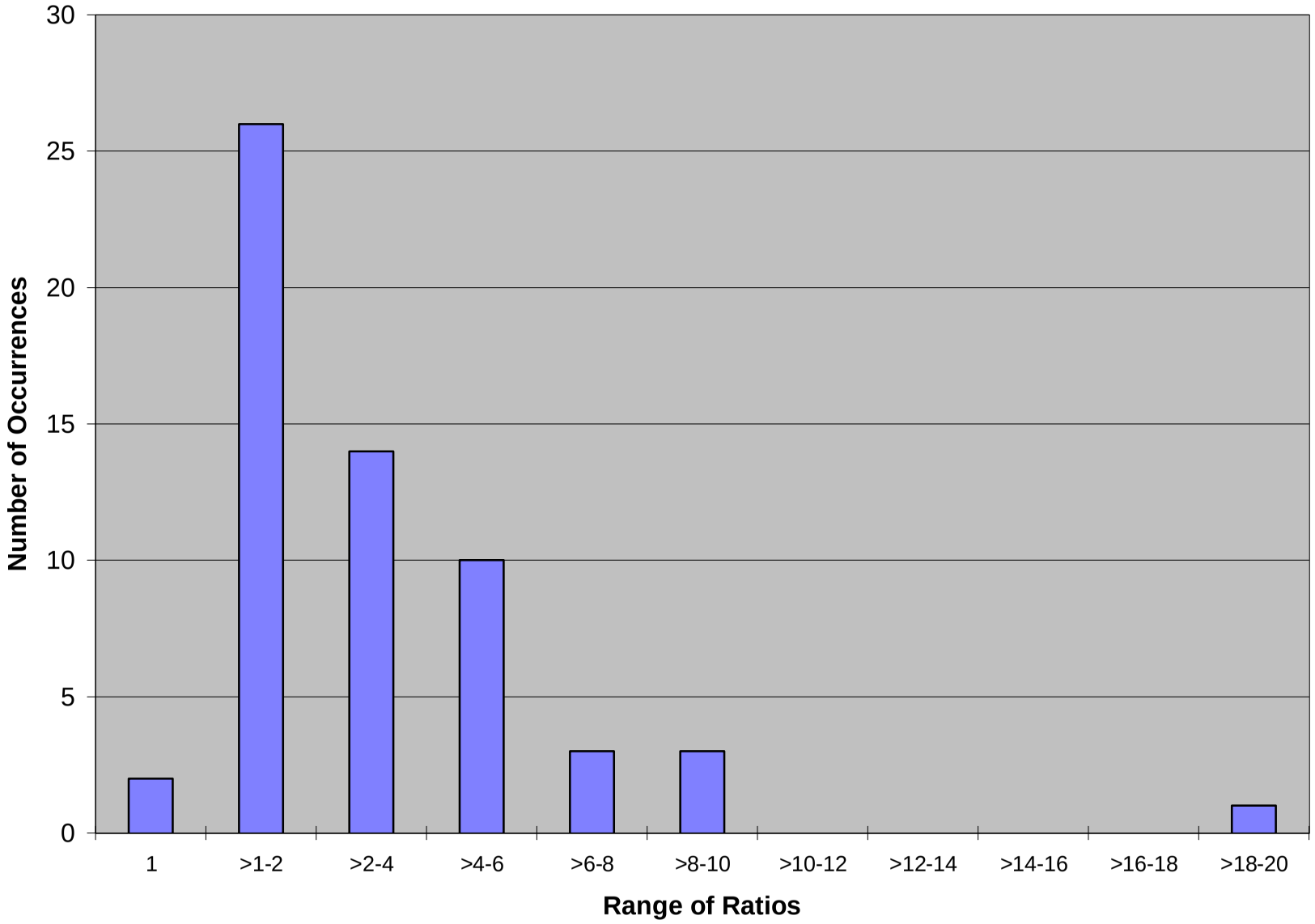
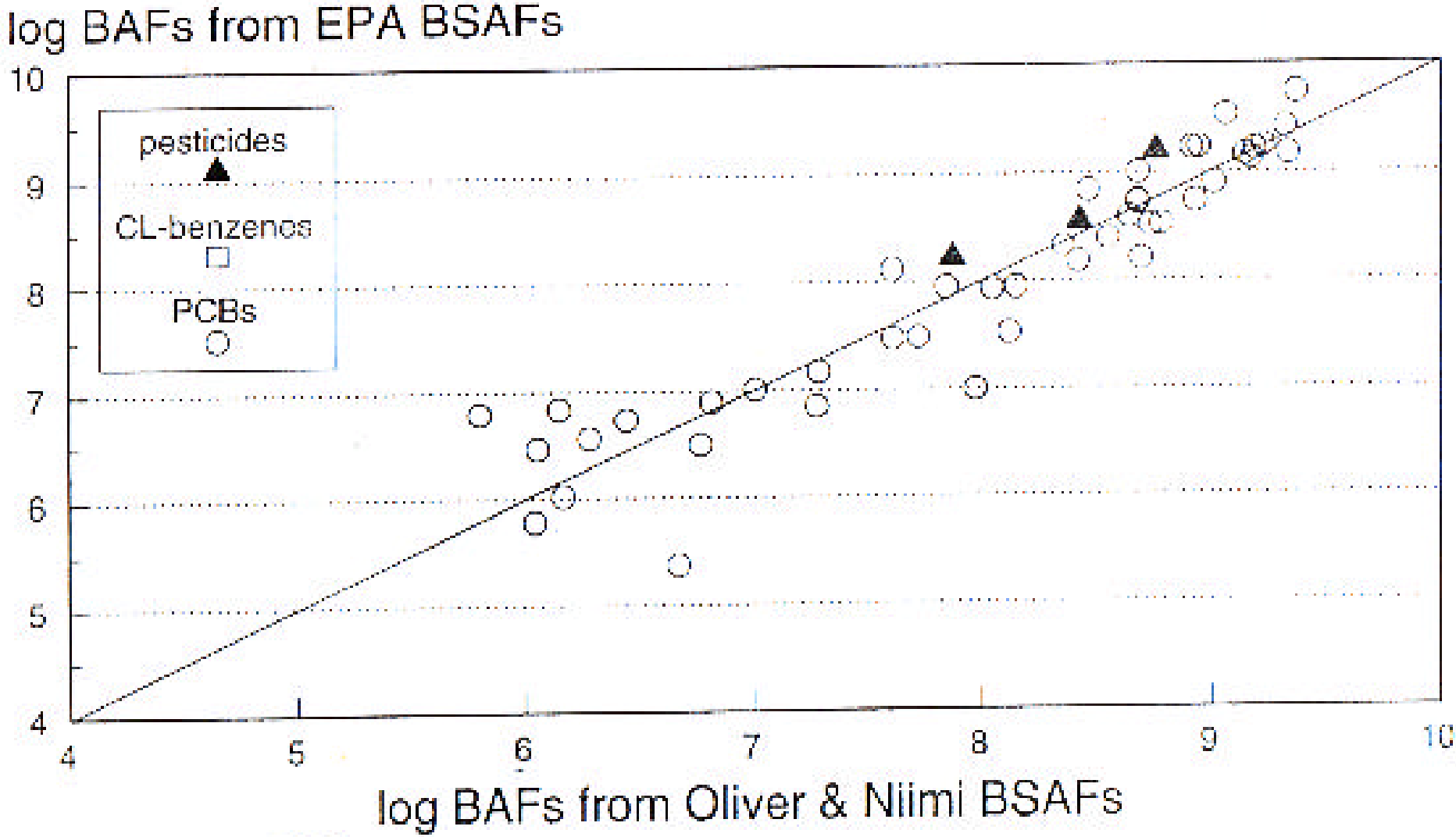


Exhibit 2.4.3: Lake Ontario Salmonid BAFs

Correlation of EPA BSAF-pred. to O-N BSAF-pred.



Referenced to BAF for PCB 52
Doc=2mg/L & Kdoc=Kow/10

Exhibit 2.4.4:
Ratios between BAFs predicted from EPA BSAFs and BAFs predicted from Oliver and Niimi (1988) BSAFs

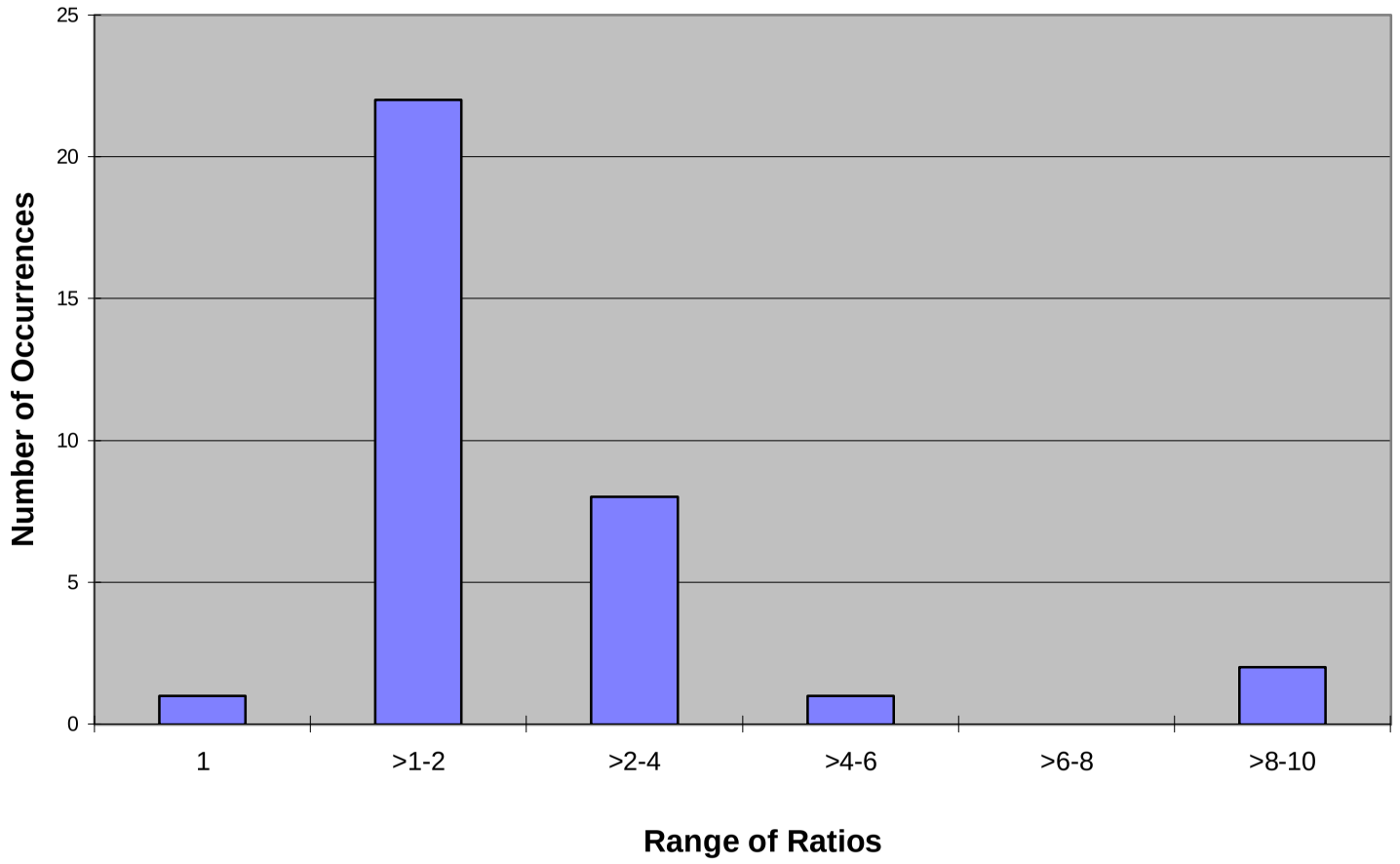
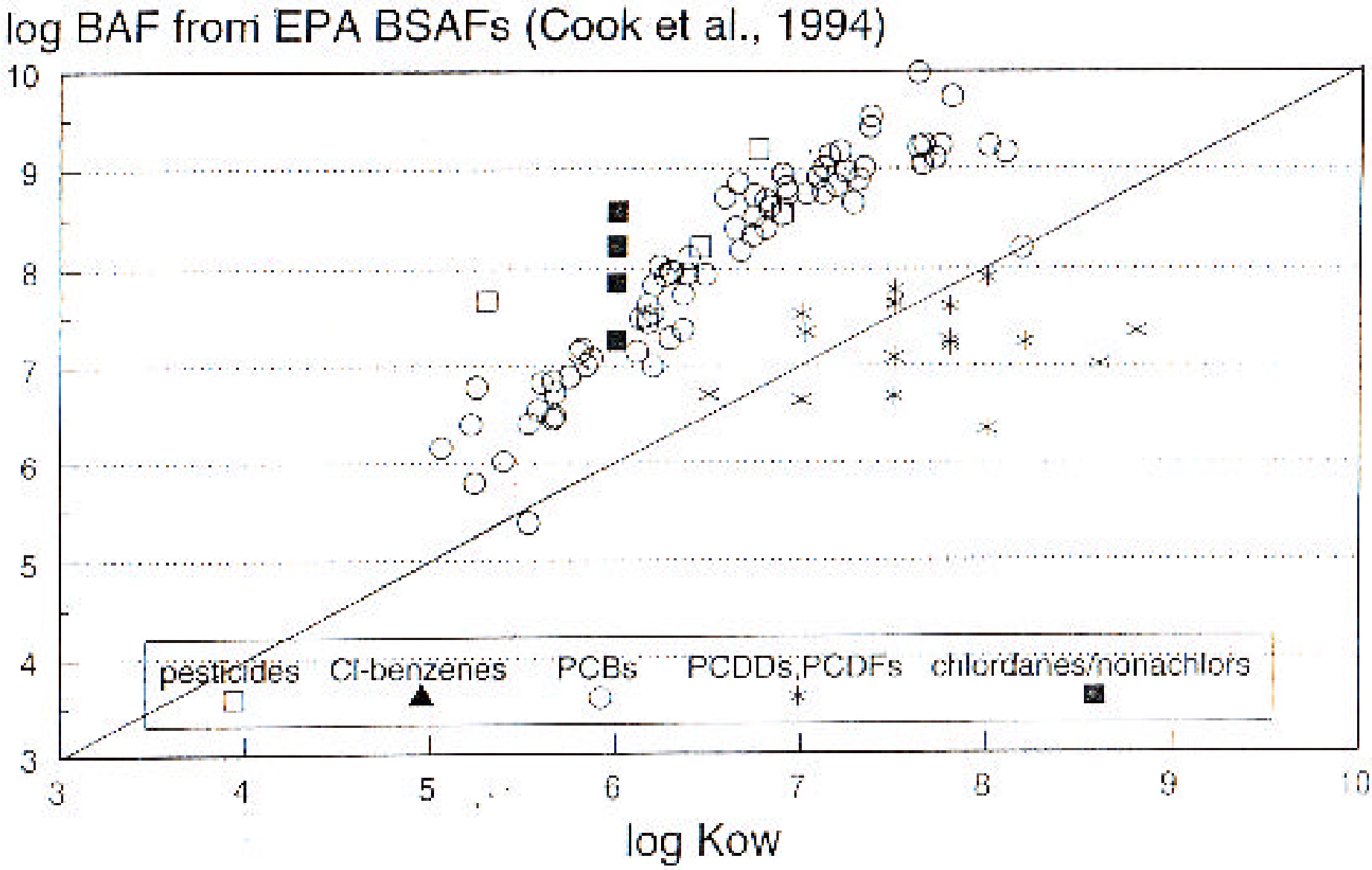
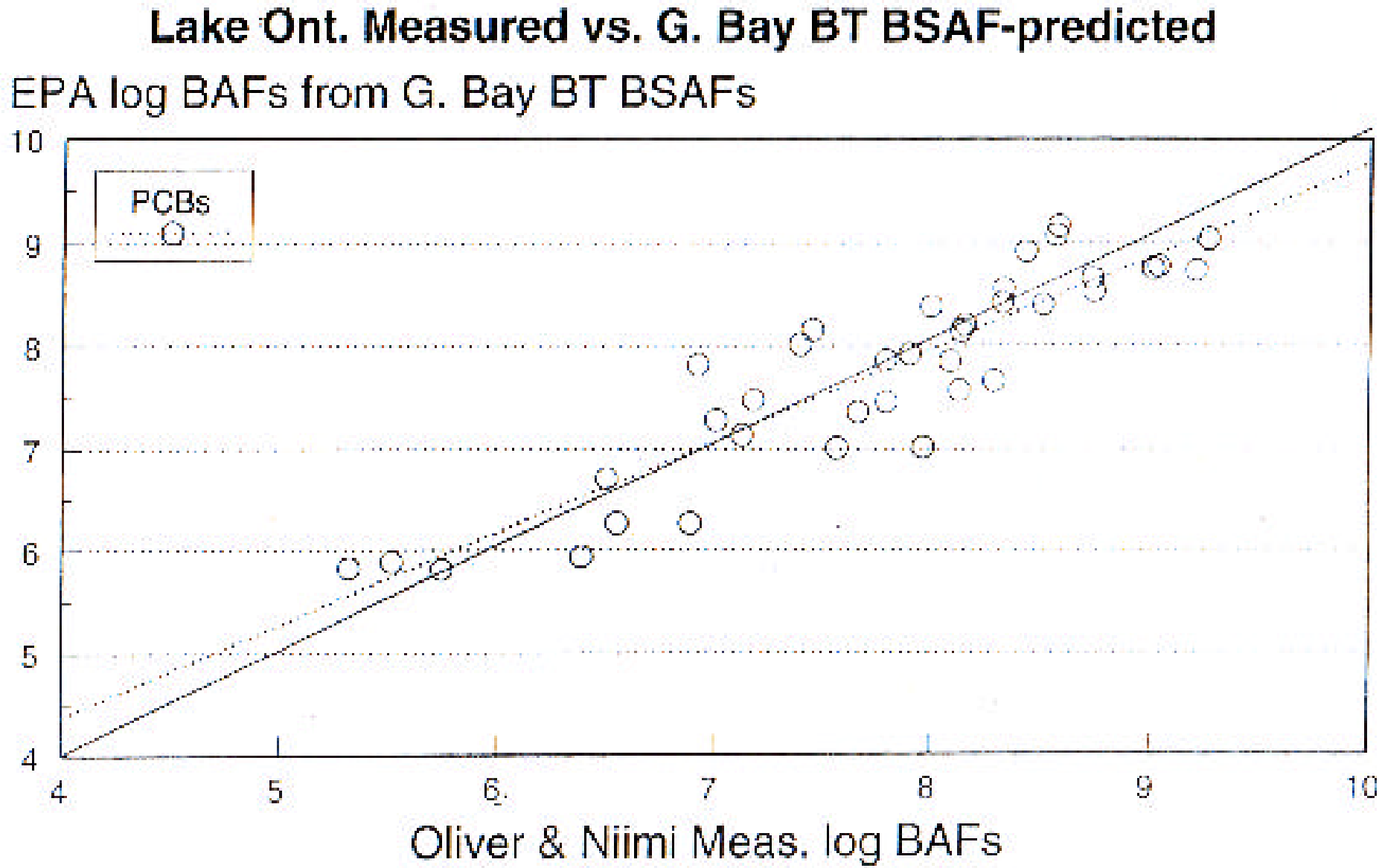


Exhibit 2.4.5: Predicted Lake Ontario Lake Trout BAFs



Referenced to O-N BAF for PCB 52
Doc=2mg/L & Kdoc=Kow/10

Exhibit 2.4.6: Correlation of L. Ont. & Green Bay BAFs



ERLD GB B.Trout Region 3A/3B BAFs ref. PCB 52
Doc=2-5mg/L & Koc=Kow/10

Exhibit 2.4.7:
Ratios between Oliver and Niimi (1988) measured BAFs and BAFs predicted from Green Bay BSAFs

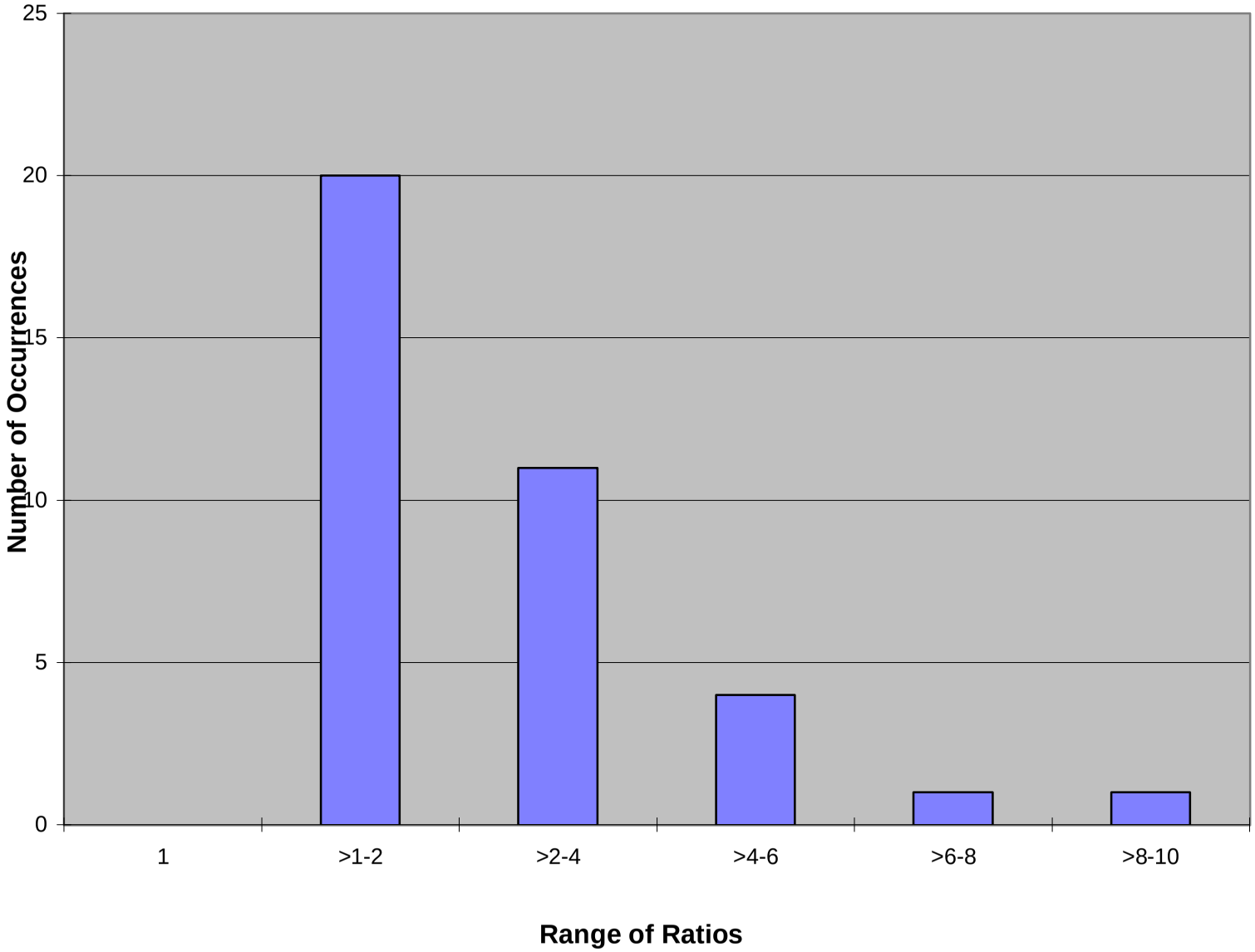
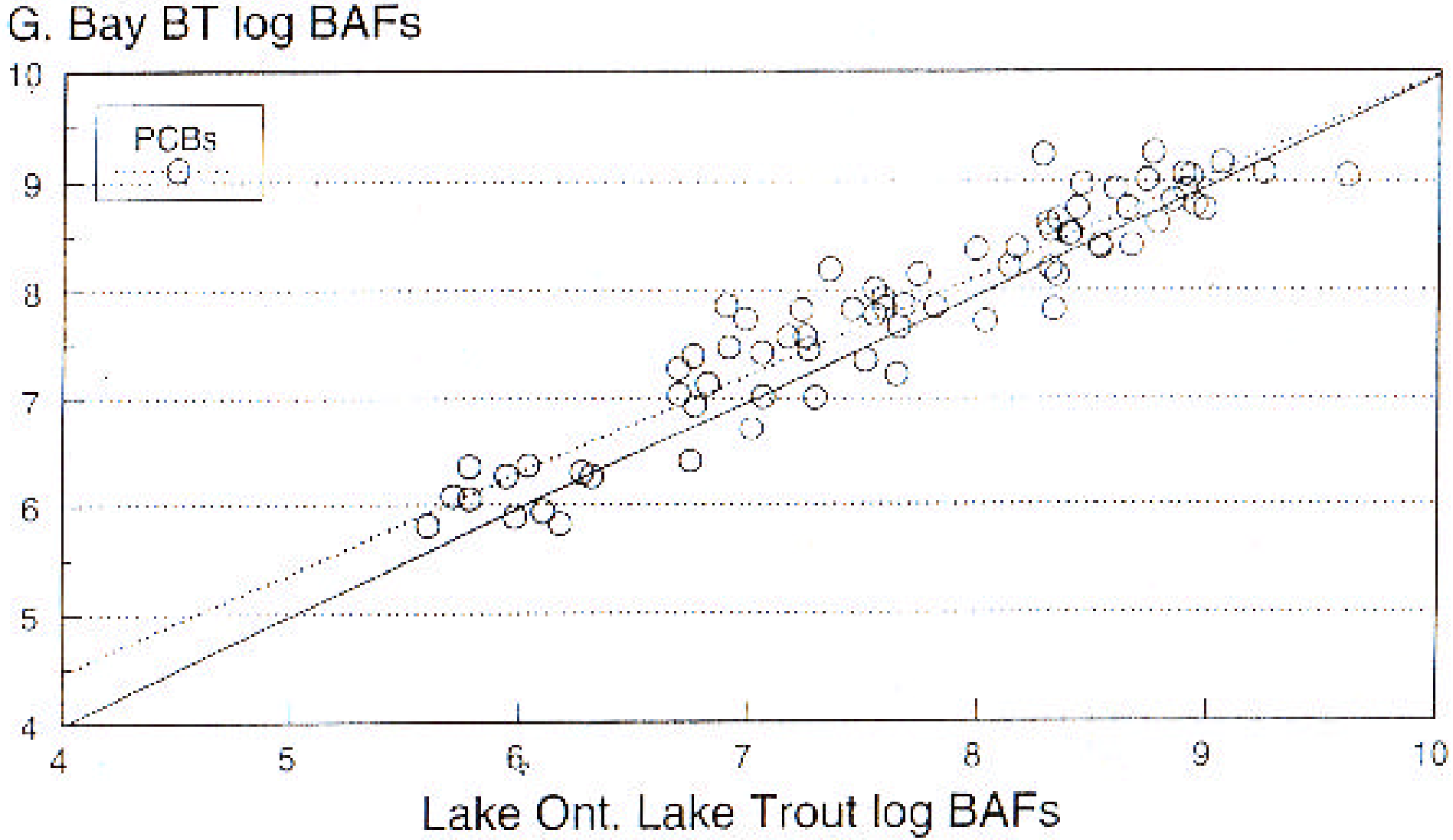


Exhibit 2.4.8: Correlation of EPA BAFs from BSAFs

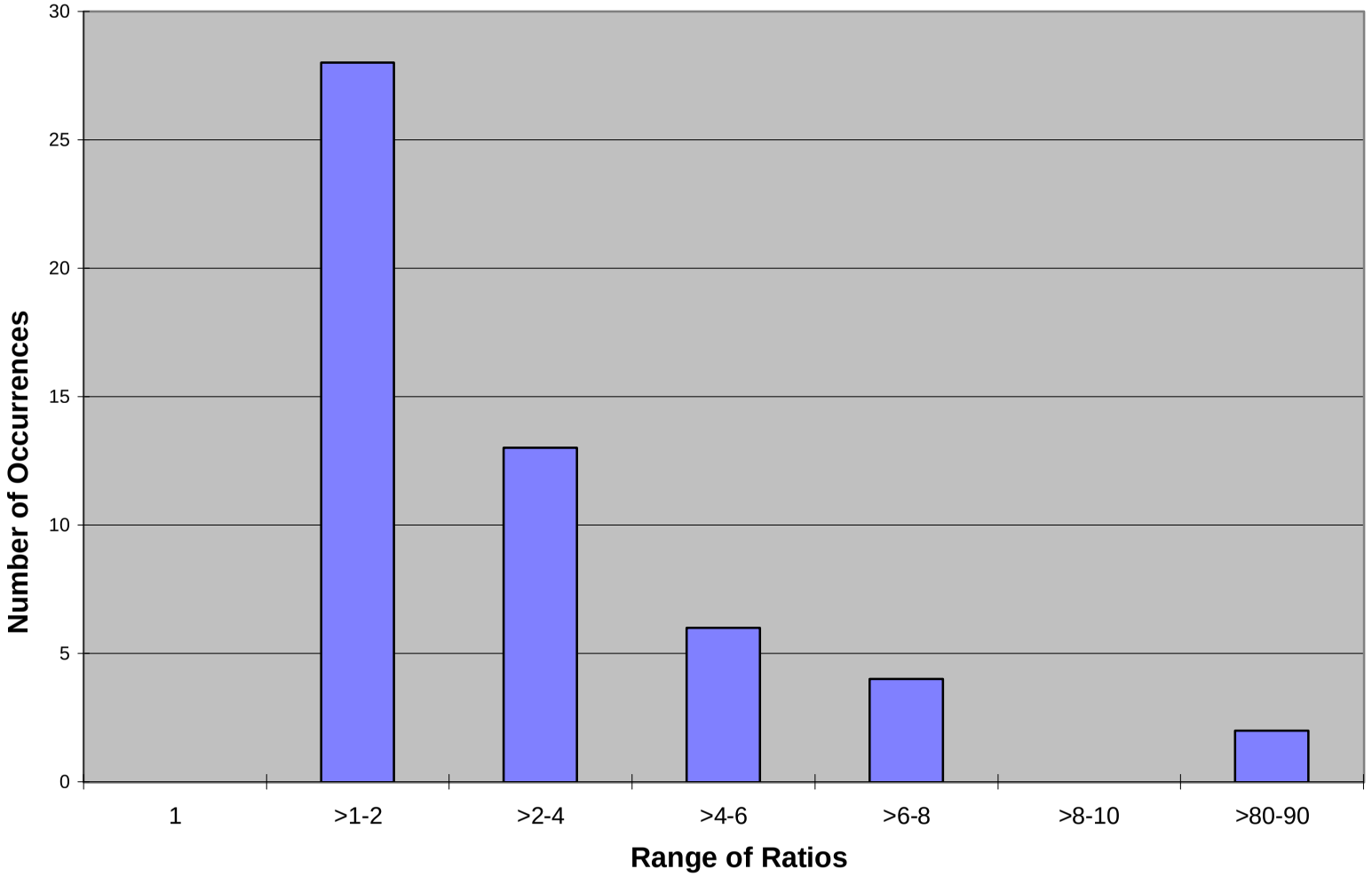
Lake Ontario Lake Trout vs. Green Bay B. Trout



BAFs referenced to PCB 52; Green Bay Region 3A/B

Doc=2-5mg/L & Koc=Kow/10

Exhibit 2.4.9:
Ratios BAFs predicted from EPA BSAFs and BAFs predicted from Green Bay BSAFs



2.4.4.3 Baseline BAF Derived from a Laboratory-Measured BCF and Food-Chain Multiplier

For the third tier in the data preference hierarchy for nonpolar organic chemicals, EPA recommends the use of a predicted BAF derived from a technically defensible, laboratory measurement of the BCF and an appropriate food chain multiplier (FCM). A FCM is determined as the ratio of the baseline BAF ($BAF^{fd)}$ of an organism at a particular trophic level to the baseline BCF (usually determined for trophic level one).[24] FCMs with values greater than 1.0 indicate biomagnification and typically apply to organic chemicals with K_{ow} values between 4.0 and 9.0. Laboratory-measured BCFs are preferred over predicted BCFs because laboratory-measured BCFs inherently account for effects of chemical metabolism on the BCF during its measurement.

The equation for calculating a baseline BAF from a laboratory-measured BCF is:

$$\text{Baseline BAF}^{fd} = (\text{FCM})\left[\frac{\text{Measured BCF}_T^t}{f_{fd}} - 1\right]\left(\frac{1}{f}\right)$$

(Equation 2.4.17)

where:

Baseline BAF^{fd}	=	BAF expressed on a freely-dissolved and lipid-normalized basis
BCF_T^t	=	BCF based on total concentration in tissue and water
f	=	Fraction of the tissue that is lipid
f_{fd}	=	Fraction of the total chemical in the test water that is freely dissolved
FCM	=	Food-chain multiplier obtained from Tables 2.4.4, 2.4.5, or 2.4.6 by linear interpolation for the appropriate trophic level as necessary (or from appropriate field data)

For each trophic level, the species mean baseline BAF is calculated as the geometric mean if more than one acceptable baseline BAF is predicted from laboratory-measured BCFs for a given species. For each trophic level, the trophic level-specific BAF is calculated as the geometric mean of the species mean baseline BAFs based on laboratory-measured BCFs.

[24]Note: Equilibrium partitioning theory would predict BCF^{fd} approximately equal to K_{ow}, thus the BCF^{fd} would not be trophic level dependent.

Procedural and Quality Assurance Requirements for Measured BCFs

A measured BCF derived from results of a laboratory exposure study is acceptable if the study has met certain specific technical criteria. These criteria include, but are not limited to:

1. The test organism should not be diseased, unhealthy, or adversely affected by the concentration of the chemical because these attributes may alter accumulation of chemicals by otherwise healthy organisms.

2. The total concentration of the chemical in the water should be measured and should be relatively constant during the steady-state time period.

3. The organisms should be exposed to the chemical using a flow-through or renewal procedure.

4. For organic chemicals, the percent lipid should be either measured or reliably estimated for the tissue used in the determination of the BCF.

5. For organic chemicals with log K_{ow} greater than four, the concentrations of POC and DOC in the test solution should be either measured or reliably estimated. For organic chemicals with log K_{ow} less than four, virtually all of the chemical is predicted to be freely dissolved, except in water with extremely high DOC and POC concentrations, which is not characteristic of laboratory dilution water used in BCF determinations.

6. Laboratory-measured BCFs should be determined using fish species, but BCFs determined with molluscs and other invertebrates may be used with caution. For example, because invertebrates metabolize some chemicals less efficiently than vertebrates, a baseline BCF determined using invertebrates is expected to be higher than a comparable baseline BCF determined using fish.

7. If laboratory-measured BCFs increase or decrease as the concentration of the chemical increases in the test solutions in a bioconcentration test, the BCF measured at the lowest test concentration above control concentrations should be used (i.e., a BCF should not be calculated from a control treatment). The concentrations of an inorganic chemical in a bioconcentration test should be greater than normal background levels and greater than levels required for normal nutrition of the test species if the chemical is a micronutrient, but below levels that adversely affect the species. Bioaccumulation of an inorganic chemical might be overestimated if concentrations are at or below normal background levels due to, for example, nutritional requirements of the test organisms.

8. For inorganic chemicals, BCFs should be used only if they are expressed on a wet weight basis. BCFs reported on a dry weight basis cannot be converted to wet weight

unless a conversion factor is measured or reliably estimated for the tissue used in the determination of the BAF.

9. BCFs for organic chemicals may be based on measurement of radioactivity only when the BCF is intended to include metabolites, when there is confidence that there is no interference due to metabolites, or when studies are conducted to determine the extent of metabolism, thus allowing for a proper correction.

10. The calculation of the BCF must appropriately address growth dilution.

11. Other aspects of the methodology used should be similar to those described by ASTM (1990).

In addition, the magnitude of the octanol-water partition coefficient (K_{ow}) and the availability of corroborating BCF data should be considered. For example, some chemicals with high log K_{ow}s may require longer than 28 days to reach steady state conditions between the organism and the water column. As with BAFs, the BCFs should be divided by the mean lipid fraction to express the value on a lipid-normalized basis.

Food-Chain Multipliers

The food-chain multiplier represents a measure of a chemical's tendency to biomagnify in aquatic food webs. For non-polar organic chemicals, FCMs can be determined from bioaccumulation models or directly from field data (tissue residues).

For model-derived FCMs, EPA recommends using the food web model by Gobas (1993) to determine FCMs for nonpolar organic chemicals. There are several advantages to using the Gobas (1993) model. First, uptake into both benthic and pelagic food chains is measured, incorporating exposure of organisms to chemicals from both the sediments and the water column. Second, the input data needed to run the model can be readily defined. Third, the model-predicted BAFs (which are used to derive the FCMs) are in agreement with field-measured BAFs for chemicals, even those with very high log K_{ow}s. Finally, the model predicts chemical residues in benthic organisms using equilibrium partitioning theory, which is consistent with EPA's sediment quality criteria effort.

The Gobas (1993) model predicts the chemical residues in the organisms, which are then used to estimate BAFs for each species in the food chain:

$$BAF^{fd} = \frac{C}{C_w^{fd}}$$

(Equation 2.4.18)

where:

BAF^{fd} = Lipid-normalized BAF using the freely dissolved concentration in the water

C_w^{fd} = Freely dissolved concentration of the chemical in the water column

C = Lipid-normalized concentration in appropriate tissue

Food-chain multipliers are then calculated from the predicted BAF^{fd}s using the following equation:

$$FCM = \frac{BAF^{fd}}{K_{ow}}$$

(Equation 2.4.19)

where:

K_{ow} = n-octanol/water partition coefficient

Data Requirements to Predict the Food-Chain Multiplier. The food chain model by Gobas (1993) requires specific data on the structure of the food chain and the water quality characteristics of the water body of interest including:

- Feeding preferences, weights, and lipid contents for each species in the food chain.
- Water temperature.
- Organic carbon content of the sediment and the water column.
- Concentrations of the chemical in the sediment and freely dissolved concentration of the chemical in the water column.
- Densities of lipid and organic carbon.
- Metabolic transformation rate constant.

- K_{ow} values, estimated using the methods described in Section 2.4.4.1 (subsection entitled: *Guidance on Selecting Appropriate K_{ow} Values*).

It should be noted that the model of Gobas (1993) does not include solubility controls or limitations; thus, the concentration of the chemical in the water used with the model is arbitrary for determining the BAFs, i.e., the ratio of the concentration of the chemical in the tissue to the concentration of the chemical in the water column (BAF) obtained using a 1 ng/L concentration of the chemical in the water will be equal to that obtained using a 150 g/L concentration of the chemical for a specified K_{ow}.

It should be noted that the model of Gobas (1993) takes the total concentration of the chemical in the water and, before doing any predictions, calculates the freely dissolved concentration of the chemical in the water. The freely dissolved concentration of the chemical in the water is then used *in all subsequent calculations by the model*. By setting the concentration of the DOC and POC to 0 mg/L, the total concentration of the chemical input to the model becomes equal to the freely dissolved concentration of the chemical in the water. This allows the fixing of the chemical concentration relationship between sediment and water phases in the model. BAFs were determined by dividing the chemical residues predicted by the model of Gobas (1993) by the freely dissolved concentration of the chemical in the water; therefore, they are not influenced by the concentration of DOC input to the model.

Measured chemical residues in fishes assigned to trophic level 3 can be higher than those in piscivorous fishes (trophic level 4) from the same food chain. Potential causes of the higher concentrations (on a lipid basis) in the trophic level 3 fish include 1) growth rates which are much slower than rates for predator fishes; 2) slower rates of metabolism than the predator fishes for the chemicals of interest; and 3) feeding preferences for trophic level 3 fish, including predation on other fish. In the development of FCMs, the feeding preferences for smelt (see Gobas 1993) consisted of a mixture of trophic level 2 and 3 organisms, i.e., mysids, *Diporeia* sp., and sculpin. This mixture of different trophic levels combined with bioenergetic factors for the smelt caused the predicted concentrations of the chemicals and subsequently, the derived FCMs, to be slightly larger than those for the piscivorous fishes (trophic level 4).

Table 2.4.3: Environmental Parameters and Species Characteristics Used With the Model of Gobas (1993) for Deriving Chain Multipliers

Environmental parameters:
Mean water temperature: 8 C Organic carbon content of the sediment: 2.7% Organic carbon content of the water column: 0.0 kg/L Density of lipids: 0.9 kg/L Density of organic carbon: 0.9 kg/L Metabolic transformation rate constant: 0.0 day^{-1} $\Pi_{socw} = 25 * \log K_{ow}$.
Species characteristics:
Phytoplankton Lipid content: 0.5%
Zooplankton: Mysids (*Mysis relicta*) Lipid content: 5.0%
Diporeia sp. Lipid content: 3.0%
Sculpin (*Cottus cognatus*) Lipid content: 8.0% Weight: 5.4 g Diet: 18% zooplankton, 82% *Diporeia* sp. (pelagic/benthic food web) 100% *Diporeia* sp. (all-benthic food web) 100% zooplankton (all-pelagic food web)
Alewives (*Alosa pseudoharengus*) Lipid content: 7.0% Weight: 32 g Diet: 60% zooplankton, 40% *Diporeia* sp. (pelagic/benthic food web) 100% *Diporeia* sp. (all-benthic food web) 100% zooplankton (all-pelagic food web)
Smelt (*Osmerus mordax*) Lipid content: 4.0% Weight: 16 g Diet: 54% zooplankton, 21% *Diporeia* sp., 25% sculpin 54% *Diporeia* sp., 46% sculpin (all-benthic food web) 68% zooplankton, 32% sculpin (all-pelagic food web)
Salmonids (*Salvelinus namaycush, Oncorhynchus mykiss, Oncorhynchus velinus namaycush*) Lipid content: 11.0% Weight: 2410 g Diet: 10% sculpin, 50% alewives, 40% smelt

Table 2.4.4:
Food-Chain Multipliers for Trophic Levels 2, 3, & 4
(Pelagic and Benthic Structure)

Log K_{ow}	Trophic Level 2	Trophic[a] Level 3	Trophic Level 4
<2.0	1.000	1.000	1.000
2.0	1.000	1.005	1.000
2.5	1.000	1.010	1.002
3.0	1.000	1.028	1.007
3.1	1.000	1.034	1.007
3.2	1.000	1.042	1.009
3.3	1.000	1.053	1.012
3.4	1.000	1.067	1.014
3.5	1.000	1.083	1.019
3.6	1.000	1.103	1.023
3.7	1.000	1.128	1.033
3.8	1.000	1.161	1.042
3.9	1.000	1.202	1.054
4.0	1.000	1.253	1.072
4.1	1.000	1.315	1.096
4.2	1.000	1.380	1.130
4.3	1.000	1.491	1.178
4.4	1.000	1.614	1.242
4.5	1.000	1.766	1.334
4.6	1.000	1.950	1.459
4.7	1.000	2.175	1.633
4.8	1.000	2.452	1.871
4.9	1.000	2.780	2.193
5.0	1.000	3.181	2.612
5.1	1.000	3.643	3.162
5.2	1.000	4.188	3.873
5.3	1.000	4.803	4.742
5.4	1.000	5.502	5.821
5.5	1.000	6.266	7.079
5.6	1.000	7.096	8.551
5.7	1.000	7.962	10.209
5.8	1.000	8.841	12.050
5.9	1.000	9.716	13.964
6.0	1.000	10.556	15.996
6.1	1.000	11.337	17.783
6.2	1.000	12.064	19.907
6.3	1.000	12.691	21.677
6.4	1.000	13.228	23.281
6.5	1.000	13.662	24.604
6.6	1.000	13.980	25.645
6.7	1.000	14.223	26.363

Table 2.4.4:
Food-Chain Multipliers for Trophic Levels 2, 3, & 4
(Pelagic and Benthic Structure)

Log K_{ow}	Trophic Level 2	Trophic[a] Level 3	Trophic Level 4
6.8	1.000	14.355	26.669
6.9	1.000	14.388	26.669
7.0	1.000	14.305	26.242
7.1	1.000	14.142	25.468
7.2	1.000	13.852	24.322
7.3	1.000	13.474	22.856
7.4	1.000	12.987	21.038
7.5	1.000	12.517	18.967
7.6	1.000	11.708	16.749
7.7	1.000	10.914	14.388
7.8	1.000	10.069	12.050
7.9	1.000	9.162	9.840
8.0	1.000	8.222	7.798
8.1	1.000	7.278	6.012
8.2	1.000	6.361	4.519
8.3	1.000	5.489	3.311
8.4	1.000	4.683	2.371
8.5	1.000	3.949	1.663
8.6	1.000	3.296	1.146
8.7	1.000	2.732	0.778
8.8	1.000	2.246	0.521
8.9	1.000	1.837	0.345
9.0	1.000	1.493	0.226

[a] The FCMs for trophic level 3 are the geometric mean of the FCMs for sculpin and alewife.

Table 2.4.5:
Food-Chain Multipliers for Trophic Levels 2, 3, & 4
(All-Pelagic Structure)

Log K_{ow}	Trophic Level 2	Trophic[a] Level 3	Trophic Level 4
<2.0	1.000	1.000	1.000
2.0	1.000	1.000	1.001
2.1	1.000	1.000	1.001
2.2	1.000	1.000	1.001
2.3	1.000	1.000	1.002
2.4	1.000	1.000	1.002
2.5	1.000	1.001	1.002
2.6	1.000	1.001	1.003
2.7	1.000	1.001	1.003
2.8	1.000	1.001	1.004
2.9	1.000	1.001	1.005
3.0	1.000	1.002	1.006
3.1	1.000	1.002	1.007
3.2	1.000	1.002	1.009
3.3	1.000	1.003	1.011
3.4	1.000	1.004	1.013
3.5	1.000	1.005	1.016
3.6	1.000	1.006	1.021
3.7	1.000	1.007	1.026
3.8	1.000	1.009	1.032
3.9	1.000	1.011	1.040
4.0	1.000	1.014	1.050
4.1	1.000	1.018	1.063
4.2	1.000	1.022	1.078
4.3	1.000	1.028	1.097
4.4	1.000	1.034	1.121
4.5	1.000	1.043	1.150
4.6	1.000	1.053	1.185
4.7	1.000	1.066	1.228
4.8	1.000	1.081	1.280
4.9	1.000	1.099	1.342
5.0	1.000	1.121	1.415
5.1	1.000	1.147	1.502
5.2	1.000	1.176	1.603
5.3	1.000	1.210	1.719
5.4	1.000	1.248	1.851
5.5	1.000	1.289	1.999
5.6	1.000	1.333	2.162
5.7	1.000	1.379	2.337
5.8	1.000	1.425	2.521
5.9	1.000	1.471	2.711

Table 2.4.5:
Food-Chain Multipliers for Trophic Levels 2, 3, & 4
(All-Pelagic Structure)

Log K_{ow}	Trophic Level 2	Trophic[a] Level 3	Trophic Level 4
6.0	1.000	1.514	2.900
6.1	1.000	1.554	3.083
6.2	1.000	1.589	3.254
6.3	1.000	1.619	3.407
6.4	1.000	1.643	3.536
6.5	1.000	1.660	3.637
6.6	1.000	1.671	3.705
6.7	1.000	1.674	3.738
6.8	1.000	1.669	3.733
6.9	1.000	1.657	3.688
7.0	1.000	1.636	3.602
7.1	1.000	1.606	3.474
7.2	1.000	1.567	3.305
7.3	1.000	1.518	3.094
7.4	1.000	1.458	2.848
7.5	1.000	1.389	2.570
7.6	1.000	1.308	2.270
7.7	1.000	1.219	1.958
7.8	1.000	1.122	1.647
7.9	1.000	1.020	1.349
8.0	1.000	0.915	1.076
8.1	1.000	0.810	0.835
8.2	1.000	0.707	0.631
8.3	1.000	0.610	0.466
8.4	1.000	0.520	0.336
8.5	1.000	0.438	0.237
8.6	1.000	0.366	0.164
8.7	1.000	0.303	0.112
8.8	1.000	0.249	0.075
8.9	1.000	0.204	0.050
9.0	1.000	0.166	0.033

[a] The FCMs for trophic level 3 are the geometric mean of the FCMs for sculpin and alewife.

Table 2.4.6:
Food-Chain Multipliers for Trophic Levels 2, 3, & 4
(All-Benthic Structure)

Log K_{ow}	Trophic Level 2	Trophic[a] Level 3	Trophic Level 4
<2.0	1.000	1.000	1.000
2.0	1.000	1.009	1.001
2.1	1.000	1.010	1.001
2.2	1.000	1.011	1.001
2.3	1.000	1.013	1.002
2.4	1.000	1.015	1.002
2.5	1.000	1.018	1.002
2.6	1.000	1.022	1.003
2.7	1.000	1.026	1.003
2.8	1.000	1.032	1.004
2.9	1.000	1.039	1.005
3.0	1.000	1.048	1.006
3.1	1.000	1.060	1.008
3.2	1.000	1.074	1.010
3.3	1.000	1.092	1.013
3.4	1.000	1.114	1.017
3.5	1.000	1.142	1.022
3.6	1.000	1.177	1.029
3.7	1.000	1.222	1.039
3.8	1.000	1.277	1.053
3.9	1.000	1.347	1.072
4.0	1.000	1.433	1.099
4.1	1.000	1.541	1.138
4.2	1.000	1.676	1.195
4.3	1.000	1.843	1.276
4.4	1.000	2.050	1.392
4.5	1.000	2.306	1.559
4.6	1.000	2.620	1.796
4.7	1.000	3.004	2.131
4.8	1.000	3.470	2.595
4.9	1.000	4.032	3.232
5.0	1.000	4.702	4.087
5.1	1.000	5.492	5.215
5.2	1.000	6.411	6.668
5.3	1.000	7.462	8.501
5.4	1.000	8.643	10.754
5.5	1.000	9.942	13.457
5.6	1.000	11.337	16.617
5.7	1.000	12.800	20.213
5.8	1.000	14.293	24.192
5.9	1.000	15.774	28.468

Table 2.4.6:
Food-Chain Multipliers for Trophic Levels 2, 3, & 4
(All-Benthic Structure)

Log K_{ow}	Trophic Level 2	Trophic[a] Level 3	Trophic Level 4
6.0	1.000	17.202	32.920
6.1	1.000	18.539	37.405
6.2	1.000	19.753	41.764
6.3	1.000	20.822	45.836
6.4	1.000	21.730	49.472
6.5	1.000	22.469	52.544
6.6	1.000	23.037	54.949
6.7	1.000	23.433	56.610
6.8	1.000	23.659	57.472
6.9	1.000	23.717	57.501
7.0	1.000	23.606	56.679
7.1	1.000	23.326	55.007
7.2	1.000	22.873	52.507
7.3	1.000	22.246	49.227
7.4	1.000	21.443	45.254
7.5	1.000	20.467	40.714
7.6	1.000	19.327	35.780
7.7	1.000	18.040	30.657
7.8	1.000	16.629	25.572
7.9	1.000	15.129	20.744
8.0	1.000	13.580	16.359
8.1	1.000	12.026	12.547
8.2	1.000	10.510	9.368
8.3	1.000	9.068	6.822
8.4	1.000	7.732	4.856
8.5	1.000	6.522	3.387
8.6	1.000	5.448	2.321
8.7	1.000	4.513	1.567
8.8	1.000	3.711	1.045
8.9	1.000	3.032	0.689
9.0	1.000	2.465	0.451

[a] The FCMs for trophic level 3 are the geometric mean of the FCMs for sculpin and alewife.

The freely dissolved concentrations of the chemicals in the water column were calculated from the data of Oliver and Niimi (1988) using the equations of Gschwend and Wu (1985) and Cook et al. (1993)[25] for freely dissolved fraction:

$$f_{fd} = \frac{1}{1 + DOC \cdot K_{doc} + POC \cdot K_{poc}}$$

(Equation 2.4.21)

and freely dissolved concentration:

$$C_w^{fd} = C_w^t \cdot f_{fd}$$

(Equation 2.4.22)

where:

f_{fd} = Fraction of the chemical which is freely dissolved in the water

DOC = Concentration of dissolved organic carbon

POC = Concentration of particulate organic carbon

K_{doc} = Partition coefficient for the chemical between the DOC and the freely dissolved phase in the water

K_{poc} = Partition coefficient for the chemical between the POC phase and the freely dissolved phase in the water

C_w^t = Total concentration of the chemical in the water

C_w^{fd} = Freely dissolved concentration of the chemical in the water

The concentrations in the water reported by Oliver and Niimi (1988) were obtained by liquid-liquid extraction of aliquots of Lake Ontario water which had passed through a continuous-flow centrifuge to remove POC. Therefore, the concentrations in the water reported by Oliver and Niimi (1988) include both the freely dissolved chemical and the chemical associated with the DOC in the water sample. The above equations were used to derive the freely dissolved concentrations of the

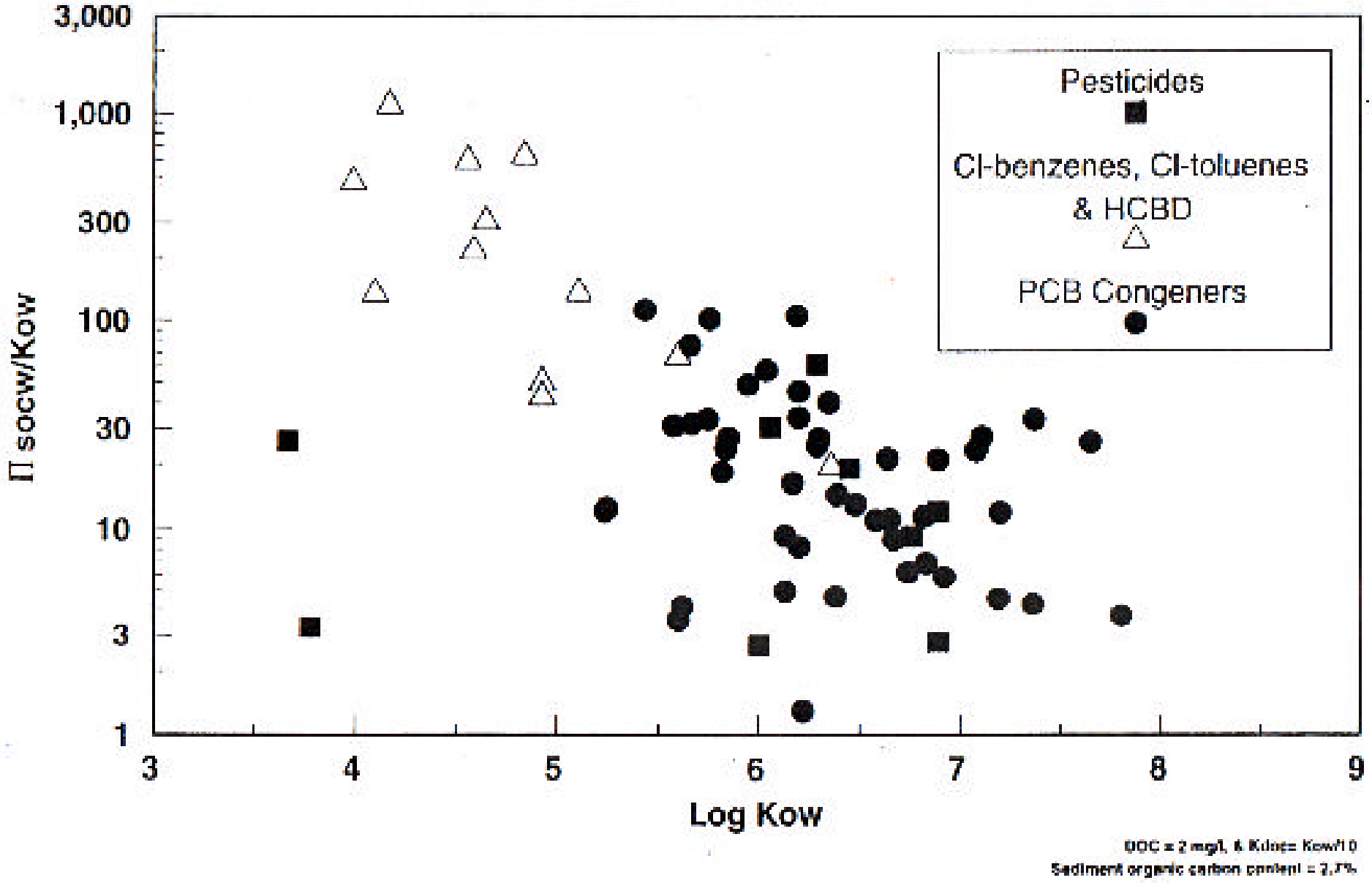
[25]These equations were used to derive the equation for f_{fd} presented in Section 2.4.4.1, and are discussed in Appendix D.

chemicals in the water by setting the POC = 0 mg/L and DOC = 2 mg/L. K_{ow}s used to derive the freely dissolved concentrations have been reported elsewhere (USEPA, 1995c).

In Exhibit 2.4.10, Π_{socw} is plotted against K_{ow} for each chemical reported by Oliver and Niimi (1988). Because the chemical residues by Oliver and Niimi (1988) for the foraging and piscivorous fishes were almost entirely for the PCBs and pesticides, a regression equation of the form log II = A x log K_{ow} + B was determined using this set of chemicals. Using the geometric mean regression technique, the slope (standard deviation) of this equation was 1.07 (0.078). This slope was not significantly different from 1.0, and thus, the relationship between the Π_{socw}/K_{ow} of the individual PCB and pesticide compounds. The average (standard deviation) ratio was 24.7 (25.7). The following relationship was therefore selected to define Π_{socw} in this investigation: $\Pi_{socw} = 25 * \log K_{ow}$.

In addition to determining FCMs for organic substances using the Gobas (1993) model, EPA also recommends the use of FCMs derived from field data where data are sufficient to enable scientifically valid and reliable determinations to be made. Currently, field-measured FCMs are the only method recommended for estimating FCMs for inorganic substances because appropriate model-derived estimates are not yet available. Similarly, field-measured FCMs can also be determined for organic substances. Compared to the model-based FCMs described previously, properly derived field-based FCMs may offer some advantages in some situations. For example, field-measured FCMs rely on measured contaminant concentrations in tissues of biota and therefore inherently account for any contaminant metabolism which may occur. Field-measured FCMs may also be useful for estimating BAFs for some highly hydrophobic contaminants whose water column concentrations are very difficult to determine with accuracy and precision. Furthermore, field-measured FCMs may better reflect local conditions that can influence bioaccumulation, such as differences in food web structure, exposure pathways, water body type, and target species. Finally, use of field-measured FCMs in estimating BAFs may enable existing data on contaminant concentrations in aquatic organisms to be used in situations where companion water column data are unavailable or are judged to be unreliable for calculating a BAF.

Exhibit 2.4.10: Sediment-water column chemical concentration quotient for Lake Ontario data of Oliver and Niimi (1988)



As discussed below and in Appendix C, FCMs are related to and can be determined from biomagnification factors (BMF). For example:

1. $FCM_{TL-2} = BMF_{TL-2}$

2. $FCM_{TL-3} = (BMF_{TL-3})\,(FCM_{TL-2})$
   $= (BMF_{TL-3})\,(BMF_{TL-2})$

3. $FCM_{TL-4} = (BMF_{TL-4})\,(FCM_{TL-3})$
   $= (BMF_{TL-4})\,(BMF_{TL-3})\,(BMF_{TL-2})$

where:

FCM = Food chain multiplier for designated trophic level (TL2, TL3, or TL4)
BMF = Biomagnification factor for designated trophic level (TL2, TL3, or TL4)

The basic difference between FCMs and BMFs is that FCMs relate back to trophic level one (or trophic level two as assumed by the Gobas (1993) model), whereas BMFs always relate back to the next lowest trophic level. For nonpolar organic chemicals, biomagnification factors can be calculated from lipid-normalized tissue residue concentrations determined in biota at a site according to the following equation.

$$BMF_{TL2} = (C_{\ell\text{-}TL2}) / (C_{\ell\text{-}TL1})$$
$$BMF_{TL3} = (C_{\ell\text{-}TL3}) / (C_{\ell\text{-}TL2})$$
$$BMF_{TL4} = (C_{\ell\text{-}TL4}) / (C_{\ell\text{-}TL3})$$

where:

C_ℓ = Lipid-normalized concentration of chemical in tissue of appropriate biota that occupy the specified trophic level (TL2, TL3, or TL4).

For inorganic chemicals, BMFs are determined as shown above, except that tissue concentrations expressed on a wet-weight basis and are not lipid normalized. In calculating field-derived BMFs for determining FCMs, care must be taken to ensure that the biota upon which they are based actually represent functional predator-prey relationships at the study site, and therefore, would accurately reflect any biomagnification that may occur at the site.

As with field-measured BAFs, the potential advantages of using field data for estimating bioaccumulation can be offset by improper collection and use of information. In calculating field-based FCMs, steps similar to those recommended for determining field-measured BAFs need to be taken to ensure that the resulting FCMs accurately represent potential exposures to the target population at the site(s) of interest. Some of the general procedural and quality assurance requirements that are important for determining field-measured FCMs include:

1. A food web analysis should be conducted for the site from which the tissue concentration data are to be determined (or have been already been determined) to identify the appropriate trophic levels for the aquatic organisms and appropriate predator-prey relationships. To assist in trophic level determinations, EPA is in the process of finalizing its draft trophic level and exposure analysis documents (USEPA 1995d; 1995e; 1995f) which include trophic level analyses of numerous species in the aquatic-based food web.

2. The aquatic organisms sampled from each trophic level should reflect the most important exposure pathways leading to human exposure via consumption of aquatic organisms. For higher trophic levels (e.g., 3 and 4), aquatic species should also reflect those that are commonly consumed by humans.

3. Collection of tissue concentration field data for a specific site for which criteria are to be derived and with the specific species of concern are preferred.

4. If data cannot be collected from every site for which criteria are to be derived, the site of the field study should not be so unique that the FCM values cannot be extrapolated to other locations where the criteria and values will apply.

5. Samples of the appropriate resident species and the water in which they reside should be collected and analyzed using appropriate, sensitive, accurate, and precise methods to determine the concentrations of bioaccumulative chemicals present in the tissues.

6. For organic chemicals, the percent lipid should be either measured or reliably estimated for the tissue used in the determination of the lipid normalized concentration in the organism's edible tissues.

7. The tissue concentrations should reflect average exposure conditions over the time period required to achieve steady-state conditions for the contaminant in the target species (usually trophic level three or four organisms).

2.4.4.4 Baseline BAF from Predicted BCF and Food-Chain Multiplier

As the fourth tier in the data preference hierarchy for nonpolar organics (e.g., when acceptable field-measured BAFs, BSAFs, or laboratory-measured BCFs are unavailable), EPA recommends multiplying the FCM by the K_{ow} for the chemical for estimating the baseline BAF. This is equivalent to the direct use of the food chain bioaccumulation model for estimating the BAF when model-derived FCMs are used. For each trophic level, the equation for calculating this baseline BAF is:

$$\text{Baseline BAF} = (\text{FCM})(\text{predicted baseline BCF}) = (\text{FCM})(K_{ow})$$

(Equation 2.4.23)

where:

Baseline BAF = BAF expressed on a lipid-normalized basis using the freely dissolved concentration of the chemical in water

FCM = Food-chain multiplier obtained from Table 2.4.3, 2.4.4, or 2.4.5 by linear interpolation (or from appropriate field data)

K_{ow} = Octanol-water partition coefficient

Use of the K_{ow} in place of the baseline BCF is supported by equilibrium partitioning theory. The linear relationship between the BCF and K_{ow} is also based on the underlying assumption that the bioconcentration process can be viewed as a partitioning of a chemical between the lipids of the aquatic organisms and water and that the K_{ow} is a useful surrogate for this partitioning process (Mackay, 1982). These authors presented a thermodynamic basis for the partitioning process for bioconcentration and, in essence, the BCF on a lipid-normalized basis (and freely dissolved concentration of the chemical in the water) should be similar if not equal to the K_{ow} for organic chemicals.

In addition, empirical data support the use of the K_{ow} in place of the BCF. As indicated by Isnard and Lambert (1988), numerous studies have demonstrated a linear relationship between the logarithm of the BCF and the logarithm of the octanol-water partition coefficient (K_{ow}) for organic chemicals for fish and other aquatic organisms. In addition, when the regression equations are constructed using BCFs reported on a lipid-normalized basis, the slopes and intercepts are not significantly different from one and zero, respectively. For example, de Wolf et al. (1992) adjusted a relationship reported by Mackay (1982) to a 100 percent lipid basis (lipid normalized basis) and obtained the following relationship:

$$\log \text{BCF} = 1.00 \log K_{ow} - 0.08$$

(Equation 2.4.24)

For chemicals with large log K_{ow} s (i.e., greater than 6.0), reported BCFs are often not equal to the K_{ow} for non-metabolizable chemicals. BCFs for non-metabolizable chemicals are equal to the K_{ow} when the BCFs are reported on lipid-normalized basis, determined using the freely dissolved concentration of the chemical in the exposure water, corrected for growth dilution, determined from steady-state conditions or determined from accurate measurements of the chemical's uptake (k_1) and elimination (k_2) rate constants from and to the water, respectively, and determined using no solvent carriers in the exposure. Therefore, EPA recommends that the K_{ow} can be used as an approximation of the BCF.

It is important to recognize the BAF estimated using this method is based on non-metabolizable chemicals. Thus, predicted BAFs will be larger than laboratory-measured BCFs for

chemicals that undergo some metabolism. For some chemicals, such as PAHs, the predicted BAF can be higher than the measured BAF.

2.4.4.5 Metabolism

One factor affecting bioaccumulation is metabolism of the chemical by aquatic organisms. Many organic chemicals that are taken up by aquatic organisms are transformed to some extent by the organism's metabolic processes, but the rate of metabolism varies widely across chemicals and species. For most organic chemicals, metabolism increases the depuration rate and reduces the BAF of the parent compound.

The procedures to measure or predict BAFs differ in the extent to which they account for metabolism. Field-measured BAFs and BSAFs inherently account for any metabolism of the chemical. Predicted BAFs that are obtained by multiplying a laboratory-measured BCF by a model-derived FCM take into account the effect of metabolism on the BCF, but not on the FCM. Use of field-derived FCMs takes into account metabolism. A food chain model prediction of the BAF (the fourth data preference for nonpolar organics) makes no allowance for chemical metabolism. Despite the differential effects of metabolism on predicted BAFs, information is not available for predicting the effect of metabolism on predicted BAFs that rely on the food-chain multiplier or predicted BCFs.

2.4.4.6 Mixtures

For chemical classes where sufficient data on the relative toxicities of individual members of the class is available, toxicity equivalency factors (TEF) can be used to assess the total toxicity risk of the mixture (for further discussion of TEFs, see Appendix I, Section A.3.f and Appendix III, Section F.4 of the *Federal Register* notice). To date, adequate data to support use of TEFs has been found in only one class of compounds (dioxins) (USEPA, 1989). Because individual chemicals of a class (e.g., PCDDs and PCDFs) not only differ in their relative toxicities, but also their relative bioaccumulation potentials, bioaccumulation equivalency factors (BEF) can also be used to account such differences. Bioaccumulation equivalency factors have been developed for PCDDs and PCDFs based on bioaccumulation data for the Great Lakes (60 FR 15366). As adequate data become available to establish TEFs for other chemical classes, the BEF methodology described in 60 FR 15366 and U.S. EPA 1995c should be considered for assessing combined risk from chemical mixtures.

2.4.5 BAFs Used in Deriving AWQC

As discussed above for nonpolar organic chemicals, after the baseline BAF has been derived for a chemical using one of the four methods, the next step is to calculate a BAF that will be used in the derivation of AWQC. This requires information on: (1) the baseline BAF for the chemical of interest using one of the four methods described above; (2) the percent lipid of the aquatic organisms consumed by humans at the site of interest; and (3) the freely dissolved fraction of the chemical in the ambient water of interest.

2.4.5.1 General Equation for an AWQC BAF

For each trophic level, the equation for deriving a BAF to be used in deriving AWQC is applicable to all four methods and is:

$$\text{BAF for AWQC}_{(TL\ n)} = [(\text{Baseline BAF}^{fd})_{TL\ n} \cdot (f)_{TL\ n} + 1] \cdot (f_{fd})$$

(Equation 2.4.25)

where:

BAF for AWQC $_{(TL\ n)}$	=	BAF at trophic level "n" used to derive AWQC based on site conditions for lipid content of consumed aquatic organisms for trophic level "n" and the freely dissolved fraction in the site water
Baseline BAF^{fd} $_{(TL\ n)}$	=	BAF expressed on a freely dissolved and lipid-normalized basis for trophic level "n"
f $_{(TL\ n)}$	=	Fraction lipid of aquatic species consumed at trophic level "n"
f_{fd}	=	Fraction of the total chemical in water that is freely dissolved

2.4.5.2 Baseline BAF

The baseline BAFs used in this equation are those derived from the equations presented in Section 2.4.3 above.

2.4.5.3 Lipid Content of Aquatic Species Eaten by Humans

The lipid content of the aquatic species consumed by humans is required when deriving BAFs for a nonpolar organic chemical that will be used for deriving ambient water quality criteria (AWQC). Information on lipid content is needed because it affects the extent of bioaccumulation of nonpolar organic chemicals in aquatic organisms (Mackay, 1982; Connolly and Pederson, 1988; Thomann, 1989) and therefore, is important in characterizing the potential contaminant exposure to the target population (e.g., general population, sport anglers, subsistence anglers).

The lipid content of aquatic organisms can vary considerably across different species, across different locations for a given species across seasons, and across different age classes (life stages) of a species at a given location. In addition to lipid content, the types and quantity of aquatic species

eaten by individuals differ substantially throughout the United States. In order to account for some of this variability in determining a representative lipid content of consumed aquatic species, EPA recommends that the lipid fraction of aquatic organism be weighted by the consumption rate of those aquatic species consumed by the target population based on information *from the local or regional survey*. Information on consumption rates and lipid content is most accurately determined on a local or regional basis and is recommended as the first choice for estimating lipid content of consumed species. Since baseline BAFs are determined for each trophic level and must be adjusted to reflect the lipid content of consumed aquatic species, EPA recommends that the consumption-weighted lipid content of consumed aquatic organisms also be determined for each trophic level. If sufficient information is not available to derive trophic level specific lipid contents, then States and Tribes may choose to calculate an overall consumption-weighted lipid content that combines data from the relevant trophic levels.

EPA recognizes that local or regional fish consumption data are not always available. Therefore, EPA has derived default, national estimates of consumption-weighted lipid content for use in deriving national AWQC, when local or regional information is unavailable. If local data on both aquatic species consumption rates and lipid contents are not available, States may wish to use national default lipid values calculated by EPA. Using the general relationship in Equation 2.4.26 and information on national finfish and shellfish consumption rates at various trophic levels, EPA has developed a national default consumption-weighted mean lipid values of 2.3% at trophic level 2, 1.5% at trophic level 3, and 3.1% at trophic level 4 (expressed to two significant digits for convenience). The data sources, calculations and assumptions supporting of these national default lipid values are described below.

Data Sources

To estimate a national default consumption-weighted percent lipid value for humans, information is needed at a national level on: (1) the type and quantity of aquatic biota consumed by humans; (2) the percent lipid of the aquatic biota consumed by humans; and (3) the trophic level of the consumed species. These data are described below.

Fish Consumption Data. Information on the types and quantity of aquatic organisms consumed in the U.S. were obtained from USDA's *Continuing Survey of Food Intake by Individuals (CSFII)* (USEPA, 1998b). This survey provided daily average per capita estimates of fish consumption for the U.S. population for categories of estuarine, freshwater, and marine fish and shellfish. Although other regional or local surveys were available, the CSFII was selected because it provided consumption information on a national basis and was the most recent data available. In this survey, consumption rates were divided into 16 categories representing mostly estuarine species and 5 categories representing mostly freshwater species. Mean per capita consumption rates were characterized for individuals 18 years and older. For a detailed discussion of the use of the CSFII data see the chapter on exposure in this TSD. Table 2.4.7 displays the habitat classification, CSFII consumption categories, mean per capita consumption rates, and the fraction of total estuarine and freshwater consumption represented by each category in the survey.

Lipid Content of Consumed Species. The second type of information required in deriving national default values for lipid content includes data on the lipid content of consumed aquatic species. Six primary data sources were used to estimate lipid content. These include: EPA's STORET data base, EPA's *National Study of Chemical Residues in Fish* (USEPA, 1992), two reviews from National Marine Fisheries Service of the National Oceanic and Atmospheric Administration (Sidwell, 1981; Kryznowek and Murphy, 1987), data from the California Toxic Substances Monitoring Program (TSMP), Green Bay Mass Balance Study (USEPA, 1992b, 1995g), and a study of the Hudson River conducted by the New York Department of Environmental Conservation (HydroQual, Inc., portions published in Armstrong and Sloan, 1988). Each of these data sources are discussed in more detail below.

STORET. Data from EPA's STORET (STOrage and RETrieval of U.S. Waterways Parametric data) data base, a waterway-related monitoring data base, were retrieved by downloading tissue and sediment chemistry data from ambient non-land-based monitoring stations, including lipid content, from 1980 through October, 1993. Data are stored in STORET by many government agencies, both federal and state. Most of the data used in this analysis were collected in the Midwest, in particular in Illinois, Minnesota, Michigan, Iowa, Kansas, Missouri, and Nebraska. The number of individual organisms per sample is not known. Information on the common and Latin name for the species sampled, the tissue sampled, the percent lipid content, the collection date and location, and the agency responsible for the data were retrieved from STORET. Data from the other data bases used in this analysis were confirmed as not being present in STORET, which could have caused double-counting of some samples.

Table 2.4.7: Aquatic Organism Categories and Average Consumption Rates from CSFII

Habitat	USDA CSFII Category	Estimated Mean Consumption Rate (g/person/day)	Percentage of Total Consumption Rate
Estuarine	shrimp	1.72959	30.08%
	perch	0.60368	10.50%
	estuarine flatfish	0.52735	9.17%
	crab	0.37126	6.46%
	flounder	0.29941	5.21%
	oyster	0.22555	3.92%
	mullet	0.08756	1.52%
	croaker	0.06749	1.17%
	herring	0.03925	0.68%
	smelt	0.03753	0.65%
	clam	0.03146	0.55%
	scallop	0.00322	0.06%
	anchovy	0.00292	0.05%
	scup	0.00068	0.01%
	sturgeon	0.00054	0.01%
Freshwater	catfish	1.18227	20.56%
	trout	0.44946	7.82%
	carp	0.05727	1.00%
	pike	0.02337	0.41%
	freshwater salmon	0.01096	0.19%

Source: USDA combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).
Notes: Estimates are projected from a sample of 8,478 individuals 18 years of age and older in the U.S. population of 177,807,000 individuals 18 years of age or older using 3-year combined survey weights.
The population for this survey consisted of individuals in the 48 conterminous states.
The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Database for individual food intake surveys.
The number of digits does not imply their significance.

National Study of Chemical Residues in Fish. This EPA study was a one-time screening investigation to determine the prevalence of selected bioaccumulative pollutants in fish (USEPA, 1992a). Three to five fish collected from one location were used for each composite sample. For each composite sample, two measurements of the percent lipid content were obtained, one from the test for dioxins/furans and one from the test for other xenobiotics. The average of the two lipid values was used to represent each sample data point. Location and sampling date information were available as was the common name of the species collected and the tissue type sampled (whole body, fillet).

NOAA Data. Data on the lipid content of estuarine species from the National Marine Fisheries Service of the National Oceanic and Atmospheric Administration were available from two reviews (Sidwell, 1981; Kryznowek and Murphy, 1987). These reviews consist of compilations of data from primary literature sources. Information on the specific location and number of individuals per value were not available in these reviews. Data not collected in North America were excluded, where information was available to make this distinction. Information was available on common and Latin name, tissue type, and method of preparation (e.g., raw, cooked). Only samples that were indicated as being fresh or raw, or for which no preparation information was available, were used in the analysis. Other information such as the number of individuals in a sample, age, weight, and sex were not available. This data source was used to augment the data from the other data sources which were very limited in quantity. For those categories (catfish, trout, carp, pike, and perch) for which we had extensive data from the other sources, data from NOAA were not used.

California Toxic Substances Monitoring Program (TSMP). This program is run by the California Environmental Protection Agency, California State Water Resources Control Board, Division of Water Quality, Monitoring and Assessment Unit. The TSMP was organized to provide a uniform statewide approach to the detection and evaluation of the occurrence of toxic substances in fresh water, and to a limited extent, in estuarine and marine waters, through the analysis of fish and other aquatic life. Samples are collected annually and composite samples of six fish are collected when possible. The data base provides information on age, sample collection date, location, number of organisms per sample, weight, and length. Most samples for the species of interest are fillet samples, although some whole organism samples are also present. Data were obtained via the Internet at World Wide Web site: http://www.swrcb.ca.gov.

Green Bay Mass Balance Study. This study includes lipid content from aquatic species from Green Bay, Lake Michigan. All data are whole body samples. Included in the data base are information on collection date, zone of bay in which the sample was collected, age, and number of fish in average or composite. Data were obtained from HydroQual, Inc. (U.S. EPA 1992b; U.S. EPA 1995g). These data are also available on the World Wide Web at www.epa.gov/glnpo/monitor.html.

Hudson River Data. The New York Department of Environmental Conservation conducted sampling from which percent lipid content for fish species from the Hudson River were available. All data are for muscle fillet samples, and there is one individual per sample. In this data base, collection

date, length, weight, and sex are available, as well as location in the form of river mile. Data were obtained from HydroQual, Inc. (U.S. EPA 1995h; 1995i and Armstrong and Sloan, 1988).

Data Analysis

Data Screening/Treatment. Several steps were required to prepare the data for the calculation of average, consumption-weighted lipid content. As described further in the following section, each record was assigned to a CSFII species category based information on the common and Latin names given in the various data bases and information on whether they could reasonably be expected to be consumed. Data for those species that could not be assigned to a CSFII species category were omitted. For the STORET data, only those data that contained the common name, Latin name, and species code were used so as to maintain consistency of species names within and across data bases. In addition, several steps were taken to correct species codes where known mistakes occurred. An upper bound lipid content was also set at 35 percent to exclude extreme values that were considered outliers. Very few values occurred above 35 percent.

Data were screened by tissue types that corresponded to those considered most commonly consumed by humans. For all finfish species, with the exception of herring, anchovy, and smelt species, data were considered only for selected tissues that include: fillet, fillet/skin, muscle, meat, and flesh samples. The great majority of samples used for the finfish species were fillet or fillet/skin samples. For crab species, data considered in the analysis included tissues designated as edible flesh, edible portion, or edible skinned, in addition to those described for finfish. For the remaining shellfish species (clam, oyster, scallop, and shrimp) and for herring, anchovy and smelt, whole body samples were considered in addition to the tissue types used for fish and crab species. These criteria were established based on the portions of a species are believed to be consumed and constraints on the availability of data.

Selection of Species for Inclusion in Lipid Analysis. Given information from the CSFII survey on the types of aquatic organisms consumed in the U.S., the next step in calculating the consumption-weighted average lipid content involved assigning species to the general CSFII categories. In most cases, information was not available from the CSFII survey to identify which species were included for determining the consumption rates listed in Table 2.4.7. Therefore, inclusion of species and accompanying lipid data into a CSFII category was based on: (1) their taxonomic and publicly-perceived linkage to a CSFII category, (2) consideration of their likelihood for being caught (either recreationally or commercially) and consumed in the U.S., and (3) their occurrence in either fresh or estuarine waters for at least some portion of their life cycle. The species included in the lipid analysis and their relationship to the CSFII consumption categories is provided in Table 2.4.8. Information from numerous published sources were used to help determine whether a species met these criteria. Because several of the CSFII species categories were broad in terms of the types of species that could be included, some species were assigned to multiple CSFII survey categories. For example, flounder species fit into both estuarine flatfish and flounder categories. In such cases, appropriate records were included in both CSFII categories. Notably, some species that

are commonly caught and consumed but did not fit into a CSFII category, such as bass and walleye, were not included in this analysis.

Lipid Content of Species in CSFII Categories. Based on lipid data from the aforementioned sources, an average lipid content was determined for each of the species in the CSFII consumption categories (Table 2.4.8). Next, the overall average lipid content of each CSFII category was determined as the average of the corresponding individual species mean lipid values. Ideally, if sufficient national consumption data were available at the species level, the overall average lipid value for each CSFII category would be determined on a consumption-weighted basis. However, sufficient national information was not available below the CSFII category level and thus, equal weights were assigned to each species mean lipid value. For example, lipid contents were available for several species of trout (e.g., rainbow trout, brown trout, and others), whereas consumption rates were available from the CSFII only for trout as a group. Thus, mean lipid values for all trout species were averaged and combined with the consumption rate for trout from the CSFII.

Trophic Level Assignments to CSFII Categories. National fish and shellfish consumption data from the CSFII (see Table 2.4.7) indicate that on average, individuals consume aquatic organisms from a variety of trophic levels (e.g., oysters and clams in trophic level two, flounder and shrimp in trophic level three, perch and certain catfish species in trophic level four). Therefore, for the purposes of calculating national AWQC using the CSFII consumption data, BAFs need to be derived that are applicable to each of these trophic levels and should be adjusted to reflect the average lipid content of organisms consumed in each of the trophic levels. To estimate the consumption-weighted average lipid content in each of the three trophic levels (and to estimate consumption rates of aquatic organisms within each of the trophic levels--see Section 2.4.8), a trophic level designation must be assigned to each of the consumption rate categories of the CSFII shown in Table 2.4.7.

In order to estimate the trophic level status of consumed aquatic species, one should ideally rely on information concerning the identity, size, age, and diets of individual aquatic species consumed. This information is useful because not only can individual species differ in their trophic status, but trophic level status can also differ for different sizes (ages) of individuals within a species because diets often change with age/size of the organism. Information on the identity, and size (age) of consumed aquatic species should be obtained from the fish consumption survey, if available. Information on the diet of consumed aquatic species might be available on a local or regional basis, but more often is scattered about in the scientific literature based on studies of various sites around the United States. If local or regional information is not available, then EPA recommends the use of the most recent version of the document: *Trophic Level and Exposure Analysis for Selected Piscivorous Birds and Mammals* (USEPA, 1995d, 1995e, 1995f), which contains information on the dietary composition of numerous aquatic species. This draft document is currently being revised based on peer review comments and is expected to be made final in 1998.

Table 2.4.8: Lipid Data for Aquatic Species Included in the Derivation of a National Default Consumption-Weighted Lipid Value

CSFII Consumption Category	Common Name	Scientific Name	Species Mean Lipid (%)	Sample Size	CSFII Mean Lipid (%)
Anchovy	Northern anchovy	*Engraulis mordax*	11.70	2	7.25
	Striped anchovy	*Anchoa hepsetus*	2.80	1	
Carp	Carp	*Cyprinus carpio*	4.45	1433	4.45
Catfish	Black bullhead	*Ameiurus melas*	1.12	11	2.36
	Brown bullhead	*Ameiurus nebulosus*	2.79	704	
	Channel catfish	*Ictalurus punctatus*	5.00	1108	
	White catfish	*Ameiurus catus*	2.15	46	
	Yellow bullhead	*Ameiurus natalis*	0.75	29	
Clam	Butter clam	*Saxidomus nuttalli*	1.22	2	1.68
	Geoduck clam	*Panope generosa*	3.20	1	
	Hard clam	*Mercenaria mercenaria*	1.04	2	
	Littleneck clam	*Protothaca staminea*	0.75	2	
	Soft shell clam	*Mya arenaria*	1.29	5	
	Venus clam	*Tapes philippinarum*	2.60	1	
Crab	Blue crab	*Callinectes sapidus*	2.33	7	1.40
	Dungeness crab	*Cancer magister*	1.15	2	
	King crab	*Paralithodes camtschatica*	0.80	1	
	Snow crab	*Chionoectes bairdi*	1.30	1	
Croaker	Atlantic croaker	*Micropogonias undulatus*	3.30	3	4.77
	Spot	*Leiostomus xanthurus*	10.35	2	
	White croaker	*Genyonemus lineatus*	2.33	7	
	Yellowfin croaker	*Umbrina roncador*	3.11	1	
Estuarine Flatfish	Gulf flounder	*Paralichthys albigutta*	0.80	1	1.48
	Rainbow smelt[1]	*Osmerus mordax*	4.50	88	
	Southern flounder	*Paralichthys lethostigma*	1.20	1	
	Starry flounder	*Platichthys stellatus*	0.97	3	
	Summer flounder	*Paralichthys dentatus*	0.40	1	
	Winter flounder	*Pseudopleuronectes americanus*	1.00	2	
Estuarine Salmon[2]	Atlantic salmon	*Salmo salar*	5.65	2	4.55
	Chinook salmon	*Oncorhynchus tshawytscha*	2.09	271	
	Chum salmon	*Oncorhynchus keta*	4.25	2	
	Coho salmon	*Oncorhynchus kistuch*	2.17	308	
	Pink salmon	*Oncorhynchus gorbuscha*	5.00	2	
	Sockeye salmon	*Oncorhynchus nerka*	8.12	4	
Flounder	Gulf flounder	*Paralichthys albigutta*	0.80	1	0.87
	Southern flounder	*Paralichthys lethostigma*	1.20	1	
	Starry flounder	*Platichthys stellatus*	0.97	3	

Table 2.4.8: Lipid Data for Aquatic Species Included in the Derivation of a National Default Consumption-Weighted Lipid Value

CSFII Consumption Category	Common Name	Scientific Name	Species Mean Lipid (%)	Sample Size	CSFII Mean Lipid (%)
	Summer flounder	*Paralichthys dentatus*	0.40	1	
	Winter flounder	*Pseudopleurnectes americanus*	1.00	2	
Freshwater Salmon	Atlantic salmon	*Salmo salar*	5.65	2	4.22
	Kokanee salmon[3]	*Oncorhynchus nerka*	2.28	3	
	Chinook salmon	*Oncorhynchus tshawytscha*	2.09	271	
	Chum salmon	*Oncorhynchus keta*	4.25	2	
	Coho salmon	*Oncorhynchus kistuch*	2.17	308	
	Pink salmon	*Oncorhynchus gorbuscha*	5.00	2	
	Sockeye salmon	*Oncorhynchus nerka*	8.12	4	
Herring	Atlantic herring	*Clupea harengus*	13.04	5	10.34
	Blueback herring	*Alosa aestivalis*	8.63	3	
	Pacific herring	*Clupea pallasi*	9.34	8	
Mullet	Striped mullet	*Mugil cephalus*	4.49	9	4.49
Oyster	Eastern oyster	*Crassostrea virginica*	1.94	8	1.62
	European oyster	*Ostrea edulis*	1.65	2	
	Olympia oyster	*Ostrea lurida*	0.50	1	
	Pacific oyster	*Crassostrea gigas*	2.40	8	
Perch	White perch	*Morone americana*	5.34	296	3.00
	Yellow perch	*Perca flavescens*	0.66	220	
Pike	Chain pickerel	*Esox niger*	1.21	5	0.84
	Northern pike	*Esox lucius*	0.47	356	
Scallop	Atlantic bay scallop	*Aequipecten irradians*	0.60	1	0.70
	Sea scallop	*Placopectens magellanicus*	0.80	2	
Scup	Scup	*Stenotomus chrysops*	3.70	1	3.70
Shrimp	Brown shrimp	*Penaeus aztecus*	0.93	3	0.75
	Northern pink shrimp	*Pandalus borealis*	0.78	2	
	Pink shrimp	*Penaeus duorarum*	0.78	2	
	White shrimp	*Penaeus setiferus*	0.52	2	
Smelt	Rainbow smelt	*Osmerus mordax*	4.50	88	4.50
Sturgeon	White sturgeon	*Acipenser transmontanus*	1.09	6	1.09
Trout	Brook trout	*Salvelinus fontinalis*	1.51	7	4.29
	Brown trout	*Salmo trutta*	3.81	142	
	Cutthroat trout	*Salmo clarki*	1.23	16	
	Lake trout	*Salvelinus namaycush*	10.90	380	
	Rainbow trout	*Oncorhynchus mykiss*	4.00	123	

[1] Information from the CSFII survey indicated that rainbow smelt were included in the calculation of fish consumption rates for estuarine flatfish.
[2] Because these species are anadromous, data on lipid content were also included for freshwater salmon category.
[3] Information from the American Fisheries Society publication: Common and Scientific Names of Fishes from the United States and Canada (AFS, 1991) indicates that freshwater stocks of sockeye salmon are commonly referred to as Kokanee.

For the national CSFII survey, very limited data were available to further delineate the identity and size of species consumed within each of the CSFII categories in Table 2.4.7. For most of the CSFII categories, this lack of information was not viewed as problematic, because rather unambiguous assignments of trophic status could be made to these categories (e.g., all oysters are considered to be trophic level two). However, for other CSFII categories, assignment of trophic status required some reasonable assumptions to be made and therefore reflect greater uncertainty. The following procedures were used in assigning trophic status to the CSFII consumption categories.

1. Data from EPA's draft trophic level document (USEPA, 1995d, 1995e, 1995f) and other sources were used to estimate the trophic level of species that could reasonably be classified in each of the CSFII consumption categories. Species level trophic assignments were performed as follows.

    a. For game fish that correspond to the CSFII categories, data were used for edible size ranges (about 20 cm [8 inches] or larger).
    b. For species where multiple size ranges were available, preferences was given to the larger specimens in determining the species trophic level.
    c. Trophic level 2 was assigned to a species if appropriate trophic level data ranged between 1.6 and 2.4; trophic level 3 if trophic level data ranged from 2.5 to 3.4; trophic level 4 if trophic level data were 3.5 or higher. This is consistent with the approach taken in the Great Lakes Water Quality Initiative guidance (USEPA, 1995c).

2. Once the species level trophic assignments were completed, this information was used to assign a trophic level to each CSFII consumption rate category as follows.

    a. In situations where a CSFII category was represented by the vast majority of species within a single trophic level, that trophic level was assigned to the CSFII category (e.g., trout, estuarine flatfish, smelt).
    b. In one situation (catfish), the CSFII consumption rate was equally divided between trophic level 3 and 4 because about half the species were determined to be trophic level 3 and about half trophic level 4.
    c. For shrimp, trophic level 3 was assigned based on data for the "general shrimp category" in USEPA (1995f) because other data (grass shrimp, mysids) were for species that are not consumed by humans.

3. The results of the trophic level assignments are shown in Table 2.4.9.

Table 2.4.9: Trophic Level Assignment of Aquatic Species Corresponding to CSFII Consumption Categories

CSFII Consumption Category	Common Name	Scientific Name	Size	Trophic Level [a] (Mean)	Trophic Level [a] (Range)	Notes [a]	Species Assigned Trophic Level [b]	CSFII Assigned Trophic Level [c]
Anchovy	Northern anchovy	*Engraulis mordax*	---	3	---	Feeds on zooplankton	3	3
			Adult	3.2	---	Feeds on large zooplankton		
			Juvenile	3	---	Feeds on zooplankton		
Carp	Common carp	*Cyprinus carpio*	---	---	2.2-3.1	Young feed on zoopl., adults on plants, molluscs, crustacea and become more herbivorous	3	3
			10-23 cm	3	2.8-3.1	Up to 23 cm, feed primarily on benthic inverts.		
			> 23 cm	2.4	2.2-2.6	Larger carp (> 23 cm approx) feed primarily on plants and detritus (60-70%), benthic inverts. (15-35%) and some zoopl (< 15%).		
Catfish	Black bullhead	*Ameiurus melas*	---	3	2.9-3.2	Seem to consume zooplankton and benthic inverts. throughout life. Indiv. > 15 cm may consume some small fish, but also plant materials.	3	3 (50%) 4 (50%)
	Blue catfish	*Ictalurus furcatus*	---	3	---	Assumption.	3	
	Brown bullhead	*Ameiurus nebulosus*	---	---	2.7-3.3	Diet changes with size.	3	
			> 10cm	3.0	2.7-3.2	> 10cm feeds on 20-30% plants & 70-100% benthic inverts (burrowing mayfly, scud, chironomid types). some consume small fish as well.		
	Channel catfish	*Ictalurus punctatus*	36-54cm	---	2.8-4	Changes with age; can grow up to 50 cm or larger. Two studies indicated they consume plants, one other did not	4	
			5-30cm	3.1	---	5-30 cm; consumes largely benthic inverts. (60-80%), detritus (10-15%) and zooplankton (10-25%)		
Catfish (cont'd)			30-35cm	3.3	3-3.5	30-35cm; consumes fish (32%), benthic inverts. (40%), zoopl. (12%), and detritus (15%). Some populations consume up to 25% algae.		

Table 2.4.9: Trophic Level Assignment of Aquatic Species Corresponding to CSFII Consumption Categories

CSFII Consumption Category	Common Name	Scientific Name	Size	Trophic Level [a] (Mean)	Trophic Level [a] (Range)	Notes [a]	Species Assigned Trophic Level [b]	CSFII Assigned Trophic Level [c]
	Channel catfish	*Ictalurus punctatus*	35-45cm	3.8	3.5-3.9	35-45cm; consumes fish (67%), benthic inverts. (25%), and detritus (8%). Some populations consume up to 25% algae		
			> 45cm	4	4.0-4.2	>45cm; consumes fish (100%)		
	Flat bullhead	*Ictalurus platycephalus*	—	3.2	3-4	Can grow to large sizes; feeds on molluscs (primarily clams), bryozoans, & worms	4	
	Flathead catfish	*Pylodictis olivaris*	---	3.8	---	Diet consists primarily of fish with some crayfish, & molluscs.	4	
	Yellow bullhead	*Ictalurus natalis*	30-46 cm	2.6	---	Scavengers, often consumes minnows, crayfish, insect larvae, worms and algae	3	
Clam	Clams (general)	---	---	2.2	2.1-2.4	Filter feeders on plankton, detritus. Includes zooplankton.	2	2
	Amethyst gemclam	—	—	2.2	2.1-2.4	Filter feeder.	2	
	Atlantic rangia	*Rangia cuneata*	---	2.2	2.1-2.4	Filter feeder.	2	
	Baltic macoma	*Macoma balthica*	—	2.2	2.1-2.4	Filter feeder.	2	
	Dwarf surf clam	*Mulina lateralis*	---	2.2	2.1-2.4	Filter feeder.	2	
Crab	Blue crab	*Callinectes sapidus*	---	3.2	2.8-3.4	Feed primarily on molluscs (39%), organic debris (20%), fish (20%), crustaceans (15%), plants (4%) worms (2%)	3	3
Croaker	Atlantic croaker	*Micropogonias undulatus*	---	3	---	Opportunistic bottom feeders; mostly on polychaetes, copepods, mysids, small clams (From: Mercer, 1989)	3	3
Estuarine Flatfish	Flounder (general)	---	---	3.2	3.0-3.4	Feeds on benthic organisms (e.g., sea urchins, sand dollars, brittle stars, shrimp, molluscs, & worms) most of which are detritivores.	—	3
	Lefteye flounders (Bothidae)	---	---	3.2	3.0-3.4	Assumed equal to general flounder diet.	3	
	European flounder	*Platichthys flesus*	---	3.2	3.0-3.4	Assumed same as general flounder diet.	3	

Table 2.4.9: Trophic Level Assignment of Aquatic Species Corresponding to CSFII Consumption Categories

CSFII Consumption Category	Common Name	Scientific Name	Size	Trophic Level [a] (Mean)	Trophic Level [a] (Range)	Notes [a]	Species Assigned Trophic Level [b]	CSFII Assigned Trophic Level [c]
	Righteye flounders	---	---	3.2	3.0-3.4	Assumed equal to general flounder diet.	3	
	Starry flounder	*Platichthys stellatus*	---	3.2	3.0-3.4	Assumed same as general flounder diet.	3	
	Winter flounder	*Pseudopleuronectes americanus*	---	3.2	3.0-3.4	Assumed same as general flounder diet.	3	
	Smelt (general)	---	---	3	---	Assumed same TL as other smelt, except for adult smelt in Great Lakes	3	
	American (Rainbow) smelt	*Osmerus mordax*	---	3.1	---	Feeds on zoopl.; some surface insects	4	
			---	3.5	---	In Great Lakes, > 1yr old feed on smaller fish and on Mysis (TL3); and other inverts & zooplankton (TL2)		
			---	3.1	---	During first year, feed on zoopl.	3	
	Juvenile night smelt	*Spirinchus starksi*	---	3	---	Assumed same as other smelt	3	
	Juvenile top smelt (Osmeridae)	---	---	3	---	Assumption	3	
	surf smelt	*Hypomesus pretiosus*	---	3	---	Assumed same TL as other smelt.	3	

Table 2.4.9: Trophic Level Assignment of Aquatic Species Corresponding to CSFII Consumption Categories

CSFII Consumption Category	Common Name	Scientific Name	Size	Trophic Level [a] (Mean)	Trophic Level [a] (Range)	Notes [a]	Species Assigned Trophic Level [b]	CSFII Assigned Trophic Level [c]
Flounder	Flounder (general)	---	---	3.2	3.0-3.4	Feeds on benthic organisms (e.g., sea urchins, sand dollars, brittle stars, shrimp, molluscs, & worms) most of which are detritivores.	---	3
	Lefteye flounders (Bothidae)	---	---	3.2	3.0-3.4	Assumed equal to general flounder diet.	3	
	European flounder	*Platichthys flesus*	---	3.2	3.0-3.4	Assumed same as general flounder diet.	3	
	Righteye flounders	---	---	3.2	3.0-3.4	Assumed equal to general flounder diet.	3	
	Starry flounder	*Platichthys stellatus*	---	3.2	3.0-3.4	Assumed same as general flounder diet.	3	
	Winter flounder	*Pseudopleuronectes americanus*	---	3.2	3.0-3.4	Assumed same as general flounder diet.	3	
Freshwater Salmon	Kokanee salmon	*Oncorhynchus nerka*		4	---	Larger specimens.	4	4
Herring	Herring (general)	---	---	3.2	3.1-3.4	Feeds primarily on copepods and krill.	---	3
	Atlantic herring	*Clupea harengus*	---	3.2	3.1-3.4	Feeds primarily on copepods and krill.	3	
	Pacific herring	*Clupea pallasi*	—	3.2	3.1-3.4	Feeds primarily on copepods and krill.	3	
Mullet	Striped mullet	*Mugil cephalus*	---	2.2	---	Feeds on plant material, detritus, & plankton.	2	2
Oyster	Molluscs (general)	---	---	2.1	2.0-2.2	Bivalves feed on plankton	---	2
	Mussels (general)	---	---	2.2	2.1-2.4	Filter feeders on plankton, detritus, zooplankton.	---	
Perch	Yellow perch	*Perca flavescens*	20-30cm	3.4	3.1-3.8	20-30cm; consumes 10% zoopl., 50% benthic inverts, 34% fish (some pops.); nearly 100% fish in other populations.	4	4

Table 2.4.9: Trophic Level Assignment of Aquatic Species Corresponding to CSFII Consumption Categories

CSFII Consumption Category	Common Name	Scientific Name	Size	Trophic Level [a] (Mean)	Trophic Level [a] (Range)	Notes [a]	Species Assigned Trophic Level [b]	CSFII Assigned Trophic Level [c]
Pike	Northern pike	*Esox lucius*	>10cm	4	---	>10cm; diet primarily all fish.	4	4
	Pickerel (redfin & grass)	*Esox americanus*	larger specimens	4	---	Larger specimens consume small fish	4	
Scallop	Molluscs (general)	---	---	2.1	2.0-2.2	Bivalves feed on plankton	2	2
Scup	Scup	*Stenotomus chrysops*	---	3	---	Bottom feeder, primarily on molluscs, worms, and small crustaceans (Jordan and Evermann, 1969)		3
Shrimp	Shrimp (general)	(Palaemonidae)	---	3.0	---	Filter feeding on zoopl.	3	3
	Grass shrimp	*Palaemonetes sp.*	---	2.1	---	Detritivore, primarily on plant material	2	
	Mysis	*Mysis relicta*	---	3.5	3-4	Cold water forms; during warm months, restricted to hypolimnion	4	
Smelt	Smelt (general)	---	---	3	---	Assumed same TL as other smelt, except for adult smelt in Great Lakes	---	3
	American (Rainbow) smelt	*Osmerus mordax*	---	3.1	---	Feeds on zoopl.; some surface insects	4	
			---	3.5	---	In Great Lakes, > 1yr old feed on smaller fish and on Mysis (TL3); and other inverts & zooplankton (TL2)		
	American (Rainbow) smelt	*Osmerus mordax*	---	3.1	---	During first year, feed on zoopl.		
	Juvenile night smelt	*Spirinchus starksi*	---	3	---	Assumed same as other smelt	3	
	Juvenile top smelt (Osmeridae)	---	---	3	---	Assumption	3	
	surf smelt	*Hypomesus pretiosus*	---	3	---	Assumed same TL as other smelt.	3	

Table 2.4.9: Trophic Level Assignment of Aquatic Species Corresponding to CSFII Consumption Categories

CSFII Consumption Category	Common Name	Scientific Name	Size	Trophic Level [a] (Mean)	Trophic Level [a] (Range)	Notes [a]	Species Assigned Trophic Level [b]	CSFII Assigned Trophic Level [c]
Sturgeon	White sturgeon	*Acipenser transmontanus*	---	---	3-4	Estimated range based on following account by Jordan & Evermann (1969): Can grow to several hundred pounds, diet reportedly consists of small plants & small animals, including small fish. One young specimen (25 in.) had 11 minnows in its stomach, larger specimens had several suckers about 12 in. long. (Jordan & Evermann, 1969).	4	4
	Lake sturgeon	*Acipenser rubicundus*	---	—	3-4	Estimated range based on following account by Jordan & Evermann (1969): Can grow up to 100 pounds, averages about 40-50 pounds for adults; primarily a bottom feeder, reportedly feeding on small gastropods, crustaceans, insect larvae and small fishes	4	
Trout	Brook trout	*Salvelinus fontinalis*	10-40cm	3.2	---	10-40cm; at most, 7-8% fish in diet; remainder primarily benthic inverts. but also some zoopl. in some populations	3	4
	Cutthroat trout	*Salmo clarki*	< 40cm	3	---	< 40cm; consumes invertebrates	4	
			> 40cm	3.2	---	> 40cm; becomes piscivorous		

Table 2.4.9: Trophic Level Assignment of Aquatic Species Corresponding to CSFII Consumption Categories

CSFII Consumption Category	Common Name	Scientific Name	Size	Trophic Level [a] (Mean)	Trophic Level [a] (Range)	Notes [a]	Species Assigned Trophic Level [b]	CSFII Assigned Trophic Level [c]
Trout (cont'd)			old adults	4	---	Assumption for oldest specimens		
	Dolly Varden trout	*Salvelinus malma*	—	---	3-4	TL changes with age	4	
			10-30cm	3	---	10-30cm; diet 100% benthic inverts.		
	Dolly Varden trout	*Salvelinus malma*	30-40cm	3.75	---	30-40cm; diet 75% fish, 17% benthic inverts.		
			> 40cm	4	---	> 40cm; diet consists of 100% fish		
	Lake trout	*Salvelinus namaycush*	20-30cm	3.7	3.5-4.0	20-30cm; feeds primarily on small fish (70%) and benthic inverts. (30%)	4	
			30-40cm	3.9	3.7-4.1	30-40cm; feeds primarily on fish (90%) and some benthic inverts. (10%)		
			>40cm	4.2	4.0-4.5	> 40cm; feeds entirely on fish; in L. Michigan, feed on alewives, which feed on *Mysis*, which feed on zoopl.		
	Rainbow trout	*Oncorhynchus mykiss*	< 30cm	3	---	< 30cm; diet completely of benthic inverts. or both inverts. & zoopl.	4	
			30-50cm	3.6	---	30-50cm; diet 35-90%fish, 25-75% benthic inverts, zoopl., terrestrial insects		
			> 50cm	4	---	> 50cm; diet of 100% fish		

Footnotes:

(a) Unless otherwise specified, information on trophic status was obtained from U.S. EPA, (1995d, 1995e, 1995f). Game fish data were limited to specimens considered to be representative of the edible size range (i.e., sizes ranges of 20cm or larger).

(b) In determining species trophic level assignments, preference was given to data on larger specimens. Trophic level 4 was assigned to a species with data indicating TL 3.5 or higher; trophic level 3 was assigned to a species with data indicating TL 2.5 to 3.4; trophic level 2 assigned for TL 1.5-2.4.

(c) In determining CSFII category trophic level assignments, best professional judgement was used. For example, the CSFII category for catfish includes 4 species that are assigned TL3 and 3 species assigned as TL4. Thus, it is assumed that half (50%) of consumption in the catfish CSFII category is from TL3 and half from TL4. Except for shrimp, all other CSFII categories included species that either were exclusively or predominately one trophic level (e.g., trout, estuarine flatfish, smelt).

Calculation of Consumption-Weighted Lipid Content, by Trophic Level. Using consumption rate data from CSFII (daily average per capita estimates of individuals 18 years and older– Table 2.4.7), the mean lipid content estimated for organisms assigned to each CSFII category (Table 2.4.8), and the trophic level assignments of each CSFII consumption category (Table 2.4.9), consumption weighted mean lipid content determined within each trophic level according to the following equation.

$$f = \sum \left[\frac{CR_i}{CR_{tot}} \bullet f_{,i} \right]$$

(Equation 2.4.26)

where:

f	=	Lipid fraction representative of aquatic species eaten by the target population that correspond to a given trophic level
CR_i	=	Consumption rate of species "i" of a given trophic level eaten by the target population
CR_{tot}	=	Consumption rate of all species at that same trophic level eaten by the target population
$f_{,i}$	=	Lipid fraction of species "i" eaten by the target population

Calculation of the consumption-weighted lipid content values is shown in Table 2.4.10. The mean, consumption weighted percent lipid values were calculated as (expressed here to 2 significant figures for convenience):

Trophic Level Two: 2.3%
Trophic Level Three: 1.5%
Trophic Level Four: 3.1%

Because of limitations in the availability and precision of the used to estimate consumption rates, lipid content, and trophic level status, uncertainty exists in the estimation of national default, consumption-weighted lipid content. To illustrate some of this uncertainty, “high” and “low” estimates of the consumption weighted lipid content values were determined using the species with the highest and lowest species mean lipid value, respectively, within each CSFII category. “High” and “low” estimates of percent lipid content values within each trophic level are:

“High” Estimate for Trophic Level Two: 3.0%
“High” Estimate for Trophic Level Three: 2.2%
“High” Estimate for Trophic Level Four: 6.2%

“Low” Estimate for Trophic Level Two: 1.5%
“Low” Estimate for Trophic Level Three: 0.77%
“Low” Estimate for Trophic Level Four: 0.91%

The reason that there is not a greater difference between the mean lipid content values (where each species within a CSFII category was given equal weighting) and the "high" and "low" estimates is likely because the mean consumption rates in the CSFII survey are weighted heavily by relatively lean aquatic organisms such as shrimp, crab, perch, and flounder. Therefore, because the consumption of aquatic organisms may differ on a local or regional basis from that reflected in the CSFII survey, EPA recommends that States and Tribes give preference to using local and regional data on consumption patterns over national default estimates, when available.

2.4.5.4 Freely Dissolved Fraction

The next step in calculating a BAF used in deriving an AWQC involves adjusting the baseline BAF to account for the freely fraction of the chemical at the site(s) to which the AWQC will apply. The same equation used to estimate the freely dissolved fraction for determining a baseline BAF (Equation 2.4.11) is used to estimate the freely dissolved fraction for determining the AWQC BAF. However, in this case, however, the POC and DOC values should be based on the site(s) where the BAF and the criterion will be applied and not where the samples were collected for determining the BAF. If POC and DOC data are not available for the site(s) to which the AWQC will apply, then data from sites closely related to those to which the AWQC sites can be used. Care should be taken to ensure that conditions affecting the POC and DOC concentrations at the surrogate sites are representative of conditions at the AWQC sites. States and tribes are encouraged to use local or regional data when appropriate and scientifically defensible. If such data are unavailable, then the default values for POC and DOC can be used. EPA has developed national default values of 0.48 mg/L (4.8×10^{-7} kg/L) for POC and 2.9 mg/L (2.9×10^{-6} kg/L) for DOC. Both of these values are 50^{th} percentile values (medians) based on an analysis of over 132,000 DOC values and 81,000 POC values contained in EPA's STORET data base. These default values reflect the combination of values for streams, lakes and estuaries across the United States. Further delineation of the POC and DOC concentrations in different water body types is provided in Table 2.4.11. These default values, which are derived at a more disaggregated level may provide more appropriate estimates of POC and DOC concentrations associated with the field BAF study compared to the national default medians listed above. The K_{ow} value for the chemical is the same as used for deriving the baseline BAF for the chemical.

Table 2.4.10: Calculation of National Default Consumption-Weighted Mean Lipid Content of Consumed Aquatic Organisms

Habitat	CSFII Category[1]	Assigned Trophic Level[2]	Trophic Level Weighting Factor[3]	Average Percent Lipids[4]	Mean Consumption Rate (g/person/day)	Trophic Level Weighted Mean Consumption rate (g/person/day)	CSFII Category Weights	Consumption-Weighted Percent Lipid Values
Estuarine	clam	2	1.0	1.68	0.03146	0.03146	0.09046	0.15219
Estuarine	mullet	2	1.0	4.49	0.08756	0.08756	0.25176	1.13069
Estuarine	oyster	2	1.0	1.62	0.22555	0.22555	0.64852	1.05162
Estuarine	scallop	2	1.0	0.70	0.00322	0.00322	0.00926	0.00648
Estuarine	anchovy	3	1.0	7.25	0.00292	0.00292	0.00078	0.00568
Freshwater	carp	3	1.0	4.45	0.05727	0.05727	0.01538	0.06842
Freshwater	catfish	3	0.5	2.36	1.18227	0.59114	0.15874	0.37486
Estuarine	crab	3	1.0	1.40	0.37126	0.37126	0.09970	0.13918
Estuarine	croaker	3	1.0	4.77	0.06749	0.06749	0.01812	0.08648
Estuarine	estuarine flatfish	3	1.0	1.48	0.52735	0.52735	0.14161	0.20927
Estuarine	flounder	3	1.0	0.87	0.29941	0.29941	0.08040	0.07022
Estuarine	herring	3	1.0	10.34	0.03925	0.03925	0.01054	0.10897
Estuarine	scup	3	1.0	3.70	0.00068	0.00068	0.00018	0.00068
Estuarine	shrimp	3	1.0	0.75	1.72959	1.72959	0.46446	0.34821
Estuarine	smelt	3	1.0	4.50	0.03753	0.03753	0.01008	0.04535
Freshwater	catfish	4	0.5	2.36	1.18227	0.59114	0.35205	0.83133
Freshwater	freshwater salmon	4	1.0	2.28	0.01096	0.01096	0.00653	0.01486
Estuarine	perch	4	1.0	3.00	0.60368	0.60368	0.35952	1.07956
Freshwater	pike	4	1.0	0.84	0.02337	0.02337	0.01392	0.01168
Estuarine	sturgeon	4	1.0	1.09	0.00054	0.00054	0.00032	0.00035
Freshwater	trout	4	1.0	4.29	0.44946	0.44946	0.26767	1.14837

Trophic Level	Sum of Consumption Rates (g/pers./day)	Sum of Weights	Consumption-Weighted Mean Percent Lipid
Trophic Level 2	0.34779	1.00	**2.34%**
Trophic Level 3	3.72389	1.00	**1.46%**
Trophic Level 4	1.67915	1.00	**3.09%**
	Total: 5.75082		

[1] Source of consumption data: USDA's *Continuing Survey of Food Intakes by Individuals (CSFII)* combined from 1989, 1990 & 1991 for individuals 18 years and older (USEPA, 1998b and Table 2.4.7).
[2] Trophic level designation of organisms corresponding to CSFII consumption categories, as described in the text and Table 2.4.9.
[3] Trophic level weighing factor used to apportion consumption rates to multiple trophic levels for catfish only (see text).
[4] Mean lipid content for species assigned to each CSFII category as described in the text and Table 2.4.8.

Table 2.4.11: National Default Values for POC and DOC in U.S. Water Bodies

WATER BODY TYPE	DOC (mg/L)		POC (mg/L)	
	50th% (Median)	Mean	50th% (Median)	Mean
Stream/River	4.0	6.2	0.70	1.3
Lake	2.1	3.0	0.31	0.43
Estuary	2.7	3.4	0.90	1.1
All Types	2.9	4.9	0.48	0.83

Source: USEPA STORET data base, data retrieval February, 1996.
Sample sizes for DOC are: 77,637 (stream/river); 40,472 (lake); 14,376 (estuary); 132,485 (all water bodies)
Sample sizes for POC are: 30,236 (stream/river); 39,931 (lake); 10,920 (estuary); 81,087 (all water bodies)

2.4.6 Determining BAFs for Inorganic Substances

Unlike organic chemicals, the lipid-BAF relationship does not generally apply to the determination of BAFs for inorganic chemicals. Thus, BAFs and BCFs for inorganics should not be expressed on a lipid-normalized basis, and are not as transferable from one species to another, or one tissue to another, as with organic chemicals. Bioaccumulation of some trace metals is substantially greater in internal organs than muscle tissue. For example, BCFs for various tissues of the rainbow trout after exposure to cadmium for 178 days are as follows (Giles, 1988):

liver	325
kidney	75
gut and skin	7
muscle	1

Merlini and Pozzi (1977) reported that lead bioconcentrated 30 times more in bluegill liver than in bluegill muscle tissue after eight days. Because of the differential uptake to different tissues and species, the BAFs should be measured in edible tissues.

BAFs or BCFs measured in plants or invertebrate animals may be available. However, these factors might be one or more orders of magnitude greater than BAFs or BCFs for the edible tissue of fish as noted in Table 5 in each of the EPA criteria documents for cadmium, copper, lead and nickel (USEPA, 1985a; USEPA, 1985b; USEPA, 1985c; and USEPA, 1986). For this reason, invertebrate BAFs and BCFs should only be used in the derivation of human health criteria when they are considered to be a significant component of the diet of the target consumers.

Although bioaccumulation of many inorganic chemicals is similar to their bioconcentration, mercury and certain other metals are subject to methylation through microbial action in nature, and may biomagnify through the food chain. For example, research demonstrates that methyl mercury is bioaccumulative in fish and biomagnifies in aquatic food webs (Grieb et al. 1990; Gardner, 1978).

The following two procedures, in order of priority, should be used to estimate BAFs for inorganic chemicals. EPA is not aware of any other generic procedures for predicting the BAF for these substances.

Field-measured BAFs are the most preferred BAFs for inorganic chemicals. Section 2.4.4.1 (*Field-Measured BAFs*) describes data requirements for measuring BAF values using field data for nonpolar organic chemicals. These requirements are applicable to field-measured BAFs for inorganic chemicals as well, except that inorganic BAFs should not be lipid-normalized because bioaccumulation of inorganics is not proportional to lipid content. However, as noted above, inorganic bioaccumulation can differ dramatically between tissues. Thus, BAFs based on uptake into edible tissue should be used to calculate human health criteria.

If field-measured BAFs are not available for inorganic chemicals, a laboratory BCF may be used to estimate bioaccumulation of inorganic substances from water. The BCF may be used because for most inorganic substances, bioaccumulation and bioconcentration are similar. Section 2.4.4.3 (*Predicted BAF Based on Laboratory-Measured BCF and a Food-Chain Multiplier*) describes acceptable data for measuring BCFs for organic chemicals in the laboratory, which are applicable to BCFs measured for inorganic chemicals. For inorganic chemicals where dietary exposure forms a significant portion of the exposure to target organisms, (e.g. mercury, selenium) BCFs should be used in conjunction with field-derived food chain multipliers.

2.4.7 Example Calculations

The two examples below illustrate how BAFs are developed using two of the four methods recommended for deriving BAFs for nonpolar organic chemicals for use in establishing AWQC for human health. The first example illustrates the development of a BAF when field-measured BAFs are available. The second example illustrates the development of BAFs using a laboratory-measured BCF and a food-chain multiplier.

2.4.7.1 Example 1: Field-Measured BAF for Chemical M

The calculation of a BAF used in the derivation of a human health criteria is a two-step process. The first step is to derive baseline BAFs for appropriate trophic levels. The second step is to derive BAFs that can be used in deriving human health AWQC. Each of these steps are illustrated below.

Baseline BAF for Chemical M

This example illustrates the development of a baseline BAF appropriate for trophic level four for a lipophilic chemical M. Data are available from Lake Washington (a hypothetical lake) on the total concentration of chemical M in fish tissue in lake trout and the water column. A review of the dietary preferences of lake trout indicates that this organism is at trophic level four for larger size ranges commonly consumed by the target population (USEPA, 1995d, 1995e, 1995f). The development of a baseline BAF for a given trophic level requires information on a field-measured BAF (Measured BAF_T^t), the fraction of the chemical that is freely dissolved in the ambient water (f_{fd}), and the fraction lipid content of the species sampled (f). The equation for calculating a baseline BAF using a field-measured BAF is:

$$\text{Baseline BAF}^{fd} = \left[\frac{\text{Measured BAF}_T^t}{f_{fd}} - 1 \right] \left(\frac{1}{f} \right)$$

(Equation 2.4.27)

To determine a field-measured BAF, information is needed on the total concentration of chemical M in fish tissue and in ambient water at the site of sampling. For this example, the mean total concentration for chemical M in fish tissue is 100 ng/g and the mean total water column concentration 160 pg/L. Data from the field studies indicates that the mean water column concentration reflects adequate temporal and spatial averaging based on the K_{ow} of this chemical and is representative of the average exposure of fish to chemical M. The field-measured BAF_T^t for chemical M is 625,000 L/kg, as demonstrated below.

$$\text{Field-measured BAF}_T^t = \frac{\text{Total concentration of chemical M in fish tissue}}{\text{Total concentration of chemical M in the water column}}$$

(Equation 2.4.28)

$$\text{Field-measured BAF}_T^t = \frac{(100 \text{ ng/g})(1{,}000 \text{ pg/ng})(1{,}000 \text{ g/kg})}{160 \text{ pg/L}} = 625{,}000 \text{ L/kg-tissue}$$

(Equation 2.4.29)

To determine the fraction of chemical M that is freely dissolved in the ambient water requires information on the particulate organic carbon (POC) and dissolved organic carbon (DOC) in the ambient water where the samples were collected and the K_{ow} of chemical M. For this example, the median POC concentration from Lake Washington, where the samples were collected, is 0.6 mg/L

(6.0×10^{-7} kg/L) and the median DOC concentration is 8.0 mg/L (8.0×10^{-6} kg/L). Importantly, the POC and DOC concentrations used in calculating the freely dissolved fraction for baseline BAFs is from the waterbody used in the BAF study. Use of default POC and DOC concentrations in the derivation of baseline BAFs is not appropriate. The K_{ow} for chemical M is 100,000 or a log K_{ow} of 5.0. The fraction freely dissolved for chemical M is 0.8722, as shown below.

$$f_{fd} = \frac{1}{[1 + (POC \cdot K_{ow}) + (DOC \cdot \frac{K_{ow}}{10})]}$$

(Equation 2.4.30)

$$f_{fd} = \frac{1}{[1 + (6.0 \times 10^{-7} \text{kg/L} \cdot 100{,}000 \text{ L/kg}) + (8.0 \times 10^{-6} \text{ kg/L} \cdot \frac{100{,}000}{10} \text{ L/kg})]} = 0.8772$$

(Equation 2.4.31)

The freely dissolved fraction has been expressed to four significant digits for convenience. The scientific basis supporting this equation for estimating the freely dissolved fraction is described in Section 2.4.4.1 and Appendix D.

Finally, the mean fraction lipid content of the fish species sampled in Lake Washington was 8 percent. Using the baseline BAF equation and information on the field-measured BAF, the fraction freely dissolved, and the fraction lipid content provides a baseline BAF for lake trout of 8,906,166, which is illustrated below.

$$\text{Baseline BAF}^{fd} = \left[\frac{625{,}000}{0.8772} - 1\right]\left(\frac{1}{0.08}\right) = 8{,}906{,}166 \text{ L/kg-lipid}$$

(Equation 2.4.32)

For the purposes of this example, it has been assumed that only one acceptable BAF value is available for trophic level four organisms. Thus, the baseline BAF for trophic level four is equal to this baseline BAF. Had other acceptable field-measured BAFs been available for trophic-level four

organisms, then the baseline BAF for trophic level four would have been calculated as the geometric mean of the acceptable baseline BAFs at trophic level four.

BAF for Chemical M to Be Used in Deriving AWQC

After the derivation of trophic level-specific baseline BAFs for chemical M (described in the previous section), the next step is to calculate BAFs that will be used in the derivation of AWQC. This step is necessary to adjust the baseline BAFs to conditions that are expected to affect the bioavailability of chemical M at the sites applicable to the AWQC. Derivation of AWQC BAFs requires information on: (1) the baseline BAF at appropriate trophic levels, (2) the percent lipid of the aquatic organisms consumed by humans at the site(s) of interest (trophic level specific), and (3) the freely dissolved fraction of the chemical in ambient water at the site(s) of interest. For each trophic level, the equation for deriving a BAF to used in deriving AWQC is:

$$\text{BAF for AWQC}_{(TL\ n)} = [(\text{Baseline BAF}^{fd})_{TL\ n} \cdot (f)_{TL\ n} + 1] \cdot (f_{fd})$$

(Equation 2.4.33)

where:

BAF for AWQC $_{(TL\ n)}$	=	BAF at trophic level "n" used to derive AWQC based on site conditions for lipid content of consumed aquatic organisms for trophic level "n" and the freely dissolved fraction in the site water
Baseline BAF^{fd} $_{(TL\ n)}$	=	BAF expressed on a freely dissolved and lipid-normalized basis for trophic level "n"
$f_{(TL\ n)}$	=	Fraction lipid of aquatic species consumed at trophic level "n"
f_{fd}	=	Fraction of the total chemical in water that is freely dissolved

For the purposes of this example, an AWQC BAF is being calculated only for aquatic organisms at one trophic level (trophic level four). If fish consumption data indicates the target population consumes significant quantities from multiple trophic levels, then AWQC BAFs should be derived for each of the appropriate trophic levels.

For chemical M, the baseline BAF at trophic level four is calculated to be 8,906,166 L/kg-lipid as described above. The fraction lipid content of aquatic species consumed by the target population at trophic level four is assumed to be 3.1% based on the national default lipid content for trophic level four derived in Section 2.4.5.3. The freely dissolved fraction of chemical M that is expected in the sites applicable to the AWQC was determined to be 0.9615. This value is calculated as shown below using hypothetical expected POC and DOC concentrations at the sites applicable to the AWQC of

0.3 mg/L (3.0×10^{-7} kg/L) and 1.0 mg/L (1.0×10^{-6} kg/L), respectively, and the same K_{ow} of 100,000 for chemical M.

$$f_{fd} = \frac{1}{[1 + (POC \cdot K_{ow}) + (DOC \cdot \frac{K_{ow}}{10})]}$$

(Equation 2.4.34)

$$f_{fd} = \frac{1}{[1 + (3.0 \times 10^{7}\ kg/L \cdot 100{,}000\ L/kg) + (1.0 \times 10^{6}\ kg/L \cdot \frac{100{,}000}{10}\ L/kg)]}$$

(Equation 2.4.35)

$$f_{fd} = 0.9615$$

Using the AWQC BAF equation described previously, the AWQC BAF for trophic level four organisms is calculated to be 265,463 L/kg as shown below.

AWQC BAF for Trophic Level Four

= [(8,906,166 L/kg-lipid)•(0.031) +1] • (0.9615)

= 265,463 L/kg-tissue

This AWQC BAF relates the total concentration in water to the total concentration in tissue of trophic level four organisms, based on the expected conditions that would affect the bioavailability of chemical M (i.e., freely dissolved fraction at AWQC sites and lipid content of consumed aquatic organisms).

2.4.7.2 Example 2: Laboratory-Measured BCF for Chemical R

When a field-measured BAF_T^t or field-measured BSAF are not available, a laboratory-measured BAF_T^t along with a food-chain multiplier should be used to derive a baseline BAF and then an AWQC BAF for use in deriving human health criteria.

Baseline BAF for Chemical R

The development of a baseline BAF^{fd} for chemical R specific to a given trophic level requires information on a laboratory measured BCF (measured BCF_T^t), the fraction of the chemical that is freely dissolved in the test water (f_{fd}), the fraction lipid content of the species sampled (f), and the food-chain multiplier for the chemical (FCM). For a given trophic level, the equation for calculating a baseline BAF^{fd} using a laboratory BCF_T^t and food-chain multiplier is:

$$\text{Baseline BAF}^{fd} = (\text{FCM})\left[\frac{\text{Measured BCF}_T^t}{f_{fd}} - 1\right]\left(\frac{1}{f}\right)$$

(Equation 2.4.36)

The basis of this equation is described in Section 2.4.4.3.

The laboratory-measured BCF requires information on the total concentration of chemical R in fish tissue and the total concentration of chemical R in the test water. For this example, the mean total fish tissue concentration for chemical R is 10 ng/g and the mean total test water concentration is 3 ng/L. The laboratory-measured BCF is 3333 L/kg.

$$\text{Laboratory measured BCF}_T^t = \frac{\text{Total concentration of chemical R in fish tissue}}{\text{Total concentration of chemical R in test water}}$$

(Equation 2.4.37)

$$\text{Laboratory measured BCF}_T^t = \frac{(10\ \text{ng/g})(1{,}000\ \text{g/Kg})}{3\ \text{ng/L}} = 3333\ \text{L/kg - tissue}$$

(Equation 2.4.38)

To determine the fraction of chemical R that is freely dissolved in the test water requires information on the particulate organic carbon (POC) and dissolved organic carbon (DOC) in the test water and the K_{ow} of chemical R. For this example, the median POC concentration in the test water is 0.6 mg/L (6.0×10^{-7} kg/L) and the median DOC concentration is 8.0 mg/L (8.0×10^{-6} kg/L). The K_{ow} for chemical R is 10,000 or a log K_{ow} of 4.0. The fraction freely dissolved for chemical R is 0.9860, as shown below.

$$f_{fd} = \frac{1}{[1 + (\text{POC} \cdot K_{ow}) + (\text{DOC} \cdot \frac{K_{ow}}{10})]}$$

(Equation 2.4.39)

$$f_{fd} = \frac{1}{[1 + (6.0 \times 10^{-7}\ \text{kg/L} \cdot 10{,}000\ \text{L/kg}) + (8.0 \times 10^{-6}\ \text{kg/L} \cdot \frac{10{,}000}{10}\ \text{L/kg})]} = 0.9862$$

(Equation 2.4.40)

The freely dissolved fraction has been expressed to four significant digits for convenience. The scientific basis supporting this equation is explained in Section 2.4.4.1 and Appendix D.

The fraction lipid content of the fish species sampled in the laboratory is 8 percent. The food-chain multiplier based on a log K_{ow} of 4 is 1.072, as indicated in Table 2.4.4 (assuming mixed benthic and pelagic food web structure and trophic level four for the tested species). Using the baseline BAF^{fd} equation and the information on the laboratory-measured BCF_T^t, the fraction freely dissolved, the fraction lipid content, and the FCM provides a baseline BAF^{fd} of 45,274 L/kg - lipid, which is used in the derivation of the BAF as described in the next section.

$$\text{Baseline BAF}^{fd} = (1.072)\left[\frac{3333}{0.9862} - 1\right]\left(\frac{1}{0.08}\right) = 45{,}274\ \text{L/kg-lipid}$$

(Equation 2.4.41)

For the purposes of this example, it has been assumed that only one acceptable baseline BAF value could be derived for trophic level four organisms. Thus, the baseline BAF for trophic level four is equal to this baseline BAF. Had other acceptable BCFs been available for trophic-level four organisms, then the trophic level four baseline BAF would have been calculated as the geometric mean of the acceptable BCF-predicted baseline BAFs for trophic level four.

AWQC BAF for Chemical R

After the derivation of trophic level-specific baseline BAFs for chemical R (described in the previous section), the next step is to calculate BAFs that will be used in the derivation of AWQC. This step is necessary to adjust the baseline BAFs to conditions that are expected to affect the bioavailability of chemical R at the sites applicable to the AWQC. Derivation of AWQC BAFs requires information on: (1) the baseline BAF at appropriate trophic levels, (2) the percent lipid of the aquatic organisms consumed by humans at the site(s) of interest (trophic level specific), and (3) the freely dissolved fraction of the chemical in ambient water at the site(s) of interest. For each trophic level, the equation for deriving a BAF to used in deriving AWQC is:

$$\text{BAF for AWQC}_{(TL\ n)} = [(\text{Baseline BAF}^{fd})_{TL\ n} \cdot (f)_{TL\ n} + 1] \cdot (f_{fd})$$

(Equation 2.4.42)

where:

BAF for AWQC $_{(TL\ n)}$	=	BAF at trophic level "n" used to derive AWQC based on site conditions for lipid content of consumed aquatic organisms for trophic level "n" and the freely dissolved fraction in the site water
Baseline BAF^{fd} $_{(TL\ n)}$	=	BAF expressed on a freely dissolved and lipid-normalized basis for trophic level "n"
$f_{(TL\ n)}$	=	Fraction lipid of aquatic species consumed at trophic level "n"
f_{fd}	=	Fraction of the total chemical in water that is freely dissolved

For the purposes of this example, an AWQC BAF for chemical R is being calculated only for aquatic organisms at one trophic level (trophic level four). If fish consumption data indicates the target population consumes significant quantities from multiple trophic levels, then AWQC BAFs should be derived for each of the appropriate trophic levels.

For chemical R, the baseline BAF at trophic level four is calculated to be 45,274 L/kg-lipid as described above. The fraction lipid content of aquatic species consumed at trophic level four is assumed to be 3.1% based on the national default lipid content for trophic level four derived in Section 2.4.5.3. The freely dissolved fraction of chemical R that is expected in the sites applicable to the AWQC was determined to be 0.9924. This value is calculated as shown below using hypothetical expected POC and DOC concentrations at the sites applicable to the AWQC of 0.48 mg/L (4.8×10^{-7} kg/L) and 2.9 mg/L (2.9×10^{-6} kg/L), respectively, and the same K_{ow} of 10,000 for chemical R.

$$f_{fd} = \frac{1}{[1 + (POC \cdot K_{ow}) + (DOC \cdot \frac{K_{ow}}{10})]}$$

(Equation 2.4.43)

$$f_{fd} = \frac{1}{[1 + (4.8 \times 10^{7}\ kg/L \cdot 10{,}000\ L/kg) + (2.9 \times 10^{6}\ kg/L \cdot \frac{10{,}000}{10}\ L/kg)}$$

(Equation 2.4.44)

$$f_{fd} = 0.9924$$

Using the AWQC BAF equation described previously, the AWQC BAF for trophic level four organisms is calculated to be 1,394 L/kg as shown below.

AWQC BAF for Trophic Level Four

= [45,274 L/kg-lipid)•(0.031) +1] • (0.9924)

= 1,394 L/kg-tissue

This AWQC BAF relates the total concentration in water to the total concentration in tissue of trophic level four organisms, based on the expected conditions that would affect the bioavailability of chemical R (i.e., freely dissolved fraction at AWQC sites and lipid content of consumed aquatic organisms).

2.4.8 Trophic Level-Specific Fish Consumption Rates

When local or regional data are unavailable for calculating fish and shellfish consumption rates, EPA has derived national default consumption rates of 17.8 g/person/d, 39 g/person/d, and 86.3 g/person/d based on the 90th, 95th and 99th percentile of average per capita fish consumption from the adult U.S. population (see Section 2.3 on exposure). These default consumption figures reflect total consumption of aquatic organisms across all trophic levels. However, as described in above, EPA recommends that BAFs be determined separately for specific trophic levels because accumulation of chemicals is often related to the trophic position of the aquatic organism, particularly for highly persistent, lipophilic organic chemicals. The question then becomes how to best relate available fish consumption rates to the trophic level-specific BAFs in the calculation of AWQC.

When calculating AWQC, EPA recommends that if possible, fish consumption rates be determined for individual trophic levels for which BAFs have been derived. For example, if available fish and shellfish consumption survey data indicate that the target population is consuming significant portions of aquatic organisms at trophic levels two, three, and four, then both BAFs and fish consumption rates should be determined for each of these trophic levels to provide the most accurate representation of contaminant exposure via the consumption of aquatic organisms. In this example, applying the total consumption rate from all three trophic levels to a BAF that is derived for a single trophic level may not accurately reflect likely exposure to the target population, if BAFs differ greatly by trophic level.

Calculating fish consumption rates for individual trophic levels requires information on the trophic status of consumed species from the consumption survey. Determination of trophic status of aquatic organisms is best determined on a local or regional basis and should involve consideration of the size (age) of aquatic organisms in addition to their dietary preferences. If local or regional information is not available, then EPA recommends the use of the most recent version of the document: *Trophic Level and Exposure Analysis for Selected Piscivorous Birds and Mammals* (USEPA 1995d, 1995e, 1995f), which contains information on the dietary composition of numerous aquatic species. This draft document is currently being revised based on peer review comments and is expected to be made final in 1998. Described below is the derivation of trophic level-specific fish consumption rates for EPA's CSFII-based, national default fish consumption rates listed above.

In estimating trophic level-specific consumption rates appropriate to the national default consumption rates from the CSFII consumption survey (USEPA, 1998b), EPA first estimated the trophic level of aquatic organisms corresponding to each of the CSFII consumption categories for mean per capita consumption of adults (see Table 2.4.9 and associated text for trophic level determinations of the various CSFII consumption categories; see Table 2.4.7 for mean per capita consumption rates from the CSFII survey). Since the national default consumption rates of 17.8, 39.0, and 86.3 g/person/day reflect consumption at the 90th, 95th and 99th percentiles, respectively, trophic level assignments would have ideally been made according to consumption patterns corresponding to these higher percentiles because consumption patterns might differ at higher percentiles. However, inherent limitations in the data from the CSFII survey prevented a meaningful assessment of consumption patterns at these upper percentiles. Therefore, the consumption pattern reflective of mean per capita consumption rates was assumed to adequately reflect consumption at the higher consumption rate percentiles.

The second step involved calculating the fraction of total fish and shellfish consumption at trophic level two, three and four using the mean per capita consumption rates of adults from CSFII survey (Table 2.4.7). The fractions of total fish consumption at specific trophic levels is shown below:

$$f_{(FI,\ TL\ n)} = \frac{FI_{(TL\ n)}}{FI_{(all\ TL)}}$$

where:

$f_{(FI, TL\ n)}$	=	Fraction of total mean per capita fish consumption at trophic level "n"
$FI_{(TL\ n)}$	=	Mean per capita fish consumption rate at trophic level "n" (g/person/day)
$FI_{(TL\ all)}$	=	Total mean per capita fish consumption rate for all trophic levels (g/person/day)

Fraction total fish consumption at:

Trophic Level Two:	0.06048	= 0.34779 (g/pers./day) / 5.75082 (g/pers./day)
Trophic Level Three:	0.64754	= 3.72389 (g/pers./day) / 5.75082 (g/pers./day)
Trophic Level Four:	0.29198	= 1.67915 (g/pers./day) / 5.75082 (g/pers./day)

These fractions indicate that on a national, per capita average basis, the majority of fish and shellfish consumption is occurring at trophic level three, followed by trophic level trophic level four. This is corroborated by the comparatively greater consumption of shrimp, catfish, perch, estuarine flatfish, trout, crab, and flounder (Table 2.4.7). Finally, the trophic level-specific consumption rates

applicable to 90th, 95th, and 99th percentile national default consumption values were calculated using the following equation:

$$FI_{(TL\ n)}^{i^{th}\ percentile} = FI_{(all\ TL)}^{i^{th}\ percentile} \cdot f_{(FI,\ TL\ n)}$$

where:

$FI_{(TL\ n)}^{ith\ percentile}$	=	Estimated fish consumption rate at trophic level "n" for the i^{th} percentile
$FI_{(TL\ all)}^{ith\ percentile}$	=	Total fish consumption rate for all trophic levels for the i^{th} percentile
$f_{(FI,\ TL\ n)}$	=	Fraction of total mean per capita fish consumption at trophic level "n" (determined above)

Trophic level-specific consumption rates (in g/person/day) corresponding to the national default consumption rates of 17.8g/d, 39.0g/d, and 86.3g/d (i.e., the 90th, 95th and 99th percentile of mean per capita consumption of adults from the CSFII survey) are shown below.

	90th	95th	99th
TL2	1.1	2.4	5.2
TL3	11.5	25.2	55.9
TL4	5.2	11.4	25.2
All TL	17.8	39.0	86.3

EPA recognizes that in some situations, States and Tribes may lack sufficient data to determine trophic level-specific fish consumption rates that are applicable to their target populations and site(s) of concern. In these situations, EPA recommends that States and Tribes assign the total fish consumption rates to the highest BAF determined across the relevant trophic levels. In most cases, this will be the BAF corresponding to trophic level four, but in some cases, it may be trophic level three. This approach reflects a assumption that may be conservative, the degree to which will depend on the actual consumption pattern of the target population.

2.4.9 References

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3. MINIMUM DATA CONSIDERATIONS

3.1 Background

The 1980 AWQC National Guidelines did not present specific minimum data requirements. However, the following minimum data requirements were implied from the text:

3.1.1 Threshold Effects Guidelines

Animal dose-response toxicity data were used in developing guidelines for deriving criteria based on noncarcinogenic responses. The following guidelines for deriving criteria were adopted:

- A free-standing Frank Effect Level (FEL) is unsuitable for the derivation of criteria.

- A free-standing No Observed Effect Level (NOEL) is unsuitable for the derivation of criteria. If multiple NOELs are available, with or without additional data on Lowest Observed Effect Levels (LOELs), No Observed Adverse Effect Levels data (NOAELs), or Lowest Observed Adverse Effect Levels (LOAELs). The highest NOEL should be used to derive a criterion.

- A NOAEL, LOEL, or LOAEL can be suitable for criteria derivation. A well-defined NOAEL from a chronic study (90-day study was considered minimum) may be used directly, applying the appropriate uncertainty factor. For a LOEL, a judgment needs to be made as to whether it actually corresponds to a NOAEL or a LOAEL. In the case of a LOAEL, an additional uncertainty factor is applied; the magnitude of the additional uncertainty factor is judgmental and should lie in the range of 1 to 10. Caution must be exercised not to substitute FELs for LOAELs.

3.1.2 Non-Threshold Effects

This section discusses lifetime animal studies or human studies where excess cancer risk has been associated with exposure to the agent.

3.1.2.1 Animal Studies

- For some chemicals, several studies conducted at several doses and different routes of exposure are available for different animal species, strains, and sexes. A choice must be made as to which of the data sets from several studies are to be used in the model. The procedures listed below, used in evaluating these data, are consistent with the estimate of a maximum-likely-risk.

- The data (i.e., dose and tumor incidence) used in the model are data sets where the incidence is statistically significantly higher than the control for at least one test dose level and/or where the tumor incidence rate shows a statistically significantly trend with respect to dose level. The data set which gives the highest estimate of lifetime carcinogenic risk, q1*, estimated from each of these data sets, is used for risk assessment.

- If sufficient data exist for two or more significant tumor sites in the same study, the number of animals with at least one of the specific tumor sites under consideration was used as incidence data in the model.

- Since to a close approximation, the surface area is proportional to the 2/3 power of the weight as would be the case for a perfect sphere, the exposure in mg/(body weight)$^{2/3}$/day is similarly considered to be an equivalent exposure.

- Use data from organ sites which are statistically higher than the control data.

3.1.3 Exposure Assumptions

The three exposure-related parameters listed below were provided in the 1980 AWQC National Guidelines. Although the concept of accounting for dietary and inhalation exposures was included, no parameters were provided.

- 2 L/day drinking water consumption;
- 6.5 g/day consumption of fish; and
- Lipid-normalized bioconcentration factor (BCF).

3.2 Minimum Data Considerations in the *Federal Register* Notice

Many sections of the *Federal Register* notice which accompanies this Technical Support Document (TSD) include discussions of data quality. While many of these discussions are qualitative in nature, they may help direct the reader to the kinds of data which meet a minimally successful risk assessment. For example, in the exposure section, there is a discussion of what constitutes acceptable data for conducting a relative source contribution assessment; in addition, there is a discussion regarding minimally acceptable fish consumption surveys and data collection. In developing bioaccumulation factors, there is a discussion in the *Federal Register* of what is regarded as a minimally acceptable BCF and K_{ow}. That section also cites a field guidance document which will contain minimum data requirements for assessing field-measured BAFs and field-measured lipid levels and POC/DOC. Once this document is finalized in 1998, the results will be cited and incorporated into the final TSD.

On the toxicological side of the human health methodology, the following minimum data is suggested for RfD development:

3.2.1 Noncancer - Data Suggestions

3.2.1.1 RfD Development (Minimal Data)

- One well-conducted subchronic (90 days) mammalian bioassay by the oral route of exposure in which a NOAEL or LOAEL can be derived.
- If the most critical endpoint is an acute effect, which occurs short-term, it should be used as the basis of the RfD.
- One short-term developmental study, if it can be shown that the developmental toxicity endpoint is the critical effect given other subchronic or chronic studies.

- One developmental study cannot be used as the basis of an RfD on its own unless other studies exist to support its use.

Of course, a more ideal data set is preferred but not always available. The following data set is considered complete and likely to have much less uncertainty associated with the resulting RfD:

3.2.1.2 RfD Development (Ideal Situation)

- One well-conducted epidemiological study; or

- Two or more adequate chronic studies in two animal species, one of which must be with rodents, by the oral route of exposure in which one can identify a NOAEL and LOAEL; and

- One adequate mammalian multi-generation reproductive toxicity study by the oral route of exposure; and

- Two adequate mammalian developmental toxicity studies by the oral route of exposure in different species; and

- Mechanistic, pharmacokinetic and target organ toxicity data; and

- If the most critical endpoint is an acute effect, which occurs short-term, it should be used as the basis of the RfD.

- The species most biologically relevant to humans is known; in the absence of the most biologically relevant species, the most sensitive species is chosen as the basis for RfD development. For example, study results from an animal whose pharmacokinetics and toxicokinetics match those of a human would be considered the most biologically relevant.

Minimum data suggestions for benchmark and categorical regression analyses are currently evolving. However, the examples and text provided in this TSD under the noncancer section do provide some information of the data needs of each of these analyses.

3.2.2 Cancer - Data Suggestions

3.2.2.1 Minimum Data

A minimally acceptable data base for cancer assessment is one similar to the weight of evidence established by the 1986 Guidelines for Carcinogen Risk Assessment (e.g., A, B, and C classifications) fully described at 51 FR 33992 and in the *Federal Register* notice which accompanies

this TSD. However, such a data base may be lacking information on mode of action, which is important for making judgments using the new Cancer Guidelines of 1996 (61 FR 17960). At a minimum, some information is needed to determine the mode of action; otherwise, the chemical must be treated as a linear compound.

3.2.2.2 Ideal Situation

The goal is to establish a complete data base which includes not only adequate tumor data from chronic studies, as described above, but data on mode of action, metabolism, pharmacokinetics, and target toxicity. The ultimate goal in any cancer assessment is to establish the mechanism by which the cancer develops. Since the number of studies for a weight-of-evidence is yet to be established, there is no quantitative guidance being presented today. These minimum data requirements may be established in time to incorporate them into the final TSD. However, as with all determinations based on a weight-of-evidence, the number of studies which demonstrate (1) a carcinogenic effect in a number of animal species and sexes, and (2) a particular mode of action, determines the confidence in the overall weight of evidence.

3.2.3 Exposure - Data Suggestions

Numerous suggestions are made at the beginning of the exposure analyses section of this TSD regarding the factors used in the AWQC derivation. These factors include (1) body weight of the individuals exposed; (2) drinking water ingestion rates; (3) fish consumption rates; (4) incidental ingestion of water; and (5) the relative source contribution factor to account for other exposures. Body weights and fish intake assumptions are used in each criterion. The suggestions made are to help the exposure assessor locate sources of information for conducting exposure analyses and do not prescribe minimum data considerations. However, the specific approach to estimating non-water sources of exposure when setting AWQC (i.e., the Exposure Decision Tree Approach) discusses data adequacy considerations. This discussion is not repeated here; the reader is referred to the data adequacy subsection in Section 2.3.4.1 of this TSD.

3.3 Site-Specific Criterion Calculation

The 1980 AWQC National Guidelines allowed for site-specific modifications to reflect local environmental conditions and human exposure patterns. The methodology stated that "local" may refer to any appropriate geographic area where common aquatic environmental or exposure patterns exist. Thus "local" may signify a Statewide, regional, river reach or entire river.

In today's proposal, site-specific criteria may be developed as long as the site-specific data, either toxicological or exposure-related, is justifiable. For example, a State should use a site-specific fish consumption rate that represents at least the central tendency (median or mean) of the population surveyed (either sport or subsistence, or both). If a site-specific fish consumption rate for sport anglers or subsistence anglers is lower than an EPA default value, it may be used in calculating AWQC. To justify such a level (either higher or lower than EPA defaults) the State should present

survey data it used in arriving at the site-specific fish consumption rate. The same conditions apply to site-specific calculations of BAF, percent fish lipid, or the RSC. In the case of deviations from toxicological values (IRIS values: verified noncancer and cancer assessments), EPA recommends that the data upon which the deviation is based be presented to and approved by the Agency before a criterion is developed.

3.4 Organoleptic Criteria

The 1980 AWQC National Guidelines provided for the development of organoleptic criteria if organoleptic data were available for a specific contaminant. The methodology also made a clear distinction that organoleptic criteria and toxicity-based criteria are derived from completely different endpoints and that organoleptic criteria have no demonstrated relationship to potential adverse human health effects. The 1992 National Experts Workshop participants and the Great Lakes Committees of the Initiative both recommended that EPA place highest priority on setting toxicity-based criteria, rather then using limited resources to set organoleptic criteria. Both efforts, the GLI and the National Experts Workshop, concluded that organoleptic effects, while significant from an aesthetic standpoint, were not a significant health concern and did not merit significant expenditures of time and effort. While it can be argued that organoleptic properties indirectly affect human health (people may drink less water or eat less fish due to objectionable taste or odor), they have not been demonstrated to result in direct adverse effects, such as cancer or other types of toxicity.

3.5 Criteria for Chemical Classes

The 1980 AWQC National Guidelines allowed for the development of criteria for chemical classes. A chemical class was defined as any group of chemical compounds which were reviewed in a single risk assessment document. The Guidelines also stated that in criterion development, isomers should be regarded as part of a chemical class rather than as a single compound. A class criterion, therefore, was an estimate of risk/safety which applied to more than one member of a class. It involved the use of available data on one or more chemicals of a class to derive criteria for other compounds of the same class in the event that insufficient data were available to derive compound-specific criteria. The criterion applied to each member of the class, rather than to the sum of the compounds within the class. The 1980 methodology also acknowledged that, since relatively minor structural changes within the class of compounds can have pronounced effects on their biological activities, reliance on class criteria should be minimized.

The 1980 methodology prescribed the following analysis when developing a class criterion:

- A detailed review of the chemical and physical properties of the chemicals within the group should be made. A close relationship within the class with respect to chemical activity would suggest a similar potential to reach common biological sites within tissues. Likewise, similar lipid solubilities would suggest the possibility of comparable absorption and distribution.

- Qualitative and quantitative data for chemicals within the group are examined. Adequate toxicological data on a number of compounds with a group provide a more reasonable basis for extrapolation to other chemicals of the same class than minimal data on one chemical or a few chemicals within the group.

- Similarities in the nature of the toxicological response to chemicals in the class provide additional support for the prediction that the response to other members of the class may be similar. In contrast, where the biological response has been shown to differ markedly on a qualitative and quantitative basis for chemicals within a class, the extrapolation of a criterion to other members is not appropriate.

- Additional support for the validity of extrapolation of a criterion to other members of a class could be provided by evidence of similar metabolic and pharmacokinetic data for some members of the class.

The proposal in the *Federal Register* allows for the development of a criterion for classes of chemicals, as long as the 1980 methodology guidance is followed and a justification is provided through the analysis of mechanistic data, pharmacokinetic data, structure-activity relationship data, and limited acute and chronic toxicity data. When potency differences between members of a class are great (such as in the case of chlorinated dioxins and furans), toxicity equivalency factors (TEFs) may be more appropriately developed than one class criterion.

3.6 Criteria for Essential Elements

The 1980 AWQC National Guidelines acknowledged that developing criteria for essential elements, particularly metals, must be a balancing act between toxicity and essentiality. The 1980 guidelines state:

> that the criteria must consider essentiality and cannot be established at levels which would result in deficiency of the element in the human population. The difference between the RDA and the daily doses causing a specified risk level for carcinogens or the ADIs (now RfDs) for noncarcinogens defines the spread of daily doses from which the criterion may be derived. Because errors are inherent in defining both essential and maximum-tolerable levels, the criterion is derived from the dose levels near the center of such dose ranges.

In the current proposal, EPA endorses the guidance from the 1980 methodology and adds that the process for developing criteria for essential elements should be similar to that used for any other chemical with minor modifications. The RfD represents concern for one end of the exposure spectrum (toxicity), whereas the RDA represents the other end (minimum essentiality). Where the RDA and RfD values might occasionally appear to be similar in magnitude to one another, it does not imply incompatibility of the two methodological approaches, nor does it imply inaccuracy or error in either calculation.

Appendices

Appendix A

TABLE A.1
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 18 Years of Age or Older in the U.S. Population - Finfish and Shellfish

Grams/person/day				
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	5.59	4.91	6.28
	50th %	0.00	0.00	0.00
	90th %	17.80	14.89	20.63
	95th %	39.04	36.13	42.16
	99th %	86.30	81.99	96.67
Marine	Mean	12.42	11.55	13.29
	50th %	0.00	0.00	0.00
	90th %	45.98	44.48	48.34
	95th %	64.08	61.61	68.05
	99th %	111.38	101.94	120.49
All Fish	Mean	18.01	16.85	19.17
	50th %	0.00	0.00	0.00
	90th %	60.64	57.06	64.63
	95th %	86.25	80.29	91.00
	99th %	142.96	134.23	154.15

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 8,478 individuals to the U.S. population of 177,807,000 using 3-year combined survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.2
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 18 Years of Age or Older in the U.S. Population - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	75.56	66.37	84.75
	50th %	0.00	0.00	0.00
	90th %	242.49	205.05	277.26
	95th %	547.61	493.47	587.37
	99th %	1,171.84	1,123.52	1,252.78
Marine	Mean	172.86	160.73	184.99
	50th %	0.00	0.00	0.00
	90th %	624.83	598.84	670.34
	95th %	911.05	877.29	952.66
	99th %	1,573.20	1,468.43	1,713.17
All Fish	Mean	248.42	232.19	264.64
	50th %	0.00	0.00	0.00
	90th %	829.02	791.06	872.61
	95th %	1,197.36	1,133.18	1,264.74
	99th %	2,014.67	1,839.55	2,180.87

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 8,478 individuals to the U.S. population of 177,807,000 using 3-year combined survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.3
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals of Age 14 and Younger in the Acute Consumers[+] - Finfish and Shellfish

	Grams/person/day	
Habitat	**Statistic**	**Estimate**
Fresh/Estuarine	Mean	45.73
n = 295	50th %	28.35
N = 6,267,000	90th %	108.36
	95th %	136.24
	99th %	214.62
Marine	Mean	73.62
n = 663	50th %	56.00
N = 13,190,000	90th %	153.20
	95th %	176.90
	99th %	337.24
All Fish	Mean	74.80
n = 807	50th %	56.49
N = 16,159,000	90th %	153.70
	95th %	178.08
	99th %	337.46

[+] Note: Acute consumer = Individual who consumed fish at least once during the 3-day reporting period.
n = sample size
N = population size

Estimates are projected from a sample of acute consumers of age 14 and younger to the population of acute consumers of age 14 and younger using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.4
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals of Age 14 and Younger in the Acute Consumers[+] - Finfish and Shellfish

Milligrams/kilogram/person/day		
Habitat	**Statistic**	**Estimate**
Fresh/Estuarine	Mean	1,721.99
n = 295	50th %	1,271.12
N = 6,267,000	90th %	3,760.67
	95th %	4,208.18
	99th %	9,789.49
Marine	Mean	2,532.95
n = 663	50th %	2,107.05
N = 13,190,000	90th %	5,068.69
	95th %	6,376.47
	99th %	8,749.02
All Fish	Mean	2,624.35
n = 807	50th %	2,172.61
N = 16,159,000	90th %	5,020.14
	95th %	6,904.83
	99th %	10,384.82

[+] Note: Acute consumer = Individual who consumed fish at least once during the 3-day reporting period.
n = sample size
N = population size

Estimates are projected from a sample of acute consumers of age 14 and younger to the population of acute consumers of age 14 and younger using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.5
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Females of Age 15 to 44 in the Acute Consumers[+] - Finfish and Shellfish

	Grams/person/day	
Habitat	**Statistic**	**Estimate**
Fresh/Estuarine	Mean	61.40
n = 445	50th %	35.22
N = 10,853,000	90th %	148.83
	95th %	185.44
	99th %	363.56
Marine	Mean	76.53
n = 774	50th %	62.96
N = 17,967,000	90th %	149.78
	95th %	178.74
	99th %	271.06
All Fish	Mean	88.80
n = 952	50th %	69.95
N = 21,924,000	90th %	170.01
	95th %	212.56
	99th %	361.04

[+] Note: Acute consumer = Individual who consumed fish at least once during the 3-day reporting period.
n = sample size
N = population size

Estimates are projected from a sample of female acute consumers of age 15 to 44 to the population of female acute consumers of age 15 to 44 using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.6
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Females of Age 15 to 44 in the Acute Consumers[+] - Finfish and Shellfish

Milligrams/kilogram/person/day		
Habitat	**Statistic**	**Estimate**
Fresh/Estuarine	Mean	961.58
n = 445	50th %	533.18
N = 10,853,000	90th %	2,578.81
	95th %	3,403.75
	99th %	6,167.24
Marine	Mean	1,227.41
n = 774	50th %	986.25
N = 17,967,000	90th %	2,469.67
	95th %	3,007.98
	99th %	4,800.68
All Fish	Mean	1,414.54
n = 952	50th %	1,100.44
N = 21,924,000	90th %	2,726.46
	95th %	3,740.83
	99th %	6,703.25

[+] Note: Acute consumer = Individual who consumed fish at least once during the 3-day reporting period.
n = sample size
N = population size

Estimates are projected from a sample acute consumers of females of age 14 and younger to the population of acute consumers of females of age 14 and younger using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.7
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 18 Years of Age or Older in the Acute Consumers[+] - Finfish and Shellfish

		Grams/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	70.91	64.16	77.65
n = 1,541	50th %	42.45	37.24	46.91
N = 37,166,000	90th %	176.58	165.08	193.26
	95th %	230.41	224.00	255.55
	99th %	402.56	358.58	518.41
Marine	Mean	91.49	87.35	95.64
n = 2,432	50th %	77.56	74.89	78.52
N = 57,830,000	90th %	172.29	168.00	182.00
	95th %	215.62	201.99	225.63
	99th %	313.05	292.80	324.81
All Fish	Mean	106.39	102.37	110.41
n = 3,007	50th %	85.36	84.00	87.36
N = 70,949,000	90th %	206.76	197.84	213.00
	95th %	258.22	241.00	266.86
	99th %	399.26	336.50	423.56

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

[+] Note: Acute consumer = Individual who consumed fish at least once during the 3-day reporting period.
n = sample size
N = population size

Estimates are projected from a sample of acute consumers 18 years of age or older to the population of acute consumers 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.8
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 18 Years of Age or Older in the Acute Consumers[+] - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	959.15	867.58	1,050.72
n = 1,541	50th %	601.88	532.31	656.86
N = 37,166,000	90th %	2,442.97	2,233.16	2,606.66
	95th %	3,116.28	2,839.90	3,303.96
	99th %	5,151.98	4,432.30	6,931.61
Marine	Mean	1,270.78	1,214.65	1,326.90
n = 2,432	50th %	1,062.93	1,019.60	1,087.06
N = 57,830,000	90th %	2,467.68	2,331.88	2,585.09
	95th %	3,116.74	2,906.16	3,264.98
	99th %	4,250.22	4,037.74	4,387.96
All Fish	Mean	1,461.71	1,406.34	1,517.09
n = 3,007	50th %	1,189.29	1,156.77	1,225.43
N = 70,949,000	90th %	2,802.28	2,685.81	2,868.73
	95th %	3,588.11	3,308.93	3,798.54
	99th %	5,355.90	5,095.58	5,766.99

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

[+] Note: Acute consumer = Individual who consumed fish at least once during the 3-day reporting period.
n = sample size
N = population size

Estimates are projected from a sample of acute consumers 18 years of age or older to the population of acute consumers 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.9
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
U.S. Population - Finfish and Shellfish

Grams/person/day				
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	4.71	4.17	5.25
	50th %	0.00	0.00	0.00
	90th %	12.62	10.91	13.98
	95th %	32.16	29.81	35.15
	99th %	82.45	77.17	86.40
Marine	Mean	10.94	10.14	11.73
	50th %	0.00	0.00	0.00
	90th %	39.51	37.29	42.91
	95th %	59.62	57.03	61.84
	99th %	106.84	104.59	114.55
All Fish	Mean	15.65	14.67	16.63
	50th %	0.00	0.00	0.00
	90th %	55.02	51.38	56.00
	95th %	78.34	75.21	80.56
	99th %	133.46	125.27	140.21

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 11,912 individuals to the U.S. population of 242,707,000 using 3-year combined survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.10
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
U.S. Population - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	74.16	65.74	82.57
	50th %	0.00	0.00	0.00
	90th %	204.00	177.97	225.16
	95th %	547.64	505.10	565.37
	99th %	1,274.55	1,197.29	1,324.90
Marine	Mean	186.06	170.81	201.31
	50th %	0.00	0.00	0.00
	90th %	663.00	627.39	717.18
	95th %	991.96	960.40	1,044.69
	99th %	1,942.17	1,815.48	2,042.99
All Fish	Mean	260.22	242.60	277.83
	50th %	0.00	0.00	0.00
	90th %	880.47	844.35	918.79
	95th %	1,308.54	1,267.15	1,346.71
	99th %	2,356.54	2,224.54	2,556.68

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 11,912 individuals to the U.S. population of 242,707,000 using 3-year combined survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.11
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
U.S. Population, Acute Consumers[+] - Finfish and Shellfish

		Grams/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	68.00	61.92	74.07
n = 1,892	50th %	39.52	36.16	44.68
N = 44,946,000	90th %	170.84	158.74	181.79
	95th %	224.78	212.91	245.98
	99th %	374.74	336.50	431.34
Marine	Mean	87.77	83.74	91.80
n = 3,184	50th %	71.77	69.73	74.23
N = 73,100,000	90th %	169.39	167.00	173.65
	95th %	209.50	198.11	221.73
	99th %	320.41	292.80	341.88
All Fish	Mean	100.63	96.66	104.60
n = 3,927	50th %	80.79	79.29	83.90
N = 89,800,000	90th %	197.44	188.74	205.12
	95th %	253.38	231.51	264.45
	99th %	371.59	359.29	401.61

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

[+] Note: Acute consumer = Individual who consumed fish at least once during the 3-day reporting period.
n = sample size
N = population size

Estimates are projected from the sample to the population of acute consumers in the 48 conterminous states, using 3-year combined survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.12
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
U.S. Population, Acute Consumers[+] - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	1,076.80	980.00	1,173.61
n = 1,892	50th %	656.62	588.84	709.37
N = 44,946,000	90th %	2,695.81	2,546.77	2,819.33
	95th %	3,399.46	3,132.65	3,839.47
	99th %	6,526.10	5,270.61	6,931.61
Marine	Mean	1,495.37	1,422.63	1,568.12
n = 3,184	50th %	1,151.58	1,120.00	1,181.14
N = 73,100,000	90th %	2,956.38	2,838.46	3,083.70
	95th %	3,887.52	3,770.65	4,113.22
	99th %	6,510.73	5,772.57	6,852.01
All Fish	Mean	1,674.31	1,606.79	1,741.83
n = 3,927	50th %	1,307.30	1,267.12	1,339.46
N = 89,800,000	90th %	3,299.54	3,133.69	3,462.35
	95th %	4,258.69	4,065.32	4,483.83
	99th %	7,126.90	6,644.11	7,794.41

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

[+] Note: Acute consumer = Individual who consumed fish at least once during the 3-day reporting period.
n = sample size
N = population size

Estimates are projected from the sample to the population of acute consumers in the 48 conterminous states, using 3-year combined survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.13
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
New England Region - Finfish and Shellfish

		Grams/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	4.94	3.87	6.01
	50th %	0.00	0.00	0.00
	90th %	17.58	6.92	25.76
	95th %	30.11	25.76	57.86
	99th %	72.04	64.61	74.67
Marine	Mean	16.96	15.57	18.35
	50th %	0.00	0.00	0.00
	90th %	56.95	49.00	66.28
	95th %	74.59	73.91	83.81
	99th %	124.64	99.13	178.05
All Fish	Mean	21.90	19.95	23.85
	50th %	0.00	0.00	0.00
	90th %	73.56	65.07	74.68
	95th %	91.33	83.81	96.30
	99th %	145.86	138.94	178.05

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 595 individuals to the regional population of 12,769,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.14
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Middle Atlantic Region - Finfish and Shellfish

Grams/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	3.79	2.62	4.96
	50th %	0.00	0.00	0.00
	90th %	12.13	9.28	13.71
	95th %	25.29	19.32	31.42
	99th %	61.72	48.00	84.21
Marine	Mean	14.89	12.76	17.02
	50th %	0.00	0.00	0.00
	90th %	52.01	46.27	55.67
	95th %	67.21	60.67	74.63
	99th %	148.91	113.21	154.15
All Fish	Mean	18.68	15.59	21.77
	50th %	0.00	0.00	0.00
	90th %	61.26	55.67	64.74
	95th %	80.54	69.72	94.85
	99th %	153.23	149.28	171.37

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 1,585 individuals to the regional population of 37,330,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.15
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
South Atlantic Region - Finfish and Shellfish

Grams/person/day				
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	4.92	3.93	5.91
	50th %	0.00	0.00	0.00
	90th %	16.72	8.63	20.77
	95th %	30.45	28.10	39.25
	99th %	77.54	72.35	86.41
Marine	Mean	11.41	9.72	13.11
	50th %	0.00	0.00	0.00
	90th %	44.56	36.43	49.55
	95th %	63.37	57.88	65.33
	99th %	102.78	91.51	107.98
All Fish	Mean	16.33	15.10	17.57
	50th %	0.00	0.00	0.00
	90th %	57.62	54.65	65.74
	95th %	83.39	77.30	92.88
	99th %	130.78	122.02	139.45

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 2,245 individuals to the regional population of 42,307,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.16
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
East North Central Region - Finfish and Shellfish

		Grams/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	2.88	1.99	3.77
	50th %	0.00	0.00	0.00
	90th %	5.10	1.71	5.94
	95th %	18.24	14.49	26.02
	99th %	58.24	56.50	66.00
Marine	Mean	10.33	8.33	12.33
	50th %	0.00	0.00	0.00
	90th %	38.82	37.33	42.96
	95th %	56.88	52.63	65.03
	99th %	113.83	104.59	132.39
All Fish	Mean	13.21	11.07	15.35
	50th %	0.00	0.00	0.00
	90th %	47.50	43.87	51.55
	95th %	72.05	65.87	80.51
	99th %	114.31	106.60	132.39

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 2,222 individuals to the regional population of 41,565,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.17
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
East South Central Region - Finfish and Shellfish

		Grams/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	10.66	5.84	15.49
	50th %	0.00	0.00	0.00
	90th %	37.64	28.11	49.93
	95th %	58.41	51.53	72.36
	99th %	165.12	86.40	224.33
Marine	Mean	5.97	4.41	7.54
	50th %	0.00	0.00	0.00
	90th %	23.87	18.54	32.27
	95th %	37.29	32.27	47.13
	99th %	61.16	56.00	76.45
All Fish	Mean	16.63	12.03	21.24
	50th %	0.00	0.00	0.00
	90th %	52.26	45.44	60.67
	95th %	69.94	66.77	86.40
	99th %	165.12	119.53	224.33

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 671 individuals to the regional population of 15,113,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.18
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
West North Central Region - Finfish and Shellfish

		Grams/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	4.48	2.22	6.74
	50th %	0.00	0.00	0.00
	90th %	4.41	0.31	9.19
	95th %	25.84	14.42	47.73
	99th %	104.32	58.05	178.33
Marine	Mean	8.37	5.71	11.03
	50th %	0.00	0.00	0.00
	90th %	31.50	27.83	39.88
	95th %	49.00	40.36	56.00
	99th %	99.62	66.20	103.24
All Fish	Mean	12.85	8.06	17.64
	50th %	0.00	0.00	0.00
	90th %	42.99	36.39	54.78
	95th %	63.05	55.03	86.40
	99th %	141.07	112.00	178.33

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 785 individuals to the regional population of 17,720,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.19
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
West South Central Region - Finfish and Shellfish

		Grams/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	7.04	4.82	9.26
	50th %	0.00	0.00	0.00
	90th %	23.85	17.18	37.48
	95th %	55.46	47.71	74.95
	99th %	112.68	77.17	115.75
Marine	Mean	6.02	4.71	7.33
	50th %	0.00	0.00	0.00
	90th %	22.23	18.72	27.67
	95th %	33.75	28.38	41.99
	99th %	92.12	55.67	100.20
All Fish	Mean	13.06	10.04	16.08
	50th %	0.00	0.00	0.00
	90th %	49.69	37.48	55.92
	95th %	74.77	57.88	85.33
	99th %	114.22	100.74	115.75

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 1,287 individuals to the regional population of 26,321,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.20
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Mountain Region - Finfish and Shellfish

		Grams/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	3.23	1.86	4.60
	50th %	0.00	0.00	0.00
	90th %	0.48	0.00	5.25
	95th %	20.90	10.51	36.00
	99th %	78.60	55.50	96.67
Marine	Mean	7.97	5.64	10.29
	50th %	0.00	0.00	0.00
	90th %	30.96	27.83	34.86
	95th %	52.68	37.80	58.73
	99th %	89.62	63.71	91.00
All Fish	Mean	11.20	8.26	14.13
	50th %	0.00	0.00	0.00
	90th %	39.32	36.89	48.20
	95th %	58.55	55.67	68.37
	99th %	95.84	91.00	136.75

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 889 individuals to the regional population of 13,385,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 21
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Pacific Region - Finfish and Shellfish

		Grams/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	3.93	2.78	5.07
	50th %	0.00	0.00	0.00
	90th %	10.16	8.53	12.08
	95th %	26.46	22.72	29.79
	99th %	68.74	51.53	91.02
Marine	Mean	12.88	10.18	15.58
	50th %	0.00	0.00	0.00
	90th %	50.78	43.68	54.65
	95th %	69.74	60.67	79.57
	99th %	111.49	106.93	121.52
All Fish	Mean	16.81	14.32	19.29
	50th %	0.00	0.00	0.00
	90th %	55.87	51.53	59.76
	95th %	83.44	71.74	95.95
	99th %	122.64	116.93	169.54

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 1,633 individuals to the regional population of 36,197,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 22
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
New England Region - Finfish and Shellfish

		Milligrams/kilogram/person/day		
			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	72.50	59.10	85.89
	50th %	0.00	0.00	0.00
	90th %	271.02	103.78	363.88
	95th %	503.29	366.45	723.60
	99th %	1,031.43	755.19	1,240.52
Marine	Mean	283.20	251.27	315.14
	50th %	0.00	0.00	0.00
	90th %	964.92	852.34	1,041.69
	95th %	1,321.16	1,163.41	1,547.33
	99th %	2,083.17	1,789.78	2,631.23
All Fish	Mean	355.70	315.28	396.12
	50th %	0.00	0.00	0.00
	90th %	1,059.55	1,019.19	1,269.56
	95th %	1,536.32	1,323.53	1,568.72
	99th %	2,362.63	2,120.35	3,014.33

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 595 individuals to the regional population of 12,769,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 23
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Middle Atlantic Region - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	63.05	45.79	80.31
	50th %	0.00	0.00	0.00
	90th %	204.00	130.89	260.42
	95th %	413.18	320.99	597.44
	99th %	1,223.45	759.78	1,324.90
Marine	Mean	239.72	211.16	268.29
	50th %	0.00	0.00	0.00
	90th %	768.83	706.68	834.11
	95th %	1,128.64	930.83	1,365.60
	99th %	2,047.28	1,697.69	2,352.51
All Fish	Mean	302.77	262.82	342.72
	50th %	0.00	0.00	0.00
	90th %	941.32	803.12	1,160.53
	95th %	1,416.61	1,209.29	1,561.31
	99th %	2,510.55	2,302.98	2,673.55

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 1,585 individuals to the regional population of 37,330,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 24
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
South Atlantic Region - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	73.39	60.04	86.73
	50th %	0.00	0.00	0.00
	90th %	256.50	150.60	290.43
	95th %	509.78	451.81	596.27
	99th %	1,216.10	1,092.18	1,353.36
Marine	Mean	178.44	154.11	202.77
	50th %	0.00	0.00	0.00
	90th %	641.43	604.63	690.25
	95th %	977.52	913.81	1,071.87
	99th %	1,690.98	1,331.69	1,943.82
All Fish	Mean	251.83	234.98	268.67
	50th %	0.00	0.00	0.00
	90th %	858.43	795.11	943.87
	95th %	1,297.53	1,192.41	1,411.80
	99th %	2,175.84	1,943.82	2,323.75

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 2,245 individuals to the regional population of 42,307,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 25
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
East North Central Region - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	44.34	29.23	59.46
	50th %	0.00	0.00	0.00
	90th %	75.18	25.97	100.90
	95th %	316.64	222.48	408.50
	99th %	858.02	808.03	1,001.91
Marine	Mean	197.24	155.33	239.14
	50th %	0.00	0.00	0.00
	90th %	682.31	624.84	747.86
	95th %	1,114.31	943.16	1,333.60
	99th %	2,128.19	1,923.34	3,430.60
All Fish	Mean	241.58	198.48	284.68
	50th %	0.00	0.00	0.00
	90th %	827.02	731.33	943.16
	95th %	1,388.72	1,241.40	1,513.97
	99th %	2,376.91	1,930.85	3,430.60

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 2,222 individuals to the regional population of 41,565,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 26
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
East South Central Region - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	199.53	106.27	292.79
	50th %	0.00	0.00	0.00
	90th %	807.10	573.22	1,021.39
	95th %	1,086.94	1,021.39	1,355.11
	99th %	2,552.93	2,257.50	3,044.97
Marine	Mean	94.04	70.81	117.28
	50th %	0.00	0.00	0.00
	90th %	340.21	258.49	425.71
	95th %	569.69	435.77	690.12
	99th %	1,370.45	880.38	1,644.42
All Fish	Mean	293.57	209.10	378.05
	50th %	0.00	0.00	0.00
	90th %	977.86	898.05	1,023.86
	95th %	1,342.17	1,035.12	1,585.92
	99th %	2,786.16	2,257.50	3,044.97

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 671 individuals to the regional population of 15,113,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 27
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
West North Central Region - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	68.68	31.08	106.29
	50th %	0.00	0.00	0.00
	90th %	44.73	5.23	99.14
	95th %	428.01	129.96	904.27
	99th %	1,819.78	929.24	2,310.54
Marine	Mean	165.41	101.17	229.64
	50th %	0.00	0.00	0.00
	90th %	546.17	438.28	711.48
	95th %	839.85	762.30	981.18
	99th %	2,354.93	1,809.91	2,890.40
All Fish	Mean	234.09	137.32	330.86
	50th %	0.00	0.00	0.00
	90th %	756.81	578.06	829.11
	95th %	1,222.04	941.54	1,653.86
	99th %	2,988.90	2,224.38	3,733.22

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 785 individuals to the regional population of 17,720,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 28
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
West South Central Region - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	106.38	74.14	138.63
	50th %	0.00	0.00	0.00
	90th %	428.38	297.04	565.37
	95th %	863.50	717.62	1,038.97
	99th %	1,398.61	1,112.73	1,416.47
Marine	Mean	96.30	71.85	120.75
	50th %	0.00	0.00	0.00
	90th %	354.59	291.60	396.92
	95th %	655.36	548.14	747.56
	99th %	1,189.90	1,088.33	1,697.71
All Fish	Mean	202.68	154.13	251.23
	50th %	0.00	0.00	0.00
	90th %	840.80	698.95	887.76
	95th %	1,085.60	920.62	1,133.18
	99th %	1,725.49	1,416.47	1,755.07

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 1,287 individuals to the regional population of 26,321,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 29
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Mountain Region - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	43.34	27.12	59.55
	50th %	0.00	0.00	0.00
	90th %	7.32	0.00	64.26
	95th %	295.74	145.18	458.98
	99th %	1,028.60	750.63	1,115.58
Marine	Mean	132.52	88.63	176.42
	50th %	0.00	0.00	0.00
	90th %	458.07	421.93	583.88
	95th %	751.69	680.90	902.64
	99th %	1,535.18	1,344.97	1,713.17
All Fish	Mean	175.86	128.71	223.01
	50th %	0.00	0.00	0.00
	90th %	641.64	542.17	729.72
	95th %	957.82	817.21	1,075.34
	99th %	1,702.77	1,421.80	1,786.53

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 889 individuals to the regional population of 13,385,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A. 30
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Pacific Region - Finfish and Shellfish

Milligrams/kilogram/person/day

			90% Interval*	
Habitat	**Statistic**	**Estimate**	**Lower Bound**	**Upper Bound**
Fresh/Estuarine	Mean	59.58	44.67	74.50
	50th %	0.00	0.00	0.00
	90th %	182.83	125.87	221.07
	95th %	416.82	345.98	472.91
	99th %	1,018.21	861.13	1,114.52
Marine	Mean	226.16	162.61	289.71
	50th %	0.00	0.00	0.00
	90th %	799.42	760.71	945.97
	95th %	1,159.26	1,096.99	1,369.73
	99th %	2,173.89	1,995.09	2,598.14
All Fish	Mean	285.75	222.88	348.61
	50th %	0.00	0.00	0.00
	90th %	946.55	873.95	1,054.94
	95th %	1,413.34	1,295.67	1,489.91
	99th %	2,589.08	2,181.37	2,661.40

* Percentile intervals were estimated using the percentile bootstrap method with 1,000 bootstrap replications.

Note: Estimates are projected from a sample of 1,633 individuals to the regional population of 36,197,000 using survey weights.

Source of individual consumption data: Combined 1989, 1990, and 1991 USDA Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.31
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 18 Years of Age or Older in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
Estuarine	Shrimp	1.72959
	Perch	0.60368
	Flatfish (Estuarine)	0.52735
	Crab (Estuarine)	0.37126
	Flounder	0.29941
	Oyster	0.22555
	Mullet	0.08756
	Croaker	0.06749
	Herring	0.03925
	Smelts	0.03753
	Clam (Estuarine)	0.03146
	Scallop (Estuarine)	0.00322
	Anchovy	0.00292
	Scup	0.00068
	Sturgeon	0.00054
Freshwater	Catfish	1.18227
	Trout	0.44946
	Carp	0.05727
	Pike	0.02337
	Salmon (Freshwater)	0.01096
Marine	Tuna	4.71788
	Flatfish (Marine)	1.28921
	Cod	1.26813
	Salmon (Marine)	0.91786
	Haddock	0.61729

Notes: Estimates are projected from a sample of 8,478 individuals 18 years of age or older to the population of 177,807,000 individuals 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.31 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 18 Years of Age or Older in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
Marine (Con't.)	Crab (Marine)	0.43234
	Pollock	0.37254
	Clam (Marine)	0.35788
	Ocean Perch	0.30679
	Porgy	0.30502
	Scallop (Marine)	0.28389
	Sea Bass	0.25467
	Lobster	0.25446
	Swordfish	0.17743
	Sardine	0.13812
	Squid	0.12760
	Pompano	0.10485
	Sole	0.10096
	Mackerel	0.07188
	Whiting	0.06481
	Shark	0.02596
	Halibut	0.02396
	Mussels	0.01911
	Whitefish	0.00888
	Snapper	0.00735
	Octopus	0.00512
	Barracuda	0.00151
	Abalone	0.00103
	Seafood	0.00057
Unknown	Fish	0.00077

Notes: Estimates are projected from a sample of 8,478 individuals 18 years of age or older to the population of 177,807,000 individuals 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.31 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 18 Years of Age or Older in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
All Species	Tuna	4.71788
	Shrimp	1.72959
	Flatfish (Marine)	1.28921
	Cod	1.26813
	Catfish	1.18227
	Salmon (Marine)	0.91786
	Haddock	0.61729
	Perch	0.60368
	Flatfish (Estuarine)	0.52735
	Trout	0.44946
	Crab (Marine)	0.43234
	Pollock	0.37254
	Crab (Estuarine)	0.37126
	Clam (Marine)	0.35788
	Ocean Perch	0.30679
	Porgy	0.30502
	Flounder	0.29941
	Scallop (Marine)	0.28389
	Sea Bass	0.25467
	Lobster	0.25446
	Oyster	0.22555
	Swordfish	0.17743
	Sardine	0.13812
	Squid	0.12760
	Pompano	0.10485
	Sole	0.10096

Notes: Estimates are projected from a sample of 8,478 individuals 18 years of age or older to the population of 177,807,000 individuals 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.31 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 18 Years of Age or Older in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
All Species (Con't.)	Mullet	0.08756
	Mackerel	0.07188
	Croaker	0.06749
	Whiting	0.06481
	Carp	0.05727
	Herring	0.03925
	Smelts	0.03753
	Clam (Estuarine)	0.03146
	Shark	0.02596
	Halibut	0.02396
	Pike	0.02337
	Mussels	0.01911
	Salmon (Freshwater)	0.01096
	Whitefish	0.00888
	Snapper	0.00735
	Octopus	0.00512
	Scallop (Estuarine)	0.00322
	Anchovy	0.00292
	Barracuda	0.00151
	Abalone	0.00103
	Fish	0.00077
	Scup	0.00068
	Seafood	0.00057
	Sturgeon	0.00054

Notes: Estimates are projected from a sample of 8,478 individuals 18 years of age or older to the population of 177,807,000 individuals 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.32
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 14 Years of Age and Younger in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
Estuarine	Shrimp	0.36872
	Perch	0.28899
	Flatfish (Estuarine)	0.17291
	Flounder	0.08613
	Oyster	0.03172
	Crab (Estuarine)	0.02880
	Mullet	0.02396
	Clam (Estuarine)	0.01273
	Croaker	0.00335
	Smelts	0.00080
	Anchovy	0.00061
	Scollop (Estuarine)	0.00034
Freshwater	Catfish	0.47501
	Trout	0.34732
	Carp	0.02862
	Pike	0.01170
	Salmon (Freshwater)	0.00321
Marine	Tuna	2.82208
	Cod	1.13423
	Pollock	0.64386
	Flatfish (Marine)	0.42271
	Ocean Perch	0.38098
	Porgy	0.32992
	Salmon (Marine)	0.26894

Notes: Estimates are projected from a sample of 2,977 individuals of age 14 and younger to the population of 55,163,000 individuals of age 14 and younger using 3 years combined survey weights.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.32 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 14 Years of Age and Younger in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
Marine (Con't.)	Haddock	0.24788
	Clam (Marine)	0.14478
	Squid	0.12532
	Sea Bass	0.07716
	Pompano	0.06221
	Lobster	0.05980
	Mackerel	0.04899
	Mussels	0.03597
	Crab (Marine)	0.03354
	Scallop (Marine)	0.02981
	Whiting	0.02808
	Whitefish	0.01170
	Halibut	0.00995
	Sardine	0.00765
	Seafood	0.00005
Unknown	Fish	0.00568
All Species	Tuna	2.82208
	Cod	1.13423
	Pollock	0.64386
	Catfish	0.47501
	Flatfish (Marine)	0.42271
	Ocean Perch	0.38098
	Shrimp	0.36872

Notes: Estimates are projected from a sample of 2,977 individuals of age 14 and younger to the population of 55,163,000 individuals of age 14 and younger using 3 years combined survey weights.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.32 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 14 Years of Age and Younger in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
All Species (Con't.)	Haddock	0.24788
	Trout	0.34732
	Porgy	0.32992
	Perch	0.28899
	Salmon (Marine)	0.26894
	Flatfish (Estuarine)	0.17291
	Clam (Marine)	0.14478
	Squid	0.12532
	Flounder	0.08613
	Sea Bass	0.07716
	Pompano	0.06221
	Lobster	0.05980
	Mackerel	0.04899
	Mussels	0.03597
	Crab (Marine)	0.03354
	Oyster	0.03172
	Scallop (Marine)	0.02981
	Crab (Estuarine)	0.02880
	Carp	0.02862
	Whiting	0.02808
	Mullet	0.02396
	Clam (Estuarine)	0.01273
	Pike	0.01170
	Whitefish	0.01170
	Halibut	0.00995
	Sardine	0.00765
	Fish	0.00568
	Croaker	0.00335

Notes: Estimates are projected from a sample of 2,977 individuals of age 14 and younger to the population of 55,163,000 individuals of age 14 and younger using 3 years combined survey weights.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.32 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Individuals 14 Years of Age and Younger in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
	Salmon (Freshwater)	0.00321
	Smelts	0.00080
	Anchovy	0.00061
	Scallop (Estuarine)	0.00034
	Seafood	0.00005

Notes: Estimates are projected from a sample of 2,977 individuals of age 14 and younger to the population of 55,163,000 individuals of age 14 and younger using 3 years combined survey weights.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.33
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Females of Age 15 to 44 in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
Estuarine	Shrimp	1.52145
	Perch	0.55348
	Flatfish (Estuarine)	0.45313
	Flounder	0.23224
	Crab (Estuarine)	0.22766
	Mullet	0.05635
	Oyster	0.02736
	Croaker	0.02672
	Clam (Estuarine)	0.01925
	Herring	0.01112
	Scallop (Estuarine)	0.00225
	Anchovy	0.00018
Freshwater	Catfish	0.81492
	Trout	0.34703
	Carp	0.07291
	Pike	0.00756
	Salmon (Freshwater)	0.00479
Marine	Tuna	4.41949
	Flatfish (Marine)	1.10778
	Cod	1.04468
	Pollock	0.48699
	Haddock	0.43548
	Salmon (Marine)	0.40098
	Crab (Marine)	0.26511

Notes: Estimates are projected from a sample of 2,891 females of age 15 to 44 to the population of 58,750,000 females of age 15 to 44 using 3-year combined survey weights.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.33 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Females of Age 15 to 44 in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
Marine (Con't.)	Porgy	0.23300
	Clam (Marine)	0.21896
	Lobster	0.20638
	Scallop (Marine)	0.19840
	Sea Bass	0.18125
	Ocean Perch	0.17925
	Swordfish	0.17758
	Squid	0.06367
	Pompano	0.06076
	Mackerel	0.04620
	Sole	0.03611
	Halibut	0.03495
	Sardine	0.03436
	Whiting	0.02711
	Whitefish	0.00756
	Octopus	0.00318
	Abalone	0.00312
	Mussels	0.00280
	Seafood	0.00046
	Shark	0.00034
All Species	Tuna	4.41949
	Shrimp	1.52145
	Flatfish (Marine)	1.10778
	Cod	1.04468
	Catfish	0.81492
	Perch	0.55348
	Pollock	0.48699

Notes: Estimates are projected from a sample of 2,891 females of age 15 to 44 to the population of 58,750,000 females of age 15 to 44 using 3-year combined survey weights.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.33 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Females of Age 15 to 44 in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
All Species (Con't.)	Flatfish (Estuarine)	0.45313
	Haddock	0.43548
	Salmon (Marine)	0.40098
	Trout	0.34703
	Crab (Marine)	0.26511
	Porgy	0.23300
	Flounder	0.23224
	Crab (Estuarine)	0.22766
	Clam (Marine)	0.21896
	Lobster	0.20638
	Scallop (Marine)	0.19840
	Sea Bass	0.18125
	Ocean Perch	0.17925
	Swordfish	0.17758
	Carp	0.07291
	Squid	0.06367
	Pompano	0.06076
	Mullet	0.05635
	Mackerel	0.04620
	Sole	0.03611
	Halibut	0.03495
	Sardine	0.03436
	Oyster	0.02736
	Whiting	0.02711
	Croaker	0.02672
	Clam (Estuarine)	0.01925
	Herring	0.01112

Notes: Estimates are projected from a sample of 2,891 females of age 15 to 44 to the population of 58,750,000 females of age 15 to 44 using 3-year combined survey weights.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.33 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
Females of Age 15 to 44 in the U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
All Species (Con't.)	Pike	0.00756
	Whitefish	0.00756
	Salmon (Freshwater)	0.00479
	Octopus	0.00318
	Abalone	0.00312
	Mussels	0.00280
	Scallop (Estuarine)	0.00225
	Seafood	0.00046
	Shark	0.00034
	Anchovy	0.00018

Notes: Estimates are projected from a sample of 2,891 females of age 15 to 44 to the population of 58,750,000 females of age 15 to 44 using 3-year combined survey weights.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.34
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
Estuarine	Shrimp	1.37241
	Perch	0.52580
	Flatfish (Estuarine)	0.43485
	Crab (Estuarine)	0.29086
	Flounder	0.24590
	Oyster	0.17419
	Mullet	0.07089
	Croaker	0.05021
	Herring	0.02937
	Smelts	0.02768
	Clam (Estuarine)	0.02691
	Scallop (Estuarine)	0.00247
	Anchovy	0.00228
	Scup	0.00050
	Sturgeon	0.00040
Freshwater	Catfish	1.06776
	Trout	0.43050
	Carp	0.04846
	Pike	0.01978
	Salmon (Freshwater)	0.00881
Marine	Tuna	4.19998
	Cod	1.22827
	Flatfish (Marine)	1.06307
	Salmon (Marine)	0.73778

Notes: Estimates are projected from a sample of 8,478 individuals 18 years of age or older to the population of 177,807,000 individuals 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.34 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
Marine (Con't.)	Haddock	0.51533
	Pollock	0.44970
	Crab (Marine)	0.33870
	Ocean Perch	0.31878
	Clam (Marine)	0.30617
	Porgy	0.29844
	Scallop (Marine)	0.21805
	Sea Bass	0.20794
	Lobster	0.20001
	Swordfish	0.13879
	Squid	0.12196
	Sardine	0.10313
	Pompano	0.09131
	Sole	0.07396
	Mackerel	0.06379
	Whiting	0.05498
	Halibut	0.02463
	Mussels	0.02217
	Shark	0.01901
	Whitefish	0.00916
	Snapper	0.00539
	Octopus	0.00375
	Barracuda	0.00111
	Abalone	0.00075
	Seafood	0.00043

Notes: Estimates are projected from a sample of 8,478 individuals 18 years of age or older to the population of 177,807,000 individuals 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.34 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
Unknown	Fish	0.00186
All Species	Tuna	4.19998
	Shrimp	1.37241
	Cod	1.22827
	Catfish	1.06776
	Flatfish (Marine)	1.06307
	Salmon (Marine)	0.73778
	Perch	0.52580
	Haddock	0.51533
	Pollock	0.44970
	Flatfish (Estuarine)	0.43485
	Trout	0.43050
	Crab (Marine)	0.33870
	Ocean Perch	0.31878
	Clam (Marine)	0.30617
	Porgy	0.29844
	Crab (Estuarine)	0.29086
	Flounder	0.24590
	Scallop (Marine)	0.21805
	Sea Bass	0.20794
	Lobster	0.20001
	Oyster	0.17419
	Swordfish	0.13879
	Squid	0.12196
	Sardine	0.10313

Notes: Estimates are projected from a sample of 8,478 individuals 18 years of age or older to the population of 177,807,000 individuals 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

TABLE A.34 (continued)
DAILY AVERAGE PER CAPITA ESTIMATES OF FISH CONSUMPTION
As Consumed Fish
U.S. Population - Mean Consumption by Species within Habitat

Habitat	Species	Estimated Mean (grams/person/day)
	Pompano	0.09131
	Sole	0.07396
	Mullet	0.07089
	Mackerel	0.06379
	Whiting	0.05498
	Croaker	0.05021
	Carp	0.04846
	Herring	0.02937
	Smelts	0.02768
	Clam (Estuarine)	0.02691
	Halibut	0.02463
	Mussels	0.02217
	Pike	0.01978
	Shark	0.01901
	Whitefish	0.00916
	Salmon (Freshwater)	0.00881
	Snapper	0.00539
	Octopus	0.00375
	Scallop (Estuarine)	0.00247
	Anchovy	0.00228
	Fish	0.00186
	Barracuda	0.00111
	Abalone	0.00075
	Scup	0.00050
	Seafood	0.00043
	Sturgeon	0.00040

Notes: Estimates are projected from a sample of 8,478 individuals 18 years of age or older to the population of 177,807,000 individuals 18 years of age or older using 3-year combined survey weights. The population for this survey consisted of individuals in the 48 conterminous states.

Source of individual consumption data: USDA Combined 1989, 1990, and 1991 Continuing Survey of Food Intakes by Individuals (CSFII).

The fish component of foods containing fish was calculated using data from the recipe file for release 7 of the USDA's Nutrient Data Base for Individual Food Intake Surveys.

Appendix B
Evaluation of the Quality of Data Set(s) for Use in Deriving an RfD

The derivation of RfDs begins with a thorough review and assessment of the toxicological data base to identify the type and magnitude of possible adverse health effects associated with a chemical. This evaluation should include an examination of the full range of possible health effects, including acute, short-term (14 to 28 days), subchronic, reproductive/developmental, and chronic effects.

To be useful for supporting the derivation of an RfD, a study must meet certain standards with regard to experimental design, conduct and data reporting. This appendix provides general guidance on criteria for appropriate study design for a variety of types of toxicity studies. These guidelines provide the assessor with a means to evaluate the quality and adequacy of data. Appropriate studies are used both for the evaluation of potential hazard of the chemical and for the derivation of the RfD.

Acute Toxicity Determination

Studies of acute exposure (one dose or multiple dose exposure occurring within a short time (e.g. less than 24 hours)) are widely available for many chemicals. Acute toxicity [often expressed in terms of the lethal dose (or concentration) to 50 percent of the population (LD_{50} or LC_{50})] is usually the initial step in experimental assessment and evaluation of a chemical's toxic characteristics. Such studies are used in establishing a dosage regimen in subchronic and other studies and may provide initial information on the mode of toxic action of a substance. Because LD_{50} or LC_{50} studies are of short duration, inexpensive and easy to conduct, they are commonly used in hazard classification systems.

Acute lethality studies are of limited use, however, in the derivation of chronic criteria, since the establishment of chronic criteria should never be based on exposures that approach acutely lethal levels. However, the data from such studies do provide information on health hazards likely to arise from individual short-term exposures. Such studies provide high dose effects data from which to evaluate potential effects from exposures which may temporarily exceed the acceptable chronic exposure level. An evaluation of the data should include the incidence and severity of all abnormalities, the reversibility of abnormalities observed other than lethality, gross lesions, body weight changes, effects on mortality, and any other toxic effects.

In recent years guidelines have been established to improve quality and provide uniformity in test conditions. Unfortunately, many published LD_{50} or LC_{50} tests were not conducted in accordance with current EPA or OECD guidelines (USEPA, 1985; OECD, 1987) since they were conducted prior to establishment of those guidelines. For this reason, it becomes necessary to examine each test or study to determine if the study was conducted in an adequate manner.

The following is a list of ideal conditions compiled from various testing guidelines which may be used for determination of adequacy of acute toxicity data. Many published studies do not report

details of test conditions making such determinations difficult. However, test conditions guidelines that might be considered ideal may include:

General:

- Animal age and species identified.
- Minimum of 5 animals per sex per dose group (both sexes should be used).
- 14-day or longer observation period following dosing.
- Minimum of 3 dose levels appropriately spaced (most statistical methods require at least 3 dose levels).
- Identification of purity or grade of test material used (particularly important in older studies).
- If a vehicle used, the selected vehicle is known to be non-toxic.
- Gross necropsy results for test animals.
- Acclimation period for test animals before initiating study.

Specific conditions for oral LD_{50}:

- Dosing by gavage or capsule.
- Total volume of vehicle plus test material remain constant for all dose levels.
- Animals were fasted before dosing.

Specific conditions for dermal LD_{50}:

- Exposure on intact, clipped skin and involve approximately 10 percent of body surface.
- Animals prevented from oral access to test material by restraining or covering test site.

Specific conditions for inhalation LC_{50}:

- Duration of exposure at least 4 hours.
- If an aerosol (mist or particulate), the particle size (median diameter and deviation) should be reported.

Although the above listed conditions would be included in an ideally conducted study, not all of these conditions need to be included in an adequately conducted study. Therefore, some discretion is required on the part of the individual reviewing these studies (USEPA, 1985; OECD, 1987).

Short-Term Toxicity Studies (14-Day or 28-Day Repeated Dose Toxicity)

Short-term exposure generally refers to multiple or continuous exposure usually occurring over a 14-day to 28-day time period. The purpose of short-term repeated dose studies is to provide information on possible adverse health effects from repeated exposures over a limited time period.

The following guidelines were derived using the OECD Guidelines for Testing of Chemicals (OECD, 1987) for determining the design and quality of a repeated dose short-term toxicity study:

- Minimum of 3 dose levels administered and an adequate control group used.
- Minimum of 10 animals per sex, per dose group (both sexes should be used).
- The highest dose level should ideally elicit some signs of toxicity without inducing excessive lethality and the lowest dose should ideally produce no signs of toxicity.
- Ideal dosing regimes include 7 days per week for a period of 14 days or 28 days.
- All animals should be dosed by the same method during the entire experiment period.
- Animals should be observed daily for signs of toxicity during the treatment period (i.e., 14 or 28 days). Animals that die during the study are necropsied and all survivors in the treatment groups are sacrificed and necropsied at the end of the study period.
- All observed results, quantitative and incidental, should be evaluated by an appropriate statistical method.
- Clinical examinations should include hematology and clinical biochemistry, urinalysis may be required when expected to provide an indication of toxicity. Pathological examination should include gross necropsy and histopathology.

The findings of short-term repeated dose toxicity studies should be considered in terms of the observed toxic effects and the necropsy and histopathological findings. The evaluation will include the incidence and severity of abnormalities, gross lesions, body weight changes, effects on mortality, and other general or specific toxic effects (OECD, 1987).

These guidelines represent ideal conditions and studies will not be expected to meet all standards in order to be considered to be adequate. For example, the National Toxicology Program's cancer bioassay program has generated a substantial data base of short-term repeated dose studies. The study periods for these range from 14 days to 20 days with 12 to 15 doses administered generally

for 5 dose levels and a control. Since the quality of this data is good, it is desirable to consider these study results even though they do not always identically follow the protocol.

Subchronic and Chronic Toxicity

Studies involving subchronic exposure (occurring usually over 3 months) and chronic exposure (those involving an extended period of time, or a significant fraction of the subject's lifetime) are designed to permit a determination of no-observed-effect levels (NOEL) and toxic effects associated with continuous or repeated exposure to a chemical. Subchronic studies provide information on health hazards likely to arise from repeated exposure over a limited period of time. They provide information on target organs, the possibilities of accumulation, and, with the appropriate uncertainty factors, may be used in establishing water quality criteria for human health. Chronic studies provide information on potential effects following prolonged and repeated exposure. Such effects might require a long latency period or are cumulative in nature before manifesting disease. The design and conduct of such tests should allow for detection of general toxic effects including neurological, physiological, biochemical, and hematological effects and exposure-related pathological effects.

The following guidelines were derived using the EPA Health Effects Testing Guidelines (USEPA, 1985), for determining the quality of a subchronic or chronic (long term) study. Additional detailed guidance may be found in that document. These guidelines represent ideal conditions and studies will not be expected to meet all standards in order to be considered for use as the basis for RfD derivation. Ideally, a subchronic/chronic study should include:

- Minimum of 3 dose levels administered and an adequate control group used.
- Minimum of 10 animals for subchronic, 20 animals for chronic studies per sex, per dose group (both sexes should be used).
- The highest dose level should elicit some signs of toxicity without inducing excessive lethality and the lowest dose should ideally produce no signs of toxicity.
- Ideal dosing regimes include dosing for 5-7 days per week for 13 weeks or greater (90 days or greater) for subchronic, and at least 12 months or greater for chronic studies in rodents. For other species, repeated dosing should ideally occur over 10 percent or greater of animal’s lifespan for subchronic studies and 50 percent or greater of the animal’s lifespan for chronic studies.
- All animals should be dosed by the same method during the entire experimental period.
- Animals should be observed daily during the treatment period (i.e., 90 days or greater).

- Animals that die during the study are necropsied and, at the conclusion of the study, surviving animals are sacrificed and necropsied and appropriate histopathological examinations carried out.

- Results should be evaluated by an appropriate statistical method selected during experimental design.

- Such toxicity tests should evaluate the relationship between the dose of the test substance and the presence, incidence and severity of abnormalities (including behavioral and clinical abnormalities), gross lesions, identified target organs, body weight changes, effects on mortality, and any other toxic effects noted in USEPA (1985).

Developmental Toxicity

Guidelines for reproductive and developmental toxicity studies have been developed by EPA (USEPA, 1985 and OECD, 1987). Developmental toxicity can be evaluated via a relatively short-term study in which the compound is administered during the period of organogenesis. Based on the EPA Health Effects Testing Guidelines (USEPA, 1985), ideal studies should include:

- Minimum of 20 young, adult, pregnant rats, mice, or hamsters or 12 young, adult, pregnant rabbits recommended per dose group.

- Minimum of 3 dose levels with an adequate control group used.

- The highest dose should induce some slight maternal toxicity but no more than 10 percent mortality. The lowest dose should not produce grossly observable effects in dams or fetuses. The middle dose level, in an ideal situation, will produce minimal observable toxic effects.

- Dose period should cover the major period of organogenesis (days 6 to 15 gestation for rat and mouse, 6 to 14 for hamster, and 6 to 18 for rabbit).

- Dams should be observed daily; weekly food consumption and body weight measurements should be taken.

- Necropsy should include both gross and microscopic examination of the dams; the uterus should be examined so that the number of embryonic or fetal deaths and the number of viable fetuses can be counted; fetuses should be weighted.

- One-third to one-half of each litter should be prepared and examined for skeletal anomalies and the remaining animals prepared and examined for soft tissue anomalies.

As with any other type of study, the appropriate statistical analyses must be performed on the data for a study to qualify as a good quality study. In addition, developmental studies are unique in

the sense that they yield two potential experimental units for statistical analysis, the litter and the individual fetus. The EPA testing guidelines do not provide any recommendation on which unit to use, but the Guidelines for the Developmental Toxicity Risk Assessment (USEPA, 1991) states that "since the litter is generally considered the experimental unit in most developmental toxicity studies . . ., the statistical analyses should be designed to analyze the relevant data based on incidence per litter or on the number of litters with a particular endpoint." Others have also identified the litter as the preferred experimental unit (Palmer, 1981 and Madson et al., 1982).

Information on maternal toxicity is very important when evaluating developmental effects because it helps determine if differential susceptibility exists for the offspring and mothers. Since the conceptus relies on its mother for certain physiological processes, interruption of maternal homeostasis could result in abnormal prenatal development. Substances which affect prenatal development without compromising the dam are considered to be a greater developmental hazard than chemicals which cause developmental effects at maternally toxic doses. Unfortunately, maternal toxicity information has not been routinely presented in earlier studies and has become a standard practice in studies only recently. In an attempt to use whatever data are available, maternal toxicity information may not be required if developmental effects are serious enough to warrant consideration regardless of the presence of maternal toxicity.

Reproductive Toxicity

The EPA Health Effects Testing Guidelines (USEPA, 1985) include guidelines for both reproduction and fertility studies and developmental studies. These EPA guidelines can serve as the ideal experimental situation with which to compare study quality. Studies being evaluated do not need to match precisely but rather should be similar enough that one can be assured that the chemical was adequately tested and that the results are a reliable estimate of the true reproductive or developmental toxicity of the chemical.

These guidelines also recommend a two-generation reproduction study to provide information on the ability of a chemical to impact gonadal function, conception, parturition and the growth and development of the offspring. Additional information concerning the effects of a test compound on neonatal morbidity, mortality, and developmental toxicity may also be provided. The recommendations for reproductive testing are lengthy and quite detailed and may be reviewed further in the EPA Health Effects Testing Guidelines. In general, the test compound is administered to the parental (P) animals (at least 20 males and enough females to yield 20 pregnant females) at least 10 weeks before mating, through the resulting pregnancies and through weaning of their offspring (F1 or first generation). The compound is then administered to the F1 generation similarly through the production of the second generation (or F2) offspring until weaning. Recommendations for numbers of dose groups and dose levels are similar to those reported for developmental studies. Details should also be provided on mating procedures, standardization of litter sizes (if possible, 4 males and 4 females from each litter are randomly selected), observation, gross necropsy and histopathology. Full histopathology is recommended on the following organs of all high dose and control P and F1 animals used in mating: vagina, uterus, testes, epididymides, seminal vesicles, prostate, pituitary gland, and target organs. Organs of animals from other dose groups should be examined when pathology has been demonstrated in high dose animals (USEPA, 1985).

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Appendix C
Derivation of Basic Equations Concerning Bioconcentration and Bioaccumulation of Organic Chemicals

Introduction

Most work dealing with the bioconcentration and bioaccumulation of organic chemicals has concerned chemicals whose log K_{ow}s are greater than 3. The purpose of this appendix is to explain why modifications of the equations generally used with such chemicals are necessary so that the equations also are appropriate for chemicals whose K_{ow}s, BCFs, or BAFs are less than 1,000, and to derive all of the appropriate equations that are used in the calculation of BAFs for the final Guidance.

Background

BCFs were originally defined as:

$$BCF_T^t = \frac{C_B^t}{C_W^t} \qquad (1)$$

where:

BCF_T^t = Total BCF (i.e., a BCF that is based on the total concentrations of the chemical in the water and in the aquatic biota)

C_B^t = Total concentration of the chemical in the aquatic biota, based on the wet weight of the aquatic biota

C_W^t = Total concentration of the chemical in the water around the aquatic biota

This is not the nomenclature that was used originally, but it is used here for clarity.

It was subsequently realized that extrapolation of BCFs for organic chemicals from one species to another would be more accurate if the BCFs were normalized on the basis of the amount of lipid in the aquatic biota. It was also realized that extrapolation of BCFs for organic chemicals from one water to another would be more accurate if the BCFs were calculated on the basis of the freely dissolved concentration of the organic chemical in the water around the aquatic biota. Thus, two additional BCFs were defined and used:

$$BCF_\ell^t = \frac{C_\ell}{C_W^t} \qquad (2)$$

$$BCF_{\ell}^{fd} = \frac{C_{\ell}}{C_W^{fd}} \tag{3}$$

where:

BCF_{ℓ}^{t} = Lipid-normalized total BCF (i.e., normalized to 100 percent lipid and based on the total concentration of the chemical in the water around the biota)

C_{ℓ} = Lipid-normalized concentration of the chemical in the aquatic biota

BCF_{ℓ}^{fd} = Lipid-normalized, freely dissolved BCF

C_W^{fd} = Freely dissolved concentration of chemical in the water around the aquatic biota

The experimental definition of C_{ℓ} is:

$$C_{\ell} = \frac{\text{the total amount of chemical in the aquatic biota}}{\text{the amount of lipid in the aquatic biota}}$$

$$= \frac{(B)(C_B^t)}{L} = \frac{(B)(C_B^t)}{(f_{\ell})(B)} = \frac{C_B^t}{f_{\ell}} \tag{4}$$

where:

B = Wet weight of the aquatic biota.

L = Weight of the lipid in the aquatic biota.

f_{ℓ} = Fraction of the aquatic biota that is lipid = L/B

Using Equation 4 to substitute for C_{ℓ} in Equation 2 and then using Equation 1:

$$BCF_{\ell}^{t} = \frac{C_B^t}{(C_W^t)(f_{\ell})} = \frac{BCF_T^t}{f_{\ell}} \tag{5}$$

If f_{fd} = the fraction of the chemical in the water around the aquatic biota that is freely dissolved, then:

$$f_{fd} = \frac{C_W^{fd}}{C_W^t} \quad (6)$$

Using Equations 4 and 6 to substitute for C_ℓ and C_W^{fd} in Equation 3 and then using Equation 1:

$$BCF_\ell^{fd} = \frac{C_B^t}{(f_\ell)(C_W^t)(f_{fd})} = \frac{BCF_T^t}{(f_\ell)(f_{fd})} \quad (7)$$

Equations 1, 5, and 7 show the relationships between the three different BCFs.

Theoretical justification for use of both lipid-normalization and the freely dissolved concentration of the organic chemical in the ambient water is based on the concept of equilibrium partitioning, whereas practical justification is provided by the general similarity of the value of BCF_ℓ^{fd} for an organic chemical across both species and waters. It will be demonstrated, however, that a more complete application of equilibrium partition theory shows that BCF_ℓ^{fd} extrapolates well only for chemicals whose K_{ow}s are greater than 1,000, whereas a different BCF extrapolates well for organic chemicals whose K_{ow}s are greater than 1,000 as well as for chemicals whose K_{ow}s are less than 1,000.

Partition Theory and Bioconcentration

Equilibrium partition theory provides the understanding necessary to ensure proper use of K_{ow}s, BCFs, and BAFs in the derivation of water quality criteria for organic chemicals. For the purpose of applying partition theory, aquatic biota can be modeled as consisting of water, lipid, and non-lipid organic matter (Barber et al., 1991). In this model, an organic chemical in aquatic biota exists in three forms:

1. Chemical that is freely dissolved in the water that is in the biota.

2. Chemical that is partitioned to the lipid that is in the biota.

3. Chemical that is partitioned to non-lipid organic matter in the biota. The total concentration of chemical in the water inside the biota includes chemical that is partitioned to lipid and non-lipid organic matter in the water.

According to this model:

$$C_B^t = (f_W)(C_{WB}^{fd}) + (f_\ell)(C_L) + (f_N)(C_N) \quad (8)$$

where:

f_W = Fraction of the aquatic biota that is water

C_{WB}^{td} = Freely dissolved concentration of the organic chemical in the water in the aquatic biota

f_ℓ = Fraction of the aquatic biota that is lipid

C_L = Concentration of the organic chemical in the lipid

f_N = Fraction of the aquatic biota that is non-lipid organic matter

C_N = Concentration of the organic chemical in the non-lipid organic matter in the aquatic biota

The most important partitioning of the organic chemical within the aquatic biota is between the lipid and the water, which is described by the following equation:

$$K_{LW} = \frac{C_L}{C_{WB}^{fd}} \qquad (9)$$

where:

K_{LW} = the lipid-water partition coefficient.

"K_{LW}" (Gobas 1993) is used herein because it is more descriptive than "K_L," which is used by DiToro et al., (1991). This partition coefficient is central to the equilibrium partition approach that is used to derive sediment quality criteria (DiToro et al., 1991), the Gobas model that is used to derive Food-Chain Multipliers for the final Guidance, and the equations given here that are used to derive BCFs and BAFs for the final Guidance.

In order for Equations 8 and 9 to be correct, partition theory requires that the concentration of the organic chemical in the lipid, C_L, be defined as:

$$C_L = \frac{\text{the amount of chemical partitioned to lipid in aquatic biota}}{\text{the amount of lipid in the aquatic biota}}$$

It is difficult to determine C_L experimentally because it is not easy to measure only the chemical that is partitioned to the lipid (i.e., it is not easy to separate the three different kinds of chemical that, according to the model, exist in aquatic biota). Because all of the organic chemical in the biota is measured when C_ℓ is determined, C_ℓ can be determined easily, and C_ℓ is higher than C_L.

It is useful to define another BCF as:

$$BCF_L^{fd} = \frac{C_L}{C_W^{fd}} \tag{10}$$

Because C_L is lower than C_ℓ, $BCF_L^{fd} < BCF_\ell^{fd}$.

The only difference between K_{LW} and BCF_L^{fd} is that the denominator in K_{LW} is C_{WB}^{fd}, whereas the denominator in BCF_L^{fd} is C_W^{fd}. When partition theory applies, however, all phases are in equilibrium and so:

$$C_W^{fd} = C_{WB}^{fd} \tag{11}$$

Therefore, when the organic chemical is not metabolized by the aquatic biota and when growth dilution is negligible:

$$BCF_L^{fd} = K_{LW} \tag{12}$$

Because octanol is a useful surrogate for lipid, a reasonable approximation is that:

$$K_{LW} = K_{ow} \tag{13}$$

where:

K_{ow} = the octanol-water partition coefficient.

Thus:

$$\text{predicted } BCF_L^{fd} = K_{LW} = K_{ow} \tag{14}$$

By using Equations 9 and 11 to substitute for C_L and C_{WB}^{fd} in Equation 8:

$$C_B^t = (f_W)(C_W^{fd}) + (f_\ell)(BCF_L^{fd})(C_W^{fd}) + (f_N)(C_N) \tag{15}$$

By using Equation 6 to substitute for C_W^{fd} in Equation 15:

$$C_B^t = (f_W)(f_{fd})(C_W^t) + (f_\ell)(BCF_L^{fd})(f_{fd})(C_W^t) + (f_N)(C_N) \tag{16}$$

Dividing by C_W^t gives:

$$\frac{C_B^t}{C_W^t} = (f_W)(f_{fd}) + (f_\ell)(BCF_L^{fd})(f_{fd}) + \frac{(f_N)(C_N)}{C_W^t} \quad (17)$$

Using Equation 1 and rearranging gives:

$$BCF_T^t = (f_{fd})[\ f_W + (f_\ell)(BCF_L^{fd}) + \frac{(f_N)(C_N)}{(f_{fd})(C_W^t)}\ ] \quad (18)$$

Using Equation 6:

$$BCF_T^t = (f_{fd})[\ f_W + (f_\ell)(BCF_L^{fd}) + \frac{(f_N)(C_N)}{C_W^{fd}}\ ] \quad (19)$$

Substituting $x = f_W + (f_N)(\frac{C_N}{C_W^{fd}})$ and rearranging gives:

$$BCF_T^t = (f_{fd})[\ x + (f_\ell)(BCF_L^{fd})\ ] \quad (20)$$

The term "$(f_\ell)(BCF_L^{fd})$" accounts for the amount of organic chemical that is partitioned to the lipid in the biota, whereas in "x," the term "f_W" accounts for the amount of organic chemical that is freely dissolved in the water in the biota and the term "$(f_N)(\frac{C_N}{C_W^{fd}})$" accounts for the amount of organic chemical that is partitioned to non-lipid organic matter in the biota. The relative magnitudes of these three terms depend on the following:

- Because of bones and other inorganic matter, the sum of $f_W + f_\ell + f_N$ must be less than 1.
- f_W is usually about 0.7 to 0.9.
- Because f_ℓ must be measured if the BAF or BCF is to be useful, f_ℓ is known for the aquatic biota; it is usually between 0.03 and 0.15.

- The term "$\left(\frac{C_N}{C_W^{fd}}\right)$" is similar to BCF_L^{fd} (see Equation 10) and is therefore probably related to K_{ow} (see Equation 14), although the affinity of the chemical for non-lipid organic matter is probably much less than its affinity for lipid.

Although such considerations aid in understanding "x," the magnitude of "x" in Equation 20 is important only for chemicals whose log K_{ow}s are in the range of 1 to 3. For organic chemicals whose log K_{ow}s are about 1, f_{fd} is about 1. In addition, such chemicals distribute themselves so as to have similar concentrations in water and in the different organic phases in the aquatic biota, which means that BCF_T^t will be approximately 1 if both metabolism and growth dilution are negligible. An organic chemical whose log K_{ow} is less than 1 will also have a BCF_T^t on the order of 1 because water is the predominant component in aquatic biota. Setting "x" equal to 1 is about right in the range of log K_{ow}s in which it is not negligible (see also McCarty et al., 1992).

Substituting x = 1 into Equation 20:

$$BCF_T^t = (f_{fd})[\ 1 + (f_\ell)(BCF_L^{fd})\ ] \tag{21}$$

Rearranging gives:

$$BCF_L^{fd} = \left(\frac{BCF_T^t}{f_{fd}} - 1\right)\left(\frac{1}{f_\ell}\right) \tag{22}$$

BCF_L^{fd} can be called the "baseline BCF" because it is the most useful BCF for extrapolating from one species to another and from one water to another for organic chemicals with both high and low K_{ow}s. The baseline BCF is intended to reference bioconcentration of organic chemicals to partitioning between lipid and water.

Equations 12, 13, and 22 demonstrate that both K_{ow} and

$$\left(\frac{BCF_T^t}{f_{fd}} - 1\right)\left(\frac{1}{f_\ell}\right)$$

are useful approximations of the baseline BCFs. It will probably be possible to improve both approximations within a few years, but such improvements might not affect the BCFs substantially and probably will not require changes in the rest of the equations or the terminology.

When BCF_T^t is greater than 1,000, the "-1" in Equation 22 is negligible and so this equation becomes equivalent to Equation 7 (i.e., when BCF_T^t is large, BCF_ℓ^{fd} is a useful approximation of the baseline BCF).

Bioaccumulation

By analogy with Equations 21 and 22:

$$BAF_T^t = (f_{fd})[\ 1 + (f_\ell)(BAF_L^{fd})\ ] \tag{23}$$

$$BAF_L^{fd} = \left(\frac{BAF_T^t}{f_{fd}} - 1\right)\left(\frac{1}{f_\ell}\right) \tag{24}$$

BAF_L^{fd} can be called the "baseline BAF" because it is the most useful BAF for extrapolating from one species to another and from one water to another for chemicals with both high and low K_{ow}s.

It is convenient to define a food-chain multiplier (FCM) as:

$$FCM = \frac{\text{baseline BAF}}{\text{baseline BCF}} = \frac{BAF_L^{fd}}{BCF_L^{fd}} \tag{25}$$

Some of the consequences of Equation 25 are:

1. Substituting Equations 22 and 24 into Equation 25:

$$FCM = \frac{BAF_T^t - f_{fd}}{BCF_T^t - f_{fd}} \tag{26}$$

Therefore, $BAF_T^t = (FCM)(BCF_T^t)$ only when f_{fd} is much less than BAF_T^t and BCF_T^t.

2. When FCM = 1 (as for trophic level 2 in the Gobas model):

$$\text{baseline BAF} = \text{baseline BCF} \tag{27}$$

3. Predicted baseline BAFs can be obtained using FCMs and the following rearrangement of Equation 25:

$$\text{predicted baseline BAF} = (\text{FCM})(\text{baseline BCF}) \tag{28}$$

a. Using a laboratory-measured BCF in Equation 22:

$$\text{predicted baseline BAF} = (\text{FCM})(\text{measured } BCF_L^{fd}) \tag{29}$$

$$= (\text{FCM})\left(\frac{BCF_T^t}{f_{fd}} - 1\right)\left(\frac{1}{f_\ell}\right) \tag{30}$$

b. Using a predicted BCF in Equation 14:

$$\text{predicted baseline BAF} = (\text{FCM})(\text{predicted } BCF_L^{fd}) \tag{31}$$

$$= (\text{FCM})(K_{OW}) \tag{32}$$

The FCMs used to calculate predicted baseline BAFs must be appropriate for the trophic level of the aquatic biota for which the predicted baseline BAF is intended to apply.

Although BAFs can be related to BCFs using FCMs, BAFs, and BCFs can also be related using Biomagnification Factors (BMFs). The two systems are entirely compatible, but confusion can result if the terms are not used consistently and clearly. Because both systems are used in the final Guidance and elsewhere, it is appropriate to explain the relation between the two here. The basic difference is that FCMs always relate back to trophic level one, whereas BMFs always relate back to the next trophic level. In the FCM system:

$$BAF_{TL1} = BCF$$

$$BAF_{TL2} = (FCM_{TL2})(BAF_{TL1})$$

$$BAF_{TL3} = (FCM_{TL3})(BAF_{TL1})$$

$$BAF_{TL4} = (FCM_{TL4})(BAF_{TL1})$$

In the BMF system:

$$BAF_{TL1} = BCF$$

$$BAF_{TL2} = (BMF_{TL2})(BAF_{TL1})$$

$$BAF_{TL3} = (BMF_{TL3})(BAF_{TL2})$$

$$BAF_{TL4} = (BMF_{TL4})(BAF_{TL3})$$

Therefore:

$$BMF_{TL2} = FCM_{TL2}$$

$$BMF_{TL3} = (FCM_{TL3})/(FCM_{TL2})$$

$$BMF_{TL4} = (FCM_{TL4})/(FCM_{TL3})$$

Both metabolism and growth dilution can cause BMFs to be less than 1.

Calculation of Criteria

Baseline BCFs and BAFs can be extrapolated between species and waters, but they cannot be used directly in the calculation of criteria that are based on the total concentration of the chemical in the water. The BCFs and BAFs that are needed to calculate such criteria can be calculated from measured and predicted baseline BCFs and BAFs using the following equations, which are derived from Equations 21 and 23:

$$BCF_T^t = [\ 1 + (\text{baseline BCF})(f_\ell)\ ](f_{fd}) \quad (33)$$

$$BAF_T^t = [\ 1 + (\text{baseline BAF})(f_\ell)\ ](f_{fd}) \quad (34)$$

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Appendix D
Derivation of the Equation Defining f_{fd}

Experimental investigations have shown that hydrophobic organic chemicals exist in water in three phases, (1) the freely dissolved phase; (2) sorbed to suspended solids (particulate organic carbon); and (3) sorbed to dissolved organic matter (Hassett and Anderson, 1979; Carter and Suffet, 1982; Landrum et al., 1984; Gschwend and Wu, 1985; McCarthy and Jimenez, 1985; Eadie et al., 1990, 1992). The total concentration of the chemical in water is the sum of the concentrations of the sorbed chemical and the freely dissolved chemical (Gschwend and Wu, 1985; Cook et al., 1993):

$$C_w^t = C_w^{fd} + POC \cdot C_{poc} + DOC \cdot C_{doc} \quad (1)$$

where:

C_w^{fd} = Concentration of freely dissolved chemical in the ambient water (kg of chemical/L of water)

C_w^t = Total concentration of the chemical in the ambient water (kg of chemical/L of water)

C_{poc} = Concentration of chemical sorbed to the particulate organic carbon in the ambient water (kg of chemical/kg of organic carbon)

C_{doc} = Concentration of chemical sorbed to the dissolved organic carbon in the water (kg of chemical/kg of organic carbon)

POC = Concentration of particulate organic carbon in the ambient water (kg of organic carbon/L of water)

DOC = Concentration of dissolved organic carbon in the ambient water (kg of organic carbon/L of water)

The above equation can also be expressed using partitioning relationships as:

$$C_w^t = C_w^{fd} \cdot (1 + POC \cdot K_{poc} + DOC \cdot K_{doc}) \quad (2)$$

where:

K_{poc} = C_{poc} / C_w^{fd} and $K_{doc} = C_{doc} / C_w^{fd}$

K_{poc} = equilibrium partition coefficient of the chemical between POC and the freely dissolved phase in the ambient water

K_{doc} = equilibrium partition coefficient of the chemical between DOC and the freely dissolved phase in the ambient water

From Equation 2, the fraction of the chemical which is freely dissolved in the water can be calculated using the following equations:

$$f_{fd} = \frac{C_w^{fd}}{C_w^{t}} \tag{3}$$

$$f_{fd} = \frac{1}{(1 + POC \cdot K_{poc} + DOC \cdot K_{doc})} \tag{4}$$

Experimental investigations by Eadie et al. (1990, 1992), Landrum et al. (1984), Yin and Hassett (1986, 1989), Chin and Gschwend (1992), and Herbert et al. (1993) have shown that K_{doc} is directly proportional to the K_{ow} of the chemical and is less than the K_{ow}. The K_{doc} can be estimated using the following equation:

$$K_{doc} \approx \frac{K_{ow}}{10} \tag{5}$$

The above equation is based upon the results of Yin and Hassett (1986, 1989), Chin and Gschwend (1992), and Herbert et al. (1993). These investigations were done using unbiased methods, such as the dynamic headspace gas-partitioning (sparging) and the fluorescence methods, for determining the K_{doc}.

Experimental investigations by Eadie at al. (1990, 1992) and Dean et al. (1993) have shown that K_{poc} is approximately equal to the K_{ow} of the chemical. The K_{poc} can be estimated using the following equation:

$$K_{poc} \approx K_{ow} \tag{6}$$

By substituting Equations 5 and 6 into Equation 4, the following equation is obtained:

$$f_{fd} = \frac{1}{(1 + POC \cdot K_{ow} + (\frac{DOC \cdot K_{ow}}{10}))} \tag{7}$$

The utility in using the freely dissolved equation described above to derive baseline BAFs applicable to multiple sites has been evaluated recently in a study conducted by Burkhard et al. (1997). In their study, Burkhard et al. measured BAFs for various chlorinated butadienes, chlorinated benzenes and hexachloroethane for three species of forage fish and blue crab in Bayou d'Inde of the Calcasieu River system, Louisiana. Using the freely dissolved equation, Burkhard et al. adjusted their field-measured BAFs to baseline BAFs (BAF_{ℓ}^{fd}) and compared these to baseline BAFs determined for other trophic level three species in two other field studies (Pereria et al., 1988; Oliver and Niimi, 1988). The field study by Pereria et al. (1988) was conducted in different sites within the Calcasieu River system and that of Oliver and Niimi (1988) in Lake Ontario. Burkhard et al. found no significant difference between BAF_{ℓ}^{fd} determined in their study and those determined by Pereria et al. (1988) (Tukey's, $\alpha = .05$). However, for one chemical (HCBD) about an order of magnitude difference was observed in the measured BAF_{ℓ}^{fd} between the two studies. Burkhard et al. further noted their baseline BAFs were not substantially different than those derived for Lake Ontario, suggesting broader applicability of properly derived baseline BAFs.

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Appendix E
Derivation of the Equation to Predict BAF from the BSAF

Several steps are involved in the derivation of the equation to predict the BAF for a chemical from the BSAF. First, in the basic equation for BAF for a given chemical, BSAF and C_{soc} can be substituted for C_ℓ for a given chemical *i* as follows:

$$(BAF_\ell^{fd})_i = (BSAF)_i \cdot \frac{(C_{soc})_i}{(C_w^{fd})_i} \quad (1)$$

The chemical concentration quotient between sediment organic carbon and a freely dissolved state in overlying water may be symbolized by Π_{soc}, as follows:

$$(\Pi_{soc})_i = \frac{(C_{soc})_i}{(C_w^{fd})_i} \quad (2)$$

Thus the ratio of BAF_ℓ^{fd}s for chemical i and a reference chemical r may be expressed as:

$$\frac{(BAF_\ell^{fd})_i}{(BAF_\ell^{fd})_r} = \frac{(BSAF)_i(\Pi_{soc})_i}{(BSAF)_r(\Pi_{soc})_r} \quad (3)$$

If both chemicals have similar fugacity ratios between water and sediment, the following assumption can be made:

$$\frac{(\Pi_{soc})_i}{(\Pi_{soc})_r} = \frac{(K_{ow})_i}{(K_{ow})_r} \quad (4)$$

therefore:

$$(BAF_\ell^{fd})_i = (BAF_\ell^{fd})_r \cdot \frac{(BSAF)_i(K_{ow})_i}{(BSAF)_r(K_{ow})_r} \quad (5)$$

The assumption of equal or similar fugacity ratios between water and sediment for each chemical is equivalent to assuming that for all chemicals used in BAF_ℓ^{fd} calculations: (1) the concentration ratios between sediment and suspended solids in the water, and (2) the degree of equilibrium between

suspended solids and C_w^{fd} are the same. Thus, errors could be introduced by inclusion of chemicals with non-steady-state external loading rates or chemicals with strongly reduced C_w^{fd} due to rapid volatilization from the water.

Appendix F
EPA New Draft Protocol for Determining Octanol-Water Partition Coefficients (K_{ow}) For Compounds with Log K_{ow} Values > 5

1. Introduction

The octanol-water partition coefficient (K_{ow}) is one of the most widely used chemical parameters. The K_{ow} of a chemical has been found to be representative of a chemical's propensity to partition into biotic and abiotic components of the environment as well as a chemical's propensity to accumulate in living organisms. Because of these associations, the K_{ow} is widely used to predict a chemical's behavior in the environment and to evaluate a chemical's impact on human health.

The octanol-water partition coefficient (K_{ow}) is a unitless measure and is defined as the ratio of the equilibrium concentrations, C, of a chemical in the two phases of a system consisting of *n* -octanol and water at standard temperature and pressure (STP, 25° C, 1 atm):

$$K_{ow} = C_{oct}/C_w$$

where C_{oct} represents the concentration in the *n* -octanol phase, and C_w represents the concentration in the water. The concentrations in the respective phases are expressed in the same volume-referenced units (i.e., mg/ml, mole/L, etc.), therefore, the K_{ow} is a unitless property. Since the value of the partition coefficient spans orders of magnitude, it is frequently expressed on a log scale (base ten) such that a given chemical has a log K_{ow} value which may range from 1 to >8. This parameter is also called the log P value.

Some specific applications of the K_{ow} within the U.S. EPA include: evaluation of a chemical's potential to bioaccumulate in aquatic life, wildlife and humans; modeling the fate, transport and distribution of a chemical in the environment; prediction of the distribution of a contaminant in a living organism; classification of persistent bioaccumulators for regulatory actions; derivation of soil screening levels; calculation of water quality benchmarks; and derivation of Sediment Quality Criteria.

Although a seemingly simple experimental determination, K_{ow} measurement is beset with difficulties. The appropriateness and accuracy of laboratory methods to directly measure a K_{ow} are influenced by a number of factors which include the magnitude of the value itself. For chemicals with log K_{ow} values at or exceeding 5, common sources of measurement error include: (1) failure to achieve equilibrium; (2) incomplete phase separation or interphase mixing during sampling; (3) emulsion effects derived from **?**excessive" mixing or induced by contaminants; (4) propensity of the chemical to self-associate, tautomerize or form hydrates; and (5) the presence of small quantities of contaminants with a lower K_{ow} value. These errors tend not to be random, but to give measured numbers lower than the true value, frequently by an order of magnitude or more. The likelihood and degree of error increases with increasing K_{ow} and also seems to be more prevalent for certain classes of chemicals (such as halogenated compounds or phthalate esters).

As a result, in addition to direct experimental measurement methods, techniques to indirectly experimentally measure or estimate K_{ow} values have been developed.

Direct experimental measurement techniques include the shake-flask approach, generator column, and slow-stir methods. The shake-flask method is the classical approach and fairly straight-forward for chemicals with log K_{ow} values below 5. For chemicals with higher log K_{ow} values, the shake-flask approach requires large volumes of water and formation of emulsions becomes a significant impediment to accurate measurements. The generator-column approach was developed to measure the partition coefficients of more hydrophobic chemicals (those with larger log K_{ow} values). This is a laborious method which results in more reliable data than the shake-flask approach for chemicals with higher log K_{ow} values, but some discontinuities in the data for higher-chlorinated PCB congeners have been observed. A third direct measurement technique is the slow-stir method. In this method, careful stirring and close temperature control can prevent or limit the formation of emulsions and reliable very high partition coefficients can be obtained relatively easily.

Because of the difficulty of directly and accurately measuring K_{ow} values, estimation methods have been developed. These methods can be divided into two types: those requiring a training set of chemicals with measured K_{ow}s and those based upon fundamental chemical thermodynamics. Those methods requiring a training set of chemicals use Quantitative Structure Property Relationships (QSPRs) or Quantitative Structure Activity Relationships (QSARs) to derive K_{ow}s. In QSPRs, K_{ow} values are correlated with the values for other chemical parameters--either measured or calculated--using data available from the training set of chemicals. In QSARs, K_{ow} values are derived from fragment constants obtained from the training set of chemicals.

One application of QSPRs is estimating K_{ow}s indirectly from other experimental measurements. In this approach, the K_{ow} is correlated with another measured property. These techniques include the use of reversed-phase high performance liquid chromatography (HPLC) and reversed-phase thin-layer chromatography (TLC). In applying these approaches, K_{ow}s are estimated from linear equations relating retention times on the reversed-phase column to the K_{ow} values. The equations are developed based on a set of reference chemicals for which K_{ow} values are well established. These are relatively efficient methods because they do not require quantification of concentrations, but the linear equations can not be extrapolated beyond the K_{ow} range represented by the reference chemicals from which the equation was derived. In application, values for the reference chemicals are usually shake-flask values obtained from the literature, resulting in unreliable K_{ow} estimates for chemicals with higher log K_{ow} values.

In addition to direct and indirect measurement methods, QSPRs are also used to establish correlations between the K_{ow} and calculated properties. For example, Hawker and Connell (1988) developed a correlative relationship between log K_{ow} and molecular surface area using approximately two dozen PCBs. They then estimated log K_{ow}s for the remaining PCBs by inputting the molecular surface area of each PCB. This technique is limited to estimating K_{ow}s for chemicals which are similar to the chemicals used in developing the relationship.

In QSARs, hydrophobic fragment values are derived from a large data base of measured K_{ow}s. These fragment constants are used to estimate K_{ow} in two ways. One approach is to estimate the K_{ow} by adding up the values for all the fragments composing the chemical, either by atom or by functional group. The other approach is to start with a measured K_{ow} value for a structurally similar compound and add or subtract the fragment constants for functional groups or atoms to estimate the K_{ow} for the specific compound. In both these cases, the calculated K_{ow} value must also be corrected for proximity effects between structurally close substituent groups, and the K_{ow} value derived is only as good as the data associated with the training set of chemicals. This method is also limited to predicting K_{ow}s for chemicals with structures similar to those within the training set. Computer-based models exist which apply QSAR approaches to estimate K_{ow}s. CLOGP[1] and LOGKOW[2] data bases are both applications of this approach.

Other computer methods are based on fundamental chemical structure theory and are not limited by nor require a training set of chemicals with measured K_{ow}s. For example, the SPARC[3] model consists of a set of core models describing intra- and inter-molecular interactions. These models are linked by appropriate thermodynamic relationships to provide estimates of reactivity parameters under desired conditions (e.g., temperature, pressure, solvent).

Given the numerous techniques available to determine the K_{ow} and its numerous and important applications across the Agency, the U.S. EPA has formed an Agency K_{ow} Work Group to draft the following guidance for selecting reliable values of K_{ow} and ultimately for developing a data base of reliable K_{ow} values. In determining these recommended K_{ow} values, the preferable option would be to recommend actual measured values. For chemicals with log K_{ow} values below 5, the classical shake-flask approach is adequate to obtain these measurements. Although recent advances in measurement technology (development of the slow stir method and increased awareness of, and compensation for, determinate errors) have significantly improved the quality of data available for chemicals with higher log K_{ow} values, there remains a serious shortage of reliable measured data for compounds with higher log K_{ow} values (log K_{ow} > 5). Unfortunately, it is frequently these chemicals that exhibit a propensity to accumulate in living tissues or bind to soils and sediments.

2. Protocol For Determining Recommended K_{ow} Values

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[1]CLOGP is a molecular fragment-based model developed at Pomona College by Albert Loe, Corwin Han (See Hansch and Leo, 1995, for model description and performance data.)

[2]LOGKOW is essentially an expanded CLOGP with more recent training data and additional fragment co Research Corporation. (See Meylan and Howard, 1994, for model details and performance information.)

[3]SPARC (SPARC Performs Automated Reasoning in Chemistry) is a mechanistic model developed at the Ecos Research and Development of the U.S. Environmental Protection Agency by Sam Karickhoff, Lionel Carreira, and The model complements the aforementioned models because development, training, and testing were done away from

Measured data are preferable for determining recommended K_{ow} values. However, the absence or scarcity of reliable data necessitates the use of estimation methods in evaluating data and in assigning K_{ow}s. K_{ow} estimates used in this exercise include: (1) QSARs (e.g., CLOGP, LOGKOW, and fragment additions or subtractions); (2) QSPRs (e.g., HPLC and TLC methods) and (3) estimation methods based on fundamental chemical structure theory (e.g. SPARC). All of these approaches except the last one listed (the SPARC model) require measured K_{ow} values for a training set of chemicals.

Assigning a K_{ow} from these data will necessarily involve scientific judgement in evaluating not only the reliability of all data inputs but also the accretion/concretion of evidence in support of the recommended K_{ow} value. Supporting rationale will be provided for each recommended value.

2.1 Operational Guidelines for K_{ow} Selection Protocol

- For chemicals with log $K_{ow} > 5$, it is highly unlikely to find multiple "high quality" measurements. (Note: "high quality" is data judged to be reliable based on the guidelines presented in Section 3)

- "High quality" measured data are preferred over estimates, but due to the scarcity of "high quality" data, the use of estimates is important in assigning K_{ow} s.

- K_{ow} measurements by slow stir are extendable to 10^8. Shake flask K_{ow} measurements are extendable to 10^6 with sufficient attention to micro emulsion effects; for classes of chemicals that are not highly sensitive to emulsion effects (i.e., PNAs) this range may extend to $10^{6.5}$.

- What is to be considered reasonable agreement in log K_{ow} data (measured or estimated) depends primarily on the log K_{ow} magnitude. The following standards for data agreement have been set for this guidance: 0.5 for log $K_{ow} > 7$; 0.4 for $6 \leq \log K_{ow} \leq 7$; 0.3 for log $K_{ow} < 6$.

- Statistical methods should be applied to data as appropriate but application is limited due to the scarcity of data, and the determinate/methodic nature of most measurement error(s).

2.2 Tiered Procedure for Setting K_{OW} Values

I. Assemble/evaluate experimental and calculated data (e.g.,CLOGP, LOGKOW, SPARC)

II. If calculated log K_{ow}s > 8,

   A. Develop independent estimates of K_{ow} using:
      1. Liquid Chromatography (LC) methods with "appropriate" standards. (See Section 3 for guidelines for LC application.)

2. Structure Activity Relationship (SAR) estimates extrapolated from similar chemicals where "high quality" measurements are available. "High quality" SARs are described in Section 3.
3. Property Reactivity Correlation (PRC) estimates based on other measured properties (solubility, etc.)

B. If calculated data are in "reasonable" agreement and are supported by independent estimates described above, report average calculated value. What is to be considered reasonable agreement in log K_{ow} data (measured or estimated) depends primarily on the log K_{ow} magnitude. The following standards for data agreement have been set for this guidance: 0.5 for log $K_{ow} > 7$; 0.4 for $6 \leq \log K_{ow} \leq 7$; 0.3 for log $K_{ow} < 6$.

C. If calculated/estimated data do not agree, use professional judgement to evaluate/blend/weight calculated and estimated data to assign a K_{ow} value.

D. Document rationale including relevant statistics.

III. If calculated log K_{ow}s range from 6 - 8,

A. Look for "high quality" measurements. These will generally be slow stir measurements, the exception being certain classes of compounds where micro emulsions tend to be less of a problem (i.e., PNAs, shake flask measurements are good to 6.5).

B. If measured data are available and are in reasonable agreement (both measurements and calculations), report average measured value.

C. If measured data are in reasonable agreement, but differ from calculated values, develop independent estimates and apply professional judgement to evaluate/blend/weight measured, calculated and estimated data to assign K_{ow} value.

D. If measured data are not in reasonable agreement (or if only one measurement is available), use II A, B, and C to produce a 'best estimate;' use this value to evaluate/screen measured data; report average value of screened data. If no measurements reasonably agree with 'best estimate,' apply professional judgement to evaluate/blend/weight measured, calculated and estimated data to assign K_{ow}.

E. If measured data are unavailable, proceed through II A, B, C and report the 'best estimate.'

F. Document rationale including relevant statistics.

IV. If calculated log K_{ow}s < 6,

A. Proceed as in III. Slow stir is the preferred method but shake flask data can be considered for all chemicals if sufficient attention has been given to emulsion problems in the measurement.

3. Guidelines for Evaluating Measured and Liquid Chromatography-estimated K_{OW}s

3.1 Assessment of Measured K_{ow} Values

3.1.1 Molecular Speciation. In order to interpret measured data, it is necessary to understand the molecular species present in both the octanol and water phases including ionization, self-association, tautomerization, and hydrate formation. For these reasons, it is difficult to conduct or interpret such measurements for mixtures of unknown composition or for single molecules of unknown structure. Solutes composed of more than one molecular species may also show substantial temperature dependence of K_{ow} reflecting relative change in speciation in the octanol and water phases.

- Ionization. For weakly ionizable molecules, shake flask measurements are conducted in solutions of a stable, non-extractable buffer to suppress ionization.

- Self-Association - For molecules able to associate through hydrogen-bonding (e.g., amines, carboxylic acids, phenols, especially if cyclic dimers can form), measurement needs to be conducted at a sufficiently low concentration that K_{ow} reflects only unassociated form of the molecule in both water and octanol phases. Measurements at several concentrations with no change in K_{ow} provide an indication that this is the case.

- Tautomerization - If the molecule is likely to exist in more than one tautomeric form, the ratio of tautomers may be different in the octanol and water phases. If that is the case, the measured K_{ow} may not be a very meaningful number. Sometimes molecules exhibit both ionization and tautomerization, leading to further complications.

- Hydrate Formation - Similar to the case of tautomerization, hydrates may exist to different degrees in the water and octanol phases thus confounding the interpretation of the measured value. A comparison of estimated and measured K_{ow} for chloral hydrate suggests that such hydration may be much less important in the octanol than water phases, making the compound more lipophilic than would be expected from the hydrate structure alone.

3.1.2 Shake Flask or Slow-Stirring Considerations. (1) Water and octanol phases should be free of impurities; (2) mixing should be of sufficient duration (e.g., 7 days for dioctyl phthalate) to reach steady state equilibrium, particularly for very hydrophobic chemicals; (3) analytical measurement of both phases is particularly important when using volatile solutes; (4) Avoid formation of emulsions during mixing and centrifuge before measuring; (5) experimental protocol should be particularly scrutinized for K_{ow} measurements 4-6; (6)

ratio of octanol to water should be reduced for high K_{ow} chemicals; and (7) sorption to glass (e.g., for pyrethroids) during workup can be a problem.

3.1.3 General Considerations. Solute should be stable to hydrolysis during the course of the experiment. Solutes should be of high purity as the presence of a less lipophilic impurity exerts a dominant effect in the measured K_{ow} value. Mixtures such as chlorinated paraffins (containing thousands of isomers, congeners, and degrees of chlorination) therefore cannot be determined except by chromatographic methods.

3.1.4 Indicators of Potential Concern. Inconsistency with other measured values, with estimated value, or inconsistency among estimated values. The importance of professional judgement and knowledge of chemistry cannot be overemphasized in making the best K_{ow} assignments. For example, inconsistency between measured and predicted may reflect only problems in the training set used based upon poor experimental values when better data have since become available.

3.2 Assessment of K_{ow} Values Estimated using Liquid Chromatographic Techniques

An estimated K_{ow} value would be considered "appropriate" provided the following experimental conditions existed during its determination:

3.2.1 K_{ow}s used for the reference compounds consist of “high quality”slow stir measurements.

- Better estimates for K_{ow}s are obtained when reference and test chemicals are similar.

3.2.2 A minimum of five chemicals are used in developing the log capacity factor (k')- log K_{ow} calibration relationship. The K_{ow}s of the reference chemicals should be evenly distributed and should span 3 to 4 orders of magnitude.

3.2.3 The log k' - log K_{ow} calibration curve is linear and has a correlation coefficient greater than 0.95.

3.2.4 The K_{ow} estimated for the test chemical is within the range of K_{ow}s for the reference compounds or does not exceed the upper end of the range of K_{ow}s for the reference compounds beyond 0.5 log units without adequate justification.

3.2.5 Chemical speciation must be accounted for in performing the measurements. For example, with ionizable chemicals, measurements must be performed on the unionized form by using an appropriate buffer with a pH below the pK for an acid and above the pK for a base.

3.2.6 Reference and test chemicals are of known purity and structure. Independent confirmation of the identity and purity of the reference and test chemicals is required or highly desirable.

3.2.7 Chemical mixtures can be used as the source of test chemicals provided accurate identities can be assigned to individual chromatographic components.

4. Estimation of K_{OW} from Molecular Fragments

For computing thermodynamic properties it is often useful to consider a molecule as a collection of molecular fragments, each making a distinct contribution to the property of interest, which is relatively independent of the rest of the molecule. The rationale behind the method is that a large number of structures can be generated from a relatively small number of fragments, and thus a large number of estimates can be derived from a small number of experimentally determined fragment constants. The accuracy of the estimation, however, necessarily improves as the specificity of the fragment environment increases, which entails an increase in the number of fragments or corrective factors that must be considered. This approach is applied at different levels of sophistication. One user may employ a few fragment constants and generate 'first order' estimates whereas another may make numerous corrections or adjustments reflecting more fragment specificity for a given molecular environment. For a more complete discussion of group fragment methods one should consult Hansch and Leo, 1995.

4.1 Addition of Ring Fragments

For condensed ring aromatics, the addition of rings is given by

$$f^{\alpha}_{(C_4H_2)} = \log K_{(OW)}\text{ (anthracene)} \quad \log K_{(OW)}\text{ (naphthalene)} \approx 1.20$$

$$f^{\beta}_{(C_3H)} = 0.5\left[\log K_{(OW)}\text{ (pyrene)} \quad \log K_{(OW)}\text{ (naphthalene)}\right] \approx 0.85$$

$$f^{\gamma}_{(C_2)} = \log K_{(OW)}\text{ (pyrene)} \quad \log K_{(OW)}\text{ (phenanthrene)} \approx 0.50$$

where $f^{\alpha}_{(C_4H_2)}$, $f^{\beta}_{(C_3H)}$, $f^{\gamma}_{(C_2)}$ are the fragment addition constants for α, β, and γ condensation respectively.

4.2 Addition of Substituents

The addition of a substituent, S (replacing a H atom) is a primary application of this method. In this case

$$\Pi_S = \log K_{(OW)}(R \quad S) \quad \log K_{(OW)}(R \quad H)$$

where R is the base molecule and Π_S is a substituent constant, which is experimentally determined. Tables for common substituents are readily available or can be easily determined from measured data. One must distinguish (i.e., have different substituent constants for) attachment to aliphatic, ethylenic, acetylenic, and aromatic carbon atoms in 'R'. Also corrections must be made for multiple substitution if attachment is to the same or adjacent carbons. The following are examples of K_{ow} estimation. The fragment constant for Cl attached to aromatic carbon can be derived from:

$$\Pi_{Cl}^{arom} = \log K_{(OW)}(\text{chlorobenzene}) \quad \log K_{(OW)}(\text{benzene}) \approx 0.71$$

With this constant, one can derive

$$\log K_{(OW)}(1,3,5\text{-trichlorobenzene}) \approx \log K_{(OW)}^{(benzene)} + 3\,(0.71) = 4.26$$

An exhaustive list of substituent constants is included in the aforementioned Hansch and Leo (1995) reference.

5. Example Application of EPA Draft K_{ow} Selection Protocol

BENZO(A)ANTHRACENE

CAS	log K_{OW}	Method	Reference/Comments
56-55-3	5.79	shake flask	Medchem
	5.61	shake flask	Steen & Karickhoff (1979)
	5.79	RP-HPLC	Wang et al (1986)
	4.00	RP-HPLC-E	Brooke et al (1986)
	5.00	RP-HPLC	Brooke et al (1986)
	5.66	CLOGP	
	5.83	SPARC	
	5.52	LOGKOW	

Calculated values < 6, therefore enter Step IV of protocol.
Go to step III of protocol with inclusion of shake flask data.

III A. Two shake-flask measurements in good agreement with one another and avg = 5.70

B. Calculators: SPARC, LOGKOW and CLOGP in good agreement with range from 5.52-5.83 and avg = 5.67.

Shake-flask measurements in excellent agreement with calculators, therefore recommended value is 5.70—average of the two shake-flask measurements.

BENZO(K)FLUORANTHENE

CAS	log K_{OW}	Method	Reference/Comments
207-08-9	6.12	CLOGP	
	6.30	SPARC	
	6.11	LOGKOW	

Calculated values in range 6-8, therefore enter Step III of protocol.

III A. No measured values available.

E. Calculators: SPARC, LOGKOW and CLOGP in excellent agreement with range from 6.11-6.30 and avg = 6.18.

- Estimate Kow from Molecular Fragment Constants:

Fluoranthene (5.12) + $f^a(C_4H_2)$ (1.20) = 6.32 This is in good agreement with calculated values.

Recommended value is average of three calculators = <u>6.18</u>.

BENZO(A)PYRENE

CAS	log K_{OW}	Method	Reference/Comments
50-32-8	5.98	gen. col.	Miller et al (1985)
	6.34	shake flask	Steen & Karickhoff (1979)
	6.04	shake flask	Medchem
	6.00	shake flask	Mallon & Harrison (1984)
	5.99	shake flask	Mallon & Harrison (1984)
	6.42	RP-HPLC	Rappaport & Eisenreich (1984)
	6.24	RP-HPLC	Hanal et al(1981) (60% solvent values
	6.04	RP-HPLC	Wang et al (1986)
	5.97	unknown	Hansch & Leo
	6.12	CLOGP	
	6.25	SPARC	
	6.11	LOGKOW	

Calculated values in range 6-8, therefore enter Step III of protocol.

III A. There are no slow-stir measurements.

There are four shake flask measurements in range 5.99-6.34 with an average = 6.09

B. Calculators: SPARC, LOGKOW and CLOGP in excellent agreement with range from 6.11-6.25 and average = 6.16

- Estimate K_{ow} from Molecular Fragment Constants:

pyrene (5.05) +$f^g(C_4H_2)$ (1.20) = 6.25 This is in good agreement with calculated and measured values.

- Three RP-HPLC values (range 6.04 - 6.42) with average 6.26.

This compound is on the border of whether shake flask data acceptable but PNAs are less susceptible to emulsification using the shake flask approach than other compounds. Therefore shake flask measurements may be acceptable up to 6.5 rather than 6.0. Therefore, we will assume the shake flask

measurements for this compound are accurate and recommend going with the average of the four shake flask measurements = 6.09

DI-N-OCTYL PHTHALATE

CAS	log K_{OW}	Method	Reference/Comments
117-84-0	8.06	RP-HPLC	McDuffie (1981)
	9.49	CLOGP	
	8.39	SPARC	
	8.54	LOGKOW	

Calculated values are >8.0 therefore enter step II of protocol.

II A. No published measured values were available, J. Ellington (EPA, Athens) measured 8.1 by slow-stir.

D. Calculators: Not in good agreement: SPARC, 8.39, CLOGP, 9.49, & LOGKOW, 8.54.

- SPARC and LOGKOW calculators are close to the Ellington value.
- Can use branching correction and estimate from diethylhexyl phthalate (2 slow stir measurements, average 7.3) . A secondary branch contributes approximately '-0.3 'per which would place the unbranched dioctyl phthalate at 7.9 (7.3 + 2(0.3)); this is close to the Ellington value.
- The RP-HPLC estimate is 8.06.

Recommended value is 8.1 (Ellington, unpublished), supported by two of the calculators and two other estimates.

PYRENE

CAS	log K_{OW}	Method	Reference/Comments
129-00-0	5.07	slow stir	Stancil (1994)
	5.18	gen. col.	Miller et al (1985)
	5.18	shake flask	Karickhoff et al (1979)
	5.09	shake flask	Means et al (1980); Hassett et al (1980)
	5.09	shake flask	Wang et al (1986)
	5.08	shake flask	Medchem
	5.05	shake flask	Ellington & Stancil (1988)
	4.88	shake flask	Hansch & Leo (1979); Medchem
	4.93	RP-HPLC-E	Hammers et al (1982)
	4.89	RP-HPLC-E	Tomlinson & Hafkenschield (1986)
	4.76	RP-HPLC-E	Hafkenschield & Tomlinson (1983)
	5.52	RP-HPLC	Rurkhard et al (1985)
	5.05	RP-HPLC	McDuffie (1981)
	4.97	RP-HPLC	Chin et al (1986)
	4.96	RP-HPLC	Rapaport & Eisenreich (1984)
	5.08	RP-HPLC	Wang et al (1986)
	4.89	RP-HPLC	Hanal et al (1981) (50% acetonitrile)
	4.95	CLOGP	
	5.02	SPARC	
	4.93	LOGKOW	

Calculated values < 6, therefore enter Step IV of protocol.
Go to step III of protocol which permits consideration of shake flask data.

III A. Seven of eight measured values are in good agreement (range = 4.88 to 5.18); shake flask, slow stir, generator column avg 5.08.

B. Calculators: All three calculators are in excellent agreement with avg = 4.94, in agreement with the measured value.
Recommended value is average of slow stir, shake flask and generator column values = <u>5.08</u>

6. References

Hansch, C. and A. Leo. 1995. Exploring QSAR. American Chemical Society.

Hawker, D. W. and D.W. Connell. 1988. Environ. Sci. Technol. 22: 382-387.

Hilal, S. H., L. A. Carreira, and S. W. Karickhoff. 1994. Quantitative Treatments of Solute/Solvent Interactions. Theoretical and Computational Chemistry 1: 291-353.

Meylan, W. M. and P. H. Howard. 1995. J. Pharm. Sci. 84: 83-92.

Appendix G
Amount of Commercial Food Items Consumed and Intake of Chemical X from Commercial Food Items

Food Item	Amount of food item consumed* (g/day)	Average chemical X concentration (ug/g)	Average intake of chemical X (mg/kg-day)	High-end chemical X concentration (ug/g)	High-end intake of chemical X (mg/kg-day)
cheddar cheese	7.07	4.55E-04	4.59E-08	2.00E-02	2.0E-06
beef roast	15.06	4.55E-04	9.78E-08	1.00E-02	2.2E-06
steak	1.93	5.00E-04	1.38E-08	1.50E-02	4.1E-07
beef loin	28.09	5.00E-04	2.01E-07	2.20E-02	8.8E-06
pork chop	8.07	8.41E-04	9.70E-08	2.10E-02	2.4E-06
pork roast	3.98	1.18E-03	4.70E-08	3.40E-02	1.9E-06
lamb chop	1.13	2.27E-04	3.66E-09	1.00E-02	1.6E-07
veal cutlet	1.11	2.05E-04	3.24E-09	9.00E-03	1.4E-07
turkey breast	3.42	7.50E-04	3.67E-08	2.30E-02	1.1E-06
bologna	7.90	1.82E-04	2.05E-08	8.00E-03	9.0E-07
cod/haddock	8.58	5.23E-04	6.40E-08	2.30E-02	1.72E-06
fishsticks	1.70	2.05E-03	5.00E-09	9.00E-03	2.18E-07
corn grits	4.03	3.64E-04	2.09E-08	1.60E-02	9.2E-07
popcorn	1.18	2.05E-04	3.44E-09	9.00E-03	1.5E-07
cornbread	7.41	2.50E-04	2.65E-08	1.10E-02	1.2E-06
biscuits	4.58	9.09E-04	5.95E-08	2.40E-02	1.6E-06
pancakes	5.51	5.45E-04	4.30E-08	2.40E-02	1.9E-06
cereal	2.23	2.45E-03	7.81E-08	6.40E-02	2.0E-06
raisins	0.34	4.77E-04	2.34E-09	2.10E-02	1.0E-07
prunes	0.34	2.73E-04	1.32E-09	1.20E-02	5.8E-08
tomato	18.26	4.55E-04	1.19E-07	2.00E-02	5.2E-06
squash	1.47	5.91E-04	1.24E-08	2.60E-02	5.5E-07
pizza	8.77	2.27E-04	2.85E-08	1.00E-02	1.3E-06

Food Item	Amount of food item consumed* (g/day)	Average chemical X concentration (ug/g)	Average intake of chemical X (mg/kg-day)	High-end chemical X concentration (ug/g)	High-end intake of chemical X (mg/kg-day)
meatloaf	8.04	6.82E-04	7.83E-08	2.30E-02	2.6E-06
potpie	1.64	5.68E-04	1.33E-08	2.50E-02	5.9E-07
margarine	4.44	4.55E-04	2.88E-08	2.00E-02	1.3E-06
butter	2.84	5.45E-04	2.21E-08	2.40E-02	9.7E-07
carmel candy	2.37	1.36E-04	4.62E-09	6.00E-03	2.0E-07
Intake from all foods containing chemical X	161.50		1.18E-06		4.26E-05
Total daily intake of all foods* = 2,582 grams/day					
Intake of Chemical X after subtracting intake from meat [Calculation = intake from all foods - (fraction of meat that is fish*chemical intake from all commercial meat)]					
general population			**1.13E-06**		**4.10E-05**
sportfisher			**1.13E-06**		**4.10E-05**
subsistence fisher			**1.06E-06**		**3.86E-05**

*These estimates are weighted averages of intakes for males and females in two age groups: 25-30 year olds and 60-65 year olds

Appendix H

Ambient Water Quality Criteria for the Protection of Human Health: Acrylonitrile

Summary

This criteria document updates the national criteria for Acrylonitrile using new methods and information described in the Federal Register Notice (USEPA, 1998a) and Technical Support Document (USEPA, 1998b) to calculate ambient water quality criteria. These new methods include approaches to determine dose-response relationships for both carcinogenic and non-carcinogenic effects, updated information for determining exposure factors (e.g., values for fish consumption), exposure assumptions, and procedures to determine bioaccumulation factors. For more detailed information please refer to the U.S. EPA Ambient Water Quality Criteria (AWQC) document for Acrylonitrile (USEPA, 1998c).

Background Information

The AWQC is being derived for acrylonitrile (CAS No. 107-13-1). The chemical formula is $C_3H_3N_2$. Acrylonitrile occurrence in environmental media is not well-documented. Several regional and local drinking water surveys were found and one limited study analyzed ambient air samples. Limited information is also available on acrylonitrile migration into foods from packaging materials.

Acrylonitrile is largely used in the manufacture of copolymers for the production of acrylic and modacrylic fibers. Other major uses include the manufacture of acrylonitrile-butadiene-styrene (ABS) and styrene acrylonitrile (SAN) (used in production of plastics), and nitrile elastomers and latexes. It is also used in the synthesis of antioxidants, pharmaceuticals, dyes, and surface-active agents.

According to the U.S. Environmental Protection Agency's (EPA) Toxic Release Inventory, the total release of acrylonitrile into the environment in 1990 by manufacturers, was 8,077,470 pounds. The two largest pathways of release were underground injection, which accounted for 61% (or 4,925,276 pounds) of the total release, and emissions into the air, which accounted for 39% (or 3,148,049 pounds) of the total release. Release of acrylonitrile into water bodies was reported at 3,877 pounds and release onto land was reported at 268 pounds.

A baseline BAF of 1.5 was calculated for acrylonitrile. The baseline BAF was calculated using a value of 0.17 for the log K_{ow} and 1.000 for the food-chain multiplier (FCM) at trophic level 4. A value of 0.17 was selected as a typical value of the log K_{ow} for acrylonitrile (USEPA 1998c). A value of 1.000 was selected as the FCM for trophic level 4, reflective of top predator fish based on a log K_{ow} of 2.0 from USEPA (1998b). Using these data, the baseline BAF was calculated as: K_{ow} * FCM = $(10^{0.17})$*1.000 = 1.5 (rounded to two significant digits).

Based upon sufficient evidence from animal studies (multiple tumor types in several strains of rats by several routes) and limited evidence from human studies (lung tumors in workers), positive mutagenicity, acrylonitrile is considered as a likely human carcinogen by any route. A linear approach is used for the low dose extrapolation.

AWQC Calculation

For Ambient Waters Used as Drinking Water Sources

The cancer-based AWQC was calculated using the RSD and other input parameters listed below:

$$AWQC = RSD \times \left(\frac{BW}{DI + \sum_{i=2}^{4} (FI_i \times BAF_i)} \right)$$

where:

RSD = Risk specific dose (1.6×10^{-6} mg/kg-day at 10^{-6} lifetime risk)
BW = Human body weight assumed to be 70 kg
DI = Drinking water intake assumed to be 2 L/day
FI = Fish intake at trophic level i, i=2,3, and 4; total intake assumed to be 0.01780 kg/day
BAF = Bioaccumulation factor at trophic level i (i=2,3, and 4) equal to 1.03, 1.02, and 1.05 L/kg-tissue for trophic levels 2,3, and 4, respectively.

This yields concentrations of 5.5×10^{-5} mg/L (or 0.05 µg/L), for a 10^{-6} (one in a million) lifetime cancer risk.

This is a preliminary summary of a criteria document being prepared for the derivation of the Ambient Water Quality Criteria (AWQC) for the protection of human health from exposure to acrylonitrile. The calculated AWQC values presented in this draft are subject to revision pending inclusion of further information concerning exposure as well as possible changes in the toxicological information used to derive the criterion.

For Ambient Waters Not Used as Drinking Water Sources

When the water body is to be used for recreational purposes and not as a source of drinking water, the drinking water value (DI above) is eliminated from the equation and it is substituted with an incidental ingestion value (II). The incidental intake is assumed to occur from swimming and other activities. The fish intake value is assumed to remain the same. The default value for incidental ingestion is 0.01 L/day. When the above equation is used to calculate the AWQC with the substitution of an incidental ingestion of 0.01 L/day an AWQC of 4.0 x 10^{-3} mg/L (or 4.0 µg/L) is obtained for a 10^{-6} lifetime cancer risk.

Site-Specific or Regional Adjustments to Criteria

Several parameters in the AWQC equation can be adjusted on a site-specific or regional basis to reflect regional or local conditions and/or specific populations of concern. These include fish consumption, incidental water consumption as related to regional/local recreational activities, BAF (including factors used to derive BAFs, percent lipid of fish consumed by target population, and species representative of given trophic levels), and the relative source contribution. States are encouraged to make adjustments using the information and instructions provided in the Technical Support Document (USEPA, 1998b).

REFERENCES

USEPA. 1998a. Federal Register Notice: Proposed Water Quality Criteria Methodology Revisions; Human Health. (See Attached Copy).

USEPA. 1998b. Ambient Water Quality Criteria Derivation Methodology; Human Health. Technical Support Document. EPA/822/B-98/005. July. (See Attached Copy).

USEPA. 1998c. Ambient Water Quality Criteria for the Protection of Human Health: Acrylonitrile. EPA/822/R-98/006. July.

Ambient Water Quality Criteria for the Protection of Human Health: 1,3-Dichloropropene (1,3-DCP)

Summary

This criteria document updates the national criteria for 1,3-DCP using new methods and information described in the Federal Register Notice (USEPA, 1998a) and Technical Support Document (USEPA, 1998b) to calculate ambient water quality criteria. These new methods include approaches to determine dose-response relationships for both carcinogenic and non-carcinogenic effects, updated information for determining exposure factors (e.g., values for fish consumption), exposure assumptions, and procedures to determine bioaccumulation factors. For more detailed information please refer to the U.S. EPA Ambient Water Quality Criteria (AWQC) document for 1,3-Dichloropropene (1,3-DCP) (USEPA, 1998c).

Background Information

The AWQC is being derived for 1,3-Dichloropropene (CAS No. 542-75-6). The chemical formula is $C_3H_4Cl_2$ and molecular weight is 110.98 (pure isomers). At 25°C, the physical state of 1,3-DCP is a pale yellow to yellow liquid. Dichloropropene (DCP) is used as soil fumigant in the United States to control soil nematodes on crops grown in sandy soils. The EPAs National Toxics Inventory data base reported air emissions of 18,820,000 pounds/year in the U.S. (USEPA, 1996a). Numerous studies have sampled for DCP (and isomers) in drinking water, groundwater and surface waters across the U.S. (Hall et al., 1987; Miller et al., 1990; RIDEM, 1990; Rutledge, 1987; STORET, 1992). All of these studies report concentrations of 1,3-DCP usually at or below the detection limits (USEPA, 1998c).

The AWQC Bioaccumulation factor (BAF) is 2.2 L/kg of tissue for 1,3-DCP. This BAF is based on the total concentration of 1,3-DCP in trophic level four biota divided by the total concentration in water, assuming default values for the freely-dissolved fraction and lipid content of consumed aquatic organisms.

The cancer risk evaluation of 1,3-DCP uses the new methods in the proposed cancer guidelines (USEPA, 1996), which are described in the Federal Register Notice (USEPA, 1998a) and in the Technical Support Document (USEPA, 1998b). Based upon sufficient evidence from animal studies (multiple tumor types in several species by oral, inhalation, and dermal routes), positive mutagenicity, and structural analogues, 1,3-DCP is considered **"likely to be carcinogenic to humans by all routes of exposure."** Based on the mutagenic mode of action, a linear low dose approach is recommended.

AWQC Calculation

For Ambient Waters Used as Drinking Water Sources

The cancer-based AWQC was calculated using the RSD and other input parameters listed below:

$$AWQC = RSD \times \left(\frac{BW}{DI + \sum_{i=2}^{4} (FI_i \times BAF_i)} \right)$$

where:

RSD = Risk specific dose 1.0 x 10^{-5} mg/kg/day (10^{-6} risk)
BW = Human body weight assumed to be 70 kg
DI = Drinking water intake assumed to be 2 L/day
FI = Fish intake at trophic level i, i=2,3,and 4 total intake assumed to be 0.01780 kg/day
BAF = Bioaccumulation factor at trophic level i (i=2,3,and 4), equal to 2.32, 1.86, and 2.78 L/kg-tissue for trophic levels 2,3,and 4, respectively.

This yields a value of 3.4 x 10^{-4} mg/L, or 0.34 µg/L (rounded from 0.343 µg/L).

For Ambient Waters Not Used as Drinking Water Sources

When the water body is used for recreational purposes and not as a source of drinking water, the drinking water value is eliminated from the equation and it is substituted with an incidental ingestion value. The incidental intake is assumed to occur from swimming and other activities. The fish intake value is assumed to remain the same. The default value for incidental ingestion is 0.01 L/day. When the above equation is used to calculate the AWQC with the substitution of an incidental ingestion of 0.01 L/day an AWQC of 1.4 x10^{-2} mg/L (14 µg/L) is obtained.

This is a preliminary summary of a criteria document being prepared for the derivation of the Ambient Water Quality Criteria (AWQC) for the protection of human health from exposure to 1,3-dichloropropene. The calculated AWQC values presented in this draft are subject to revision pending inclusion of further information concerning exposure as well as possible changes in the toxicological information used to derive the criterion.

Site-Specific or Regional Adjustments to Criteria

Several parameters in the AWQC equation can be adjusted on a site-specific or regional basis to reflect regional or local conditions and/or specific populations of concern. These include fish consumption; incidental water consumption as related to regional/local recreational activities; BAF (including factors used to derive BAFs , percent lipid of fish consumed by the target population, and species representative of given trophic levels); and the relative source contribution. States are encouraged to make adjustments using the information and instructions provided in the Technical Support Document (USEPA, 1998b).

REFERENCES

USEPA. 1998a. Federal Register Notice: Proposed Water Quality Criteria Methodology Revisions; Human Health. (See Attached Copy).

USEPA. 1998b. Ambient Water Quality Criteria Derivation Methodology; Human Health. Technical Support Document. EPA/822/B-98/005. July. (See Attached Copy).

USEPA. 1998c. Ambient Water Quality Criteria for the Protection of Human Health: 1,3-Dichloropropene (1,3-DCP). EPA/822/R-98/005. July.

Ambient Water Quality Criteria for the Protection of Human Health: Hexachlorobutadiene (HCBD)

Summary

This criteria document updates the national criteria for HCBD using new methods and information described in the Federal Register Notice (USEPA, 1998a) and Technical Support Document (USEPA, 1998b) to calculate ambient water quality criteria. These new methods include approaches to determine dose-response relationships for both carcinogenic and non-carcinogenic effects, updated information for determining exposure factors (e.g., values for fish consumption), exposure assumptions, and procedures to determine bioaccumulation factors. For more detailed information please refer to the U.S. EPA Ambient Water Quality Criteria (AWQC) document for hexachlorobutadiene (HCBD)(USEPA, 1998c).

Background Information

The AWQC is being derived for hexachlorobutadiene (CAS No. 87-68-3). The chemical formula is C_4Cl_6 and molecular weight is 260.76. At 25°C, HCBD is a colorless liquid. HCBD is used as a solvent in chlorine gas production, as an intermediate in the manufacture of rubber compounds and lubricants, and as a pesticide. The EPA's National Toxics Release Inventory data base reported total emissions to the environment in 1990 of 5,591 pounds/year in the U.S., of which 4,906 pounds was to air. Numerous studies have sampled for HCBD in drinking water, groundwater and surface waters across the U.S. (see USEPA 1998c for a summary). The vast majority of samples are at trace levels or below the detection limits (DL ≈ 0.1 µg/L).

The AWQC Bioaccumulation factor (BAF) is 620 L/kg of tissue for HCBD. This BAF is based on the total concentration of HCBD in trophic level four biota divided by the total concentration in water, assuming default values for the freely-dissolved fraction and lipid content of consumed aquatic organisms.

The cancer risk evaluation of HCBD uses the new methods described in the Federal Register Notice (USEPA, 1998a) and in the Technical Support Document (USEPA, 1998b). Based on a renal tumor finding in one chronic feeding study at one high dose in one species (both sexes of Sprague-Dawley rats), **"via oral route, HCBD is considered as likely to be carcinogenic to humans only at very high exposure conditions, where significant renal toxicity occurs."** There is some mutagenic activity in the presence of metabolic activation. Thus, a mutagenic mode of action cannot be ruled out. As a result, both the cancer-based, linear low dose approach and the non-linear margin of exposure approaches are used for deriving the AWQC.

AWQC Calculation

For Ambient Waters Used as Drinking Water Sources

The cancer-based AWQC was calculated using the RSD and other input parameters listed below:

$$AWQC = RSD \times \left(\frac{BW}{DI + \sum_{i=2}^{4} (FI_i \times BAF_i)} \right)$$

where:

RSD = Risk specific dose 2.5 x 10^{-5} mg/kg/day (10^{-6} risk)
BW = Human body weight assumed to be 70 kg
DI = Drinking water intake assumed to be 2 L/day
FI = Fish intake at trophic level i, i=2,3, and 4; total intake assumed to be 0.01780 kg/day
BAF = Bioaccumulation factor at trophic level i (i=2,3, and 4) equal to 1,518, 2,389, and 1,294 L/kg-tissue for trophic levels 2,3, and 4, respectively.

This yields a value of 4.6 x 10^{-5} mg/L, or 0.046 µg/L (rounded from 0.0462 µg/L).

The AWQC using the margin of exposure approach was calculated using the following equation and input parameters listed below.

$$AWQC = \left(\frac{Pdp}{SF} - RSC \right) \times \left(\frac{BW}{DI + \sum_{i=2}^{4} (FI_i \times BAF_i)} \right)$$

This is a preliminary summary of a criteria document being prepared for the derivation of the Ambient Water Quality Criteria (AWQC) for the protection of human health from exposure to HCBD. The calculated AWQC values presented in this draft are subject to revision pending inclusion of further information concerning exposure as well as possible changes in the toxicological information used to derive the criterion.

where:

Pdp = Point of departure (0.054 mg/kg/day)
SF = Safety factor of 300
RSC = Relative source contribution from air of 1.2×10^{-4} mg/kg-day, subtracted in this case
BW = Human body weight assumed to be 70 kg
DI = Drinking water intake assumed to be 2 L/day
FI = Fish intake at trophic level i, i=2,3, and 4; total intake assumed to be 0.01780 kg/day
BAF = Bioaccumulation factor at trophic level i (i=2,3, and 4) equal to 1,518, 2,389, and 1,294 L/kg-tissue for trophic levels 2,3, and 4, respectively.

This yields an AWQC of 1.1×10^{-4} mg/L (0.11 μg/L).

For Ambient Waters Not Used as Drinking Water Sources

When the waterbody is used for recreational purposes and not as a source of drinking water, the drinking water value is eliminated from the equation and it substituted with an incidental ingestion value. The incidental intake is assumed to occur from swimming and other activities. The fish intake value is assumed to remain the same. The default value for incidental ingestion is 0.01 L/day. When the linear approach is used to calculate the AWQC with the substitution of an incidental ingestion of 0.01 L/day a cancer-based AWQC of 4.9×10^{-5} mg/L (or 0.049 µg/L, rounded from 0.0487 µg/L) is obtained. When the non-linear margin of exposure approach is used with the substitution of an incidental ingestion of 0.01 L/day, the AWQC is 1.2×10^{-4} mg/L (or 0.12 µg/L, rounded from 0.117 µg/L).

Site-Specific or Regional Adjustments to Criteria

Several parameters in the AWQC equations can be adjusted on a site-specific or regional basis to reflect regional or local conditions and/or specific populations of concern. These include fish consumption; incidental water consumption as related to regional/local recreational activities; BAF (including factors used to derive BAFs, percent lipid of fish consumed by the target population, and species representative of given trophic levels); and the relative source contribution. States are encouraged to make adjustments using the information and instructions provided in the Technical Support Document (USEPA, 1998b).

REFERENCES

USEPA. 1998a. Federal Register Notice: Proposed Water Quality Criteria Methodology Revisions; Human Health. (See Attached Copy).

USEPA. 1998b. Ambient Water Quality Criteria Derivation Methodology; Human Health. Technical Support Document. EPA/822/B-98/005. July. (See Attached Copy).

USEPA. 1998c. Ambient Water Quality Criteria for the Protection of Human Health: Hexachlorobutadiene (HCBD). EPA/822/R-98/004. July.